Introducing Neuropsychology

Second Edition

John Stirling and Rebecca Elliott

Introducing Neuropsychology

Introducing Neuropsychology, second edition investigates the functions of the brain and explores the relationships between brain systems and human behaviour. The material is presented in a jargon-free, easy to understand manner and aims to guide students new to the field through current areas of research.

Following a brief history of the discipline and a description of methods in neuropsychology, the remaining chapters review traditional and recent research findings. Both cognitive and clinical aspects of neuropsychology are addressed to illustrate the advances scientists are making (on many fronts) in their quest to understand brain–behaviour relationships in both normal and disturbed functioning. The rapid developments in neuropsychology and cognitive neuroscience resulting from traditional research methods as well as new brain-imaging techniques are presented in a clear and straightforward way. Each chapter has been fully revised and updated and new brain-imaging data are incorporated throughout, especially in the later chapters on Emotion and Motivation, and Executive Functions. As in the first edition, key topics are dealt with in separate focus boxes, and "interim comment" sections allow the reader a chance to "take stock" at regular intervals.

The book assumes no particular expertise on the reader's part in either psychology or brain physiology. Thus, it will be of great interest not only to those studying neuropsychology and cognitive neuroscience, but also to medical and nursing students, and indeed anyone who is interested in learning about recent progress in understanding brain–behaviour relationships.

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Introducing Neuropsychology

Second Edition

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Psychology Press
Taylor & Francis Group
HOVE AND NEW YORK

First published 2008
by Psychology Press
27 Church Road, Hove, East Sussex BN3 2FA

Simultaneously published in the USA and Canada
by Psychology Press
270 Madison Avenue, New York, NY 10016

This edition published in the Taylor & Francis e-Library, 2010.

To purchase your own copy of this or any of Taylor & Francis or Routledge's collection of thousands of eBooks please go to www.eBookstore.tandf.co.uk.

Psychology Press is an imprint of the Taylor & Francis Group, an informa business

British Library Cataloguing in Publication Data
A catalogue record for this book is available from the British Library

Library of Congress Cataloging-in-Publication Data
A catalog record for this book is available from the Library of Congress
Stirling, John D., 1951–
Introducing neuropsychology / John Stirling and Rebecca Elliott. – 2nd ed.
p. ; cm.
Includes bibliographical references and index.
ISBN 978-1-84169-653-9 (hardcover) – ISBN 978-1-84169-654-6 (pbk.)
1. Neuropsychology. I. Elliott, Rebecca, 1969– II. Title.
[DNLM: 1. Neuropsychology. WL 103.5 S861i 2008]
QP360.S793 2008
612.8–dc22 2007048903

ISBN 0-203-84120-4 Master e-book ISBN

ISBN: 978–1–84169–653–9 (hbk)
ISBN: 978–1–84169–654–6 (pbk)

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PREFACE

TO THE SERIES

The Psychology Focus series provides short, up-to-date accounts of key areas in psychology without assuming the reader's prior knowledge in the subject. Psychology is often a favoured subject area for study, because it is relevant to a wide range of disciplines such as sociology, education, nursing, and business studies. These relatively inexpensive but focused short texts combine sufficient detail for psychology specialists with sufficient clarity for non-specialists.

The series authors are academics experienced in undergraduate teaching as well as research. Each takes a topic within their area of psychological expertise and presents a short review, highlighting important themes and including both theory and research findings. Each aspect of the topic is clearly explained with supporting glossaries to elucidate technical terms.

The series has been conceived within the context of the increasing modularisation which has been developed in higher education over the last decade and fulfils the consequent need for clear, focused, topic-based course material. Instead of following one course of study, students on a modularisation programme are often able to choose modules from a wide range of disciplines to complement the modules they are required to study for a specific degree. It can no longer be assumed that students studying a particular module will necessarily have the same background knowledge (or lack of it!) in that subject. But they will need to familiarise themselves with a particular topic rapidly because a single module in a single topic may be only 15 weeks long, with assessments arising during that period. They may have to combine eight or more modules in a single year to obtain a degree at the end of their programme of study.

One possible problem with studying a range of separate modules is that the relevance of a particular topic or the relationship between topics may not always be apparent. In the Psychology Focus series, authors have drawn where possible on practical and applied examples to support the points being made so that readers can see the wider relevance of the topic under study. Also, the study of psychology is usually broken up into separate areas, such as social psychology, developmental psychology, and cognitive psychology, to take three examples. While the books in the Psychology Focus series will provide excellent coverage of certain key topics within these "traditional" areas, the authors have not been constrained in their examples and explanations and may draw on material across the whole field of psychology to help explain the topic under study more fully.

Each text in the series provides the reader with a range of important material on a specific topic. They are suitably comprehensive and give a clear account of the important issues involved. The authors analyse and interpret the material as well as present an up-to-date and detailed review of key work. Recent references are provided along with suggested further reading to allow readers to investigate the topic in more depth. It is hoped, therefore, that after following the informative review of a key topic in a Psychology Focus text, readers not only will have a clear understanding of the issues in question but will be intrigued, and challenged to investigate the topic further.

PREFACE

TO THE SECOND EDITION

For this revised and fully updated edition of *Introducing Neuropsychology*, John Stirling has been joined by Rebecca Elliott as co-author.

Although the first edition of *Introducing Neuropsychology* was published just 5 years ago, such has been the growth of interest in research into brain–behaviour relationships that we felt an updated edition would be timely. Much of this growth has been driven by the more widespread availability of in-vivo imaging techniques, an area of expertise for the second author. Such techniques, of course, provide opportunities for researchers to identify brain regions that are engaged as participants undertake all manner of activities. Recently, these have ranged widely, from basic cognitive tasks designed to tap working memory processes (Fletcher et al., 2003) to more elaborate "emotional" challenges aimed, for example, at invoking sympathy/empathy in healthy controls and/or psychopaths (Farrow et al., 2001; Vollm et al., 2004).

Data from such studies have been amalgamated with more basic science research in the areas of molecular genetics, neurophysiology, and psychopharmacology, initially in the US but increasingly in the rest of the world, to provide a knowledge-base for the discipline called "cognitive neuroscience" (Gazzaniga, Ivry, & Mangun, 2003). We considered whether we too should acknowledge this emerging enterprise by re-titling our book "Introducing Cognitive Neuroscience". On balance, however, we felt that neuropsychology, as a subject area, was not yet ready to be subsumed under the cognitive neuroscience banner. This may be seen as an exercise in hair-splitting, but the facts of the matter are that not everything in this second edition could be said to be either strictly "cognitive" or even strictly "neuroscientific"—yet we hope all our material falls within the domain of neuropsychology.

In truth of course, such dividing lines are seen as more important by some people than others. Take, for instance, animal research, which is quite widespread in the field of cognitive neuroscience, but rare in neuropsychology—rare, but not unheard of (see Rizzolatti et al.'s study of mirror neurons in macaque monkeys which we review in Chapter 5). Case study, on the other hand, could reasonably claim to be the modus operandi of traditional "clinical" neuropsychology. But combine it with longitudinal neuroimaging or some other basic science assaying—such as analysis of cerebrospinal fluid (CSF) or blood, for example—and it would unquestionably qualify as cognitive neuroscience research. In short, what we have is a difference of emphasis, but with many areas of overlap. Both authors have published research in cognitive neuroscience journals, and attended/spoken at neuroscience conferences. However, both are psychologists by training, and this edition, like the first, is written primarily with the needs of psychology students in mind. Thus, on balance we felt we should retain the original title yet be entirely open to describing research that some authors might consider more cognitive neuroscience than neuropsychology. Three later chapters in this edition, covering Attention and Consciousness (Chapter 9), Emotion and Motivation (Chapter 10), and Executive Functions (Chapter 11), attest to the

common ground between the two approaches and we expect that such instances of overlap will become more commonplace in the years to come. However, it is instructive to note that just as the rise of "cognitive science" in the US in the early 1960s (Miller, 2003) did not bring about the demise of mainstream psychology, so the rise of "cognitive *neuro*science" from the 1990s onwards has not yet brought about the demise of *neuro*psychology.

In planning the format of this second edition we have tried to adapt and revise the first in light of a dramatically expanded research base and important refinements of existing research techniques and methods, plus the arrival on the scene of some completely new procedures that are now beginning to bear fruit. In no particular order, this work has included the following:

- Promising efforts to further characterise the fractionation (functional subdivisions) of the frontal lobes and the anterior cingulate gyrus (Botvinick, Cohen, & Carter, 2004; Wagner et al., 2001).
- New insights into and models of consciousness (Cooney & Gazzaniga, 2003).
- Expansion and refinement of the concept of brain modularity (Catani & ffytche, 2005; Cavanna & Trimble, 2006).
- Refinement of paradigms aimed at informing models of attention, including attentional blink and inattentional blindness (Rensink, 2002; Sergent, Baillet, & Dehaene, 2005).
- Confirmation of the existence of mirror neurons, and their possible role in imitation and perhaps even in empathy (Brass & Heyes, 2005; Rizzolatti & Buccino, 2004).
- Development of the field sometimes called "social neuroscience" encompassing research into autism and Asperger's syndrome, psychopathy, and pathological gambling (Frith & Frith, 2003; Rilling et al., 2007).
- Developments in the field of brain plasticity and recovery of function coupled with confirmation of the growth of new neurons (neurogenesis) in specific regions of the mature adult mammalian brain (Brown et al., 2003; Carlen et al., 2002; Mirescu, Peters, & Gould, 2004).
- Refinements in functional imaging including pathway tracing using diffusion tensor imaging (DTI) (e.g., Minati & Aquino, 2006).
- The use of transcranial magnetic stimulation (TMS) to reversibly manipulate brain activity, and as a possible therapeutic procedure (Heiser et al., 2003; Hilgetag, Theoret, & Pascual-Leone, 2001).

Of course, these changes need to be accommodated within the framework of the Psychology Focus series, meaning that we have tried to adhere to the criteria set out by Perry Hinton (series editor) outlined above. As with the first edition, our book is written principally with the "interested beginner" in mind but we have not used this as an excuse for failing to be up to date. Nevertheless, two early warnings may be in order: First, some readers might find sections of coverage in this edition rather complicated for an introductory text. Our only excuse is that the brain, the principal subject of our book, has rightly been characterised as *the most complex entity known to man*. We have tried hard to keep things simple wherever possible, but admit to not always succeeding. However, skipping complex sections (often separated from the general text in boxes) should not, we hope, detract from your general understanding of the material. Second, despite the rapid growth in research, many fundamental neuropsychological questions remain to be answered. Our view is that in such instances it is better to admit to uncertainty (while presenting the relevant material) than to offer glib but premature conclusions, even if the reader may find such lack of resolution frustrating.

As in the first edition, we have made liberal use of "interim comment" sections in each chapter in order variously to pull ideas together, identify inconsistencies in the data, describe continued uncertainties about what particular research findings mean, or simply to summarise a body of research before the "gist" is lost. We have tried to avoid unnecessary jargon, and where this has been impossible have sought to explain or define a term or concept there and then, with additional information provided in the expanded glossary. We have included an appendix (also somewhat expanded in this edition) on the structure and basic workings of the brain and its key constituent components as a reference for information rather than as obligatory reading. Our book should be understandable to readers with a fairly modest working knowledge of the structure and functioning of the mammalian nervous system, but if you want to know more, we offer sources in the Further Reading section at the end of the book. We have identified some key journal articles/reading assignments for each chapter

to aid further understanding of particular topics and issues, along with some general recommended reading and some interesting, accessible, and relevant web-pages for you to explore.

In the interests of continuity we have retained the broad chapter structure of the first edition, although each has been revised and updated. One entirely new chapter, on Emotion and Motivation (Chapter 10), has been added, and the Summary and Conclusions chapter from the first edition has been removed to make space for it. The methods chapter (Chapter 2) has been expanded to accommodate recent advances in imaging technology now available to the researcher, such as magnetoencephalography (MEG) and diffusion tensor imaging, and consideration is also given to recent research in which TMS has been used to induce temporary reversible disruptions to brain functioning. The chapter on somatosensation (Chapter 4) now additionally includes an extended section on neuroplasticity. The chapter on attention (Chapter 9) has been extensively revised and now includes an extended section reviewing neuropsychological investigations into consciousness, an area that has recently seen dramatic and exciting new developments. Other chapters have changed more modestly, being updated wherever possible to provide a flavour of the direction that research (in that area) is going, and how it is affecting the way we think about the subject material. Nevertheless, this edition contains over 600 new journal references, many post-dating publication of the first edition, and 60 or more additional/revised figures and diagrams.

We are particularly grateful to Andrew Parker from MMU who has contributed Chapter 7: Memory and Amnesia, and made helpful comments on other sections of the book. We would also like to thank Marilyn Barnett from MMU both for her work on collating references for this edition and for her help with numerous other administrative chores. Elsewhere in writing the book, while one or other of us has initially taken the role of lead author for a section or chapter, the other has edited, revised, and even re-drafted. Thus, in the spirit of collective responsibility, we (JS and RE) consider ourselves equally culpable!

We hope you find the second edition of *Introducing Neuropsychology* a useful entry point into the neuropsychology literature, and that our interest in trying to understand brain–behaviour relationships through neuropsychological (and cognitive neuroscience) research whets your appetite to learn more about the structure and functioning of the astonishing 1200 to 1500 grams of tissue we call the (mature) human brain.

JOHN STIRLING AND REBECCA ELLIOTT
Manchester, August 2007

PREFACE

TO THE FIRST EDITION

Just over 18 months ago I completed the first draft of an introductory book about the brain entitled *Cortical Functions*, subsequently published by Routledge in the *Modular Psychology* series in 1999. While researching the material for that book, I accumulated more information than could be shoe-horned into the *Modular* series format, and in discussing the fate of my surplus chapters/material with the editors at Routledge the idea of writing a concise up-to-date introductory text in the area of neuropsychology slowly took shape. *Introducing Neuropsychology* is, somewhat belatedly, the result.

As with other books in the "Psychology Focus" series, this one is intended as an accompanying text for courses in neuropsychology for students new to the subject area. I have written the book in such a way that a detailed understanding of neurophysiology (neurons, action potentials, synapses and so on) is not a necessary prerequisite to getting something out of it, so the book should also be accessible to non-psychology students too. However, to be on the safe side, I have included an appendix to which the reader may want to refer for a quick reminder of the basic layout of the nervous system, the structure and function of neurons, and the ways we might usefully wish to divide up the central nervous system in order to make more sense of it. Complete novices may prefer to read the entire appendix before tackling the rest of the book. This is allowed!

Mindful of the difficulties students sometimes have with the subject matter of neuropsychology, I have tried to write *Introducing Neuropsychology* in a jargon-free style (insofar as this is possible). However, a glossary is included to cover highlighted first use terms that may be new to the reader. I have also provided a large number of figures and diagrams to illustrate key points, and I have included several boxes dotted throughout the book encompassing key research findings or, in some cases, the results of neuropsychological case studies. Shaded "interim comment" sections can also be found at regular intervals in every chapter. As their name suggests, these summaries are intended to allow the reader to make sense of particular passages of material in manageable chunks, before progressing further.

Although *Introducing Neuropsychology* aims to do what the title says—with coverage of the core ideas, concepts and research findings in each of the substantive chapters—I have also tried to add a flavour of recent/current research in each area, but particularly in the later chapters. The recommended reading for each chapter (set out in the "Further reading" section) also reflects my wish to encourage readers to seek out up-to-date research reports if they want to take their studies of a topic further. There are several excellent texts with a broader and deeper coverage of the material than can be achieved in *Introducing Neuropsychology*, and I would urge enthusiastic readers to research these resources too. I have listed some of my preferred texts in the "Further reading" section. Similarly, there is some valuable material available on the Internet. The sites listed in the "Selected neuropsychology web sites" section provide an entry point to this material, and links will soon take you to 3D images

of the brain, lists of gory neurological disorders and the web pages of research institutions and even individual neuroscientists and neuropsychologists. Happy surfing!

For me, neuropsychology represents a confluence of most of the things I am interested in as a psychologist: normal and particularly abnormal behaviour, the workings of the brain, lifespan changes, the common ground between neurology, psychology and psychiatry, and even the concept of "consciousness". The more we learn about neuropsychology the more amazed I am about how a structure weighing as little as an adult human brain (usually less than 1500 grams) can do everything it does, often faultlessly, for 70, 80 or even more years! I hope that as you read this book, you come to share my wonder about this rather insignificant-looking lump of tissue, and that *Introducing Neuropsychology* whets your appetite to learn more about it.

JOHN STIRLING
Manchester, July 2001

"Into the highlands of the mind let us go"

(Adapted from the emblem on the portico of the State Supreme Court, Capital Building, Sacramento, CA. Source: "Shakespeare", from *A hundred poems by Sir William Watson, selected from his various volumes*. New York: Dodd-Mead & Co., 1923.)

CHAPTER 1

CONTENTS

1

The foundations of neuropsychology

INTRODUCTION

We take the view that a proper understanding of the current status of neuropsychology cannot be formed without at least a rudimentary appreciation of its origins. Thus, in this chapter we offer a brief history of the beginnings of scientific research into the brain, and we introduce some of the theories (and debates) that have surfaced as our understanding of the relationship between structure and functions has developed. We describe some discoveries that led to the development of the so-called "brain hypothesis", a concept that is central to neuropsychology (if not to psychology as a whole). We then introduce the "localisation of function" debate, which has rumbled on from its origins in the work of the 19th-century neuroanatomists, and continues to influence the distinct approaches and methodologies of clinical and cognitive neuropsychologists that we describe towards the end of the chapter. Fodor's concept of modularity (of mind: he is a philosopher rather than a researcher) is introduced and re-assessed in light of recent findings. Its current status is considered, by way of illustration, in relation to the neuroanatomy and connectivity of a little-known region of cortex called the precuneus (Cavanna & Trimble, 2006).

NEUROPSYCHOLOGY AS A DISTINCT DISCIPLINE

Neuropsychology is a bridging discipline that draws on material from neurology, cognitive psychology, and even psychiatry. However, its principal aim is to try to understand the operation of *psychological* processes in relation to brain structures and systems. It is the oldest branch of scientific psychology and it retains a degree of distinctiveness that distinguishes it from other related areas. It has, for example, historically relied on small *N* or even single-case study designs, a tradition that continues to this day. Like cognitive neuroscience (see preface to this edition) it embraces the concept of *converging operations* (in which research findings from different sources and even different levels of inquiry are "used" to inform a particular debate). But unlike cognitive neuroscience, we should expect some fairly direct reference to human behaviour, and also unlike cognitive neuroscience, the

brain itself may seem quite marginalised from the debate. Brain structures barely merit mention in Ellis and Young's classic text *Human cognitive neuropsychology* (1996), for example. (See also Coltheart, 2001, whose ideas are summarised later in this chapter.)

The term "neuropsychology" was used as a subtitle in Donald Hebb's influential book *The organisation of behaviour: A neuropsychological theory*, published in 1949, although the term itself was not defined. With the demise of **behaviourism** (terms in bold type in the text indicate that the term is included in the Glossary section at the end of the book) and renewed interest in cognitive processes in the 1950s and 1960s, the term appeared with increasing frequency, although its definition remained vague and it was used in different senses by different people. Although, as you will see, researchers had been interested in the effects of brain damage and disease on behaviour for many years, it was arguably some time after behaviourism's fall from grace that neuropsychology came to develop a distinct identity within psychology, and its parameters were further clarified by the publication of the first edition of Kolb and Whishaw's *Fundamentals of human neuropsychology* and Lezak's *Neuropsychological assessment* in 1980 and 1983 respectively.

It would be misleading for us to suggest that, following its protracted birth, neuropsychology has emerged as an entirely unified discipline. In reality there remain different emphases among practitioners and researchers, which broadly divide into two domains: those of **clinical** and **cognitive neuropsychology**. At the risk of oversimplifying the distinction, the former tends to focus on the effects of brain damage/disease on psychological processes such as memory, language, and attention, and often has a clinical remit for assessment and even treatment. Conversely, the latter tries to understand impairments to psychological processes in terms of disruptions to the information-processing elements involved. In other words, the clinical approach goes from the damaged brain to psychological dysfunction and its remediation, whereas the cognitive approach goes from psychological dysfunction to hypothetical models about the individual stages of information processing that could explain such dysfunctions, which may (or may not) then be "mapped" onto various brain regions. This division has led to quite heated debates among neuropsychologists about, for instance, the merits/shortcomings of single-case versus group research designs, and the extent to which cases of localised brain damage can *ever* definitively be used as evidence in support of functional localisation. (We take up each of these points in the following chapters. However, see the special issue of the journal *Cognitive Neuropsychology*, 2004, vol 21, for a flavour of the arguments.)

Incidentally, a glimpse at the chapter titles in this book might suggest to the reader that we too have chosen to take a cognitive approach to neuropsychology. However, this is not the case, and it is our hope that you will see that both approaches have much to offer in our quest to understand the relationship(s) between psychological processes and brain functioning. Besides, the ever-increasing use of **in-vivo imaging techniques** has inevitably blurred this distinction, chiefly because they provide the researcher with the opportunity to observe brain activity in healthy individuals as they undertake some sort of cognitive or other psychological challenge, arguably permitting a more direct (i.e., less inferential) link between structure and function.

KEY TERMS

Behaviourism: The school of psychology founded by Thorndike and popularised by Skinner, which places emphasis on the acquisition of behaviour through learning and reinforcement.

Clinical neuropsychology: A branch of clinical psychology that specialises in the assessment of patients with focal brain injury or neurocognitive deficits.

Cognitive neuropsychology: A branch of neuropsychology that studies how brain structure and function relate to specific psychological processes.

In-vivo imaging techniques: A range of imaging techniques that explore structure and/or function in living subjects.

THE ORIGINS OF THE BRAIN HYPOTHESIS

We know from historical records from the Middle East (e.g., the Edwin Smith Surgical Papyrus, found in Luxor, Egypt, in 1862) that the importance of the brain as a "behaviour control centre" (henceforth referred to as the brain hypothesis) was first considered at least 5000 years ago, although the predominant view then, and for many centuries thereafter, was that the heart was the organ of thinking and other mental processes. The ancient Greeks debated the relative merits of heart and brain, and Aristotle, noting that the brain was relatively cool in comparison with the heart, came down in support of the heart as the seat of mental processes, arguing that the brain's principal role was to cool blood. Hippocrates and Plato, on the other hand, both had some understanding of brain structure, and attributed various aspects of behaviour to it: Hippocrates, for example, warned against probing a wound in the brain in case it might lead to **paralysis** in the opposite side of the body.

In first-century (AD) Rome, the physician Galen spent some time working as a surgeon to gladiators and became all too well aware of the effects that brain damage could have on behaviour. The "heart hypothesis" was fundamentally undermined by Galen's descriptions of his clinical observations: he showed that **sensory nerves** project to the brain rather than the heart, and he also knew that physical distortion of the brain could affect movement whereas similar manipulation of the heart could not.

For reasons that are never entirely clear, the knowledge and understanding of these early writers was lost or forgotten for the next 1500 years or so of European history. Those with any interest in the brain concentrated on attempts to find the location of the soul. Their search focused on easily identifiable brain structures including the pineal gland and the corpus callosum, structures that today are known to be involved in the control of bodily rhythms and communication between the two sides of the brain respectively.

LOCALISATION OF FUNCTION

The renewed interest in rationalism and science that accompanied the Renaissance in Europe in the 15th and 16th centuries prompted scientists of the day to revisit the brain and to try to establish the functions of particular brain structures. Because a lot of brain tissue appears relatively undifferentiated to the naked eye, these researchers also concentrated their efforts on the same easily identified structures as the earlier "soul-searchers". They explored, for example, the functions of the fluid cavities of the brain (the ventricles), the pineal and pituitary glands, and corpus callosum. However, their ideas about the functions of these structures were usually well wide of the mark: **Descartes** (1664), for example, mistakenly argued that the pineal gland was the point of convergence of bodily sensory inputs giving rise to a non-physical sense of awareness—thus encapsulating the key idea of the **mind–body problem**, although it should, perhaps, have been more aptly described as the mind–brain (or even the brain–mind) problem! To reiterate, the pineal gland is today regarded as an entirely soul-less endocrine gland involved in the control of bodily rhythms.

Nevertheless, implicit in this early work was the core idea of **localisation of function**—that different regions of the brain are involved in specific and separate aspects of (psychological) functioning. This idea later intrigued both Gall, the

KEY TERMS

Paralysis: Loss of movement in a body region (such as a limb).

Sensory nerves: Nerves carrying action potentials from sensory receptors towards the CNS (e.g., the optic nerve).

Descartes: French philosopher famous for his ideas about the separate identities of mind and body.

Mind–body problem: Explaining what relationship, if any, exists between mental processes and bodily states.

Localisation of function: The concept that different parts of the brain carry out different functions and, conversely, that not all parts of the brain do the same thing.

Austrian physician, and his student Spurzheim, whose work represents the starting point of what we might call the modern era of brain–behaviour research. It should be noted at the outset that Gall and Spurzheim, like modern-day neuropsychologists, were more interested in localisation of function within the **cerebral cortex** (the outer surface of the brain), with its characteristic bumps (**gyri**) and folds (**sulci**), than in the subcortical structures mentioned earlier. Gall (1785–1828) readily accepted that the brain rather than the heart was the control centre for mental function and, with Spurzheim, made several important discoveries about the anatomy of the brain, its connections with the spinal cord, and its ability to control muscles that have stood the test of time. For example, Gall was the first person to distinguish between grey and white matter (**neuron cell bodies** and their bundled **axons** respectively) in the brain, and also described the first case of **aphasia** (impaired language production) associated with frontal damage resulting from a fencing injury.

THE RISE AND FALL OF PHRENOLOGY

Despite their other notable lasting contributions, Gall and Spurzheim are primarily remembered for their ideas about what is sometimes called "strict" localisation of function in the brain. Through a combination of serendipity and chance observations, Gall came to the view that each of the two sides of the cerebral cortex (also sometimes called the left and right *cerebral hemispheres*) consisted of 27 compartments or regional faculties. These ranged from commonsense (or at least recognisable) ones such as language and perception, to ambiguous and obscure ones including hope and self-esteem. Accordingly, the more a person used particular faculties, the bigger the brain in that region grew, causing the shape of the skull to be distorted. Thus was born the "science" of phrenology, which claimed to be able to describe an individual's personality and other "faculties" on the basis of the physical size and shape of the skull (see Figure 1.1a and b). Interest in phrenology gradually spread widely through both Europe and the US (thanks largely to Spurzheim's efforts; he and Gall fell out over the matter of phrenology's popularisation and the attendant commercial benefits). In England, for example, it received royal support when Queen Victoria had her children's heads measured and analysed, and gradually an entire industry of phrenological "science" was spawned, involving journals, books, and pamphlets offering advice on marital compatibility and, of course, the opportunity for a personal assessment.

Over time, thousands of phrenology measurements were collected, including a series taken from the skulls of 25 murderers, and even from an amorous widow who was described as having prominent features (bumps) behind her ears. Each observation was simply taken as confirmation of the general theory, except that the number of faculties crept up to 35. When, for example, cases were found of individuals with unilateral (one-sided) cortical damage but incomplete loss of function, phrenologists were able to say that the other (intact) hemisphere had taken over responsibility for the faculty in question. However, doubts about phrenology first arose when it became apparent that the shape of the skull bore little relationship to the shape of the underlying brain. Obviously, Gall and Spurzheim had no way of measuring internal brain structure in living people, save for those rare instances of individuals surviving (and often not for very long)

KEY TERMS

Cerebral cortex: The outer surface of the brain which has, in higher mammals, a creased and bumpy appearance.

Gyri: Elongated bumps (convexities) in the cortex (singular: gyrus).

Sulci: The smaller folds or indents on the surface of the cortex (singular: sulcus). Larger ones are called fissures.

Neuron cell bodies: The central part of neurons (nerve cells) that contain the nucleus.

Axon: Long, thin projection from a neuron that carries electrical impulses from the cell body.

Aphasia: Deficit in the production and/or comprehension of language.

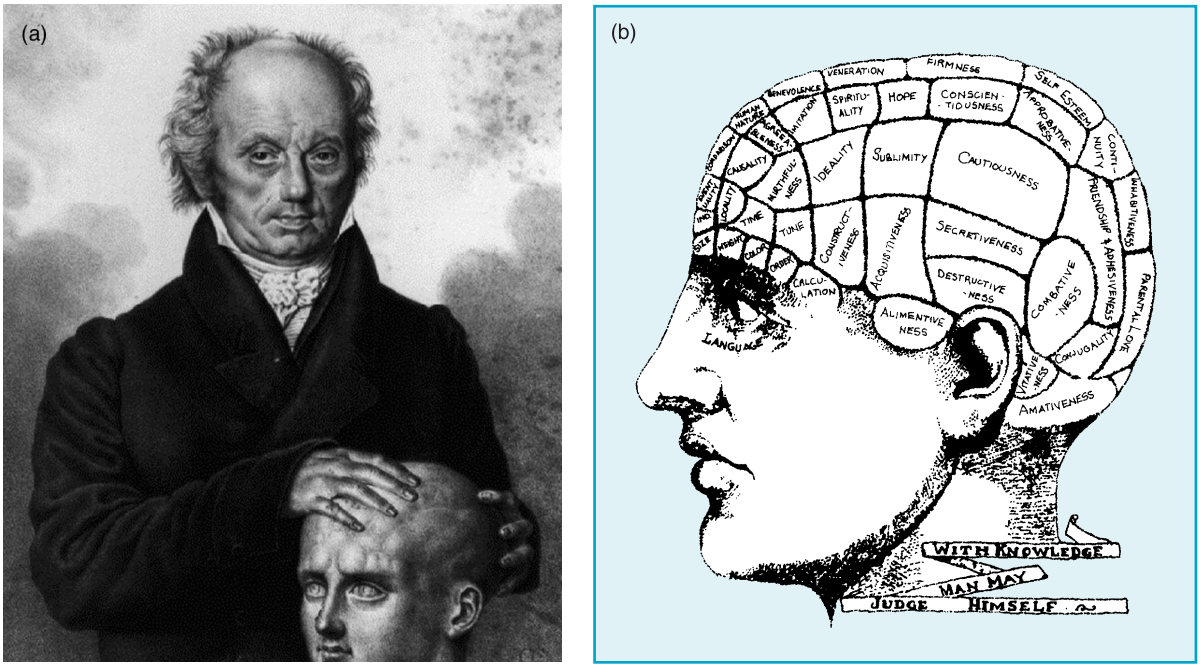


FIG. 1.1 (a) Franz Joseph Gall (1785–1828). (b) A phrenology skull. The concept of phrenology stemmed from Gall's ideas but was developed by Spurzheim. Although most scientists dismissed it as a pseudo-science, it enjoyed popular support in the mid-1800s, gaining royal patronage in the UK and spawning a mini-industry in charts, journals, and consultants.

open head injuries. Actually, records show that Gall had access to a small number of such cases, but unfortunately he seemed to regard them as being of only anecdotal interest, failing to realise that brain-injured people could offer an important test of his theory. Instead, he and Spurzheim continued to accumulate more and more measurements from members of the general population that "confirmed" their ideas.

Just as phrenology was catching on with the general population in Victorian England, Europe, and North America, the French scientist Pierre Flourens (1824) provided the first scientific evidence questioning its validity. Working mainly with birds, he developed the technique of surgically removing small areas of brain tissue and, after a period of recovery, observing the effects of the surgery on behaviour. (We now refer to these procedures as **lesion** and **ablation**, and they are described more extensively in Chapter 2.) Flourens' research led him to the conclusion that the degree of behavioural impairment was more closely linked to the *amount* of damage than to its *location*, a finding that runs counter to the principle of localisation of function that Gall and Spurzheim had so vigorously promoted. Flourens believed that the entire brain operated as a single faculty to serve the functions of perception, memory, volition, and so on, as required—an idea that came to be known as "aggregate field theory". He also believed that undamaged regions could take over the responsibilities of damaged ones—an idea giving rise to the popular (but mistaken) belief that people only use a small proportion of their brains, keeping other areas in reserve for learning new skills or replacing damaged areas.

KEY TERMS

Open head injuries: Head injuries involving damage to the cranium so that the brain is exposed or visible. Often compared with "closed head injury" in which brain damage has occurred although the cranium has not been penetrated: for example, dementia pugilistica (brain damage associated with boxing).

Lesion: A cut in (or severing of) brain tissue. This may occur as the result of an accident or may be part of a surgical procedure.

Ablation: The surgical removal of brain tissue.

Although Flourens' findings dealt something of a blow to Gall and Spurzheim's ideas about localisation (and, by implication, phrenology), hindsight suggests that his conclusions were probably wrong. First, he worked with pigeons and chickens, which are now known to have almost no cortex. Second, his behavioural measures assessed activities (such as eating, movement, and so on) unrelated to Gall and Spurzheim's faculties. Third, his surgical procedure was imprecise, leaving open the possibility that behavioural changes were caused by damage or lesions to brain structures beyond the cortex.

INTEREST IN APHASIA

Despite Flourens' lack of enthusiasm for localisation of function, interest in it was rekindled following a series of case studies of aphasia. French physicians Bouillaud and Dax had independently described a handful of patients they had seen who had lost the power of speech after brain damage. Those with left-sided damage often became paralysed in the right side of their bodies too, despite no apparent loss in intelligence. Bouillaud's work was reported in 1825, and Dax's in 1836 (although neither actually published their findings in a journal), yet little interest was shown until Auburtin (who happened to be Bouillaud's son-in-law) described the same work at a conference in 1861 that was also attended by Paul Broca. A few days later, Broca met Monsieur Leborgne, a patient who became known as Tan because this was almost the only sound he could utter. However, Tan could understand speech well and could, for example, follow quite complicated instructions. Like many of Dax's patients, he too was paralysed on his right side. Broca proposed that Tan had suffered damage to the same area of cortex (the left frontal region) earlier identified as crucial for language production by Dax and Bouillard. When Tan died from an unrelated disease later that year, Broca conducted a superficial post-mortem on his brain and confirmed that he had indeed incurred damage to the left frontal cortical region variously attributed to epilepsy, syphilis, or a **stroke**.

Within two years, Broca had collected post-mortem data on eight similar cases. This research led him to conclude that language production depended on intact left frontal function, and that, in more general terms, the two sides of the brain controlled the opposite sides of the body. (In fact, neither of these ideas was new—the relationship of one side of the brain to the opposite side of the body had been described by Galen at the beginning of the first millennium, and the link between left-sided damage and aphasia could be dated back to Gall.) Nevertheless, Broca seemed to gain the credit, and the region of brain he described (part of the left frontal cortex) is now known as Broca's area.

Soon, other regions of the cortex on the left side were identified as being important for various aspects of language. In 1874 Carl Wernicke described two additional forms of aphasia that were distinct from Broca's type. In **fluent aphasia** the patient could speak at a normal rate but what was said usually made little sense. In **conduction aphasia** the patient seemed able to understand what was said to them but was unable to repeat it. Wernicke surmised (on the basis of just one documented post-mortem investigation) that fluent aphasia was caused by damage to the posterior region of the left **temporal lobe**. He speculated that conduction aphasia was caused by a **disconnection** (literally a break in the pathway) between this region (which we now know as Wernicke's area) and Broca's area.

KEY TERMS

Stroke: A catch-all term for disturbances of the blood supply to the brain. Most commonly, strokes are caused by obstruction to, or rupture of, blood vessels in the brain.

Fluent aphasia: Another name for Wernicke's aphasia. Language is fluent but nonsensical.

Conduction aphasia: Aphasia in which the principal deficit is an inability to repeat spoken language.

Temporal lobe: The region of the cortex (on both sides of the brain) running forward horizontally above and in front of the ear, known to be involved in language, memory, and visual processing.

Disconnection: The general term for a group of disorders thought to be caused by damage to a pathway between two undamaged regions (e.g., split-brain syndrome).

INTERIM COMMENT

Two important consequences followed from Wernicke's observations. First, language could no longer be considered a unitary "faculty" and would have to be subdivided (at least) in terms of receptive and expressive functions. Second, it was clear that focal disease could cause specific deficits. The first observation meant that the scientists of the day would have to rethink the concept of "faculty". The second lent considerable weight to the idea of localisation of function. When, in 1892, Dejerine identified the cortical area (these days called the **angular gyrus**) related to the loss of the ability to read from text (known as **alexia**), three language areas, all on the left side, had been identified, and the localisation of function concept had received a major boost (see Figure 1.2).

To this work on aphasia, we might add the pioneering work of Fritsch and Hitzig (1870) who showed that discrete electrical stimulation of dogs' brains could induce movement of specific body parts in a consistent and predictable way. We might also note the subsequent cytoarchitectonic maps (maps of cortical regions differentiated by cell type and density) of Vogt (Vogt & Vogt, 1903) and Brodmann (1909). The latter has stood the test of time (with minor modification to some of his regional boundaries), and present-day researchers still frequently identify cortical locations by their Brodmann number (see Figure 1.3). BA 44 (and into BA 45) on the left, for example, correspond with Broca's area, and BA 7 corresponds to the precuneus, which we will discuss towards the end of this chapter. Cytoarchitectonic maps are primarily concerned with structure, but there is general agreement that most of the mappers anticipated there would be correspondences between structurally distinct regions and underlying functions.

KEY TERMS
Angular gyrus: A region of cortex on the temporal/parietal border roughly equivalent to Brodmann's area 39. The left side is probably involved in reading (sentences).
Alexia: Inability to read.

MASS-ACTION AND EQUIPOTENTIALITY

Despite the evidence presented in the previous section, it would be misleading to suggest that after Dejerine's findings all researchers quickly accepted the basic principles of cortical localisation. For instance, the renowned British neurologist John Hughlings-Jackson supported localisation for some cortical functions, but was also aware that focal damage rarely led to complete loss of the function. As if to underline this point, the German physiologist Goltz regularly attended scientific meetings in the 1880s with a dog whose behaviour seemed relatively "normal" despite Goltz himself having removed a large chunk of its cortex!

At the beginning of the 20th century European psychology came under the influence of the "Gestalt" movement, which emphasised the importance of "the whole as being greater than the

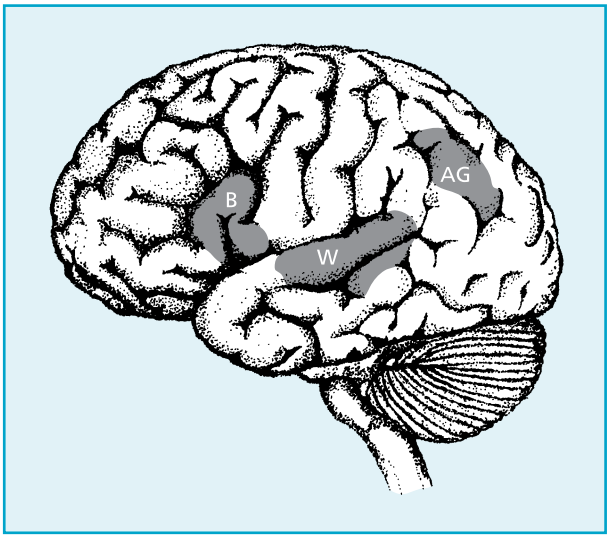


FIG. 1.2 Some language areas in the brain. W is Wernicke's area, conceptualised as the region responsible for linking speech sounds to stored representations of words. B is Broca's area, identified as involved in the generation of speech. AG depicts the angular gyrus, known to be important in understanding visually presented material.

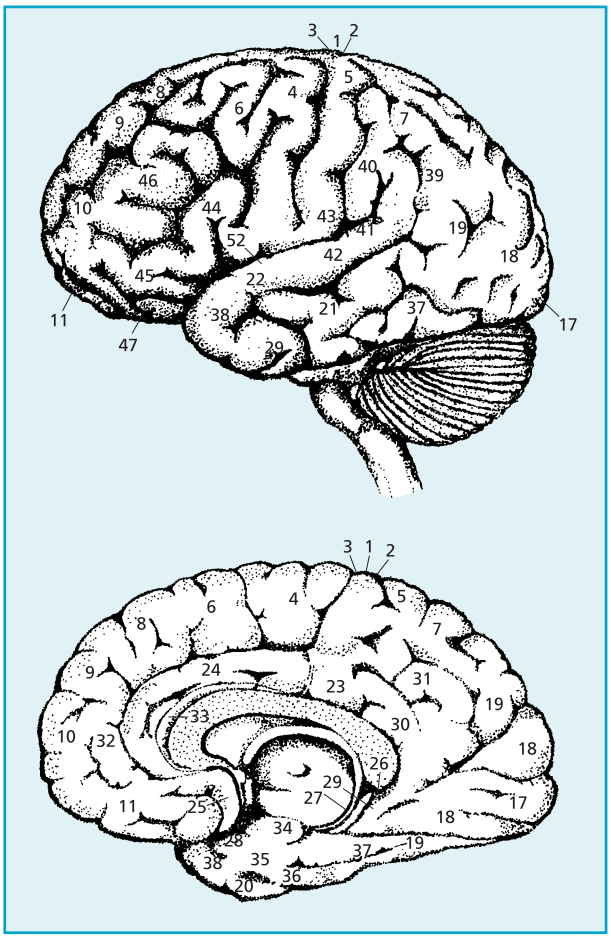


FIG. 1.3 Brodmann areas. Brodmann used a light microscope to analyse the cellular organisation of the cortex, identifying 52 distinct regions. Many (though not all) of these are still recognised and used today to identify particular locations.

sum of its parts". This view was anathema to localisationists but it prompted other scientists, such as the British neurologist Henry Head, to describe the brain as a dynamic, interconnected system that should be considered in its own right rather than as a collection of independently functioning units. Head's ideas were shared by Karl Lashley, an American psychologist, whose theories of **mass-action** (that the entire cortex is involved in all functions), and **equipotentiality** (that each cortical region can assume control for any given behaviour) were based on the same "holistic" principles, and were, for a while, extremely influential, particularly in psychology.

Lashley's ideas can be traced back to the earlier work of Flourens: like him, Lashley used brain lesions and worked exclusively with animals. Many of his studies were designed in an attempt to establish the anatomical location of the "engram"—the representation of memory in the brain. To address this, he measured the effects of lesions and ablations (cutting or removal of brain tissue) on maze learning in rodents (see Figure 1.4a). Initially there would be a period of orientation during which an animal learned its way around a maze to locate a food pellet. Then Lashley would remove a small region of cortex and, following a period of recovery, see how many trials it took the animal to relearn the maze and find the food pellet (see Figure 1.4b). After many such experiments, Lashley came to the view that his quest to locate the engram would never succeed. On the contrary, his research had shown that the amount of lesioned brain tissue rather than its location best predicted how long it would take the rat to relearn the maze. This finding is clearly at odds with the idea of a localised memory system, and lends weight to the ideas of mass-action and equipotentiality.

These findings jibed well with new ideas about behaviourism emanating from American experimental psychology at the beginning of the 20th century. This approach stressed the importance of learning and **reinforcement** at the expense of interest in the brain. However (and notwithstanding the difficulties in generalising from rat to human behaviour), there are a number of flaws in Lashley's argument, and his findings could, in fact, be used to support localisation of function. Think for a moment about the information a rat might use to find food in a maze—this is likely to include sensory information from the visual, tactile, and olfactory modalities, in addition to any more sophisticated conceptual information such as sense of direction, distance travelled, and so on. Indeed, effective maze learning probably depends on the integration of all this information. When Lashley

KEY TERMS

Mass-action: The principle (alongside equipotentiality) that cortical regions of the brain are inherently non-specialised, and have the capacity to engage in any psychological function.

Equipotentiality: The term associated with Lashley, broadly meaning that any region of cortex can assume responsibility for a given function (memory being the function of interest for Lashley).

Reinforcement: Typically some form of reward (positive reinforcement) or punishment (negative reinforcement) that affects the likelihood of a response being repeated.

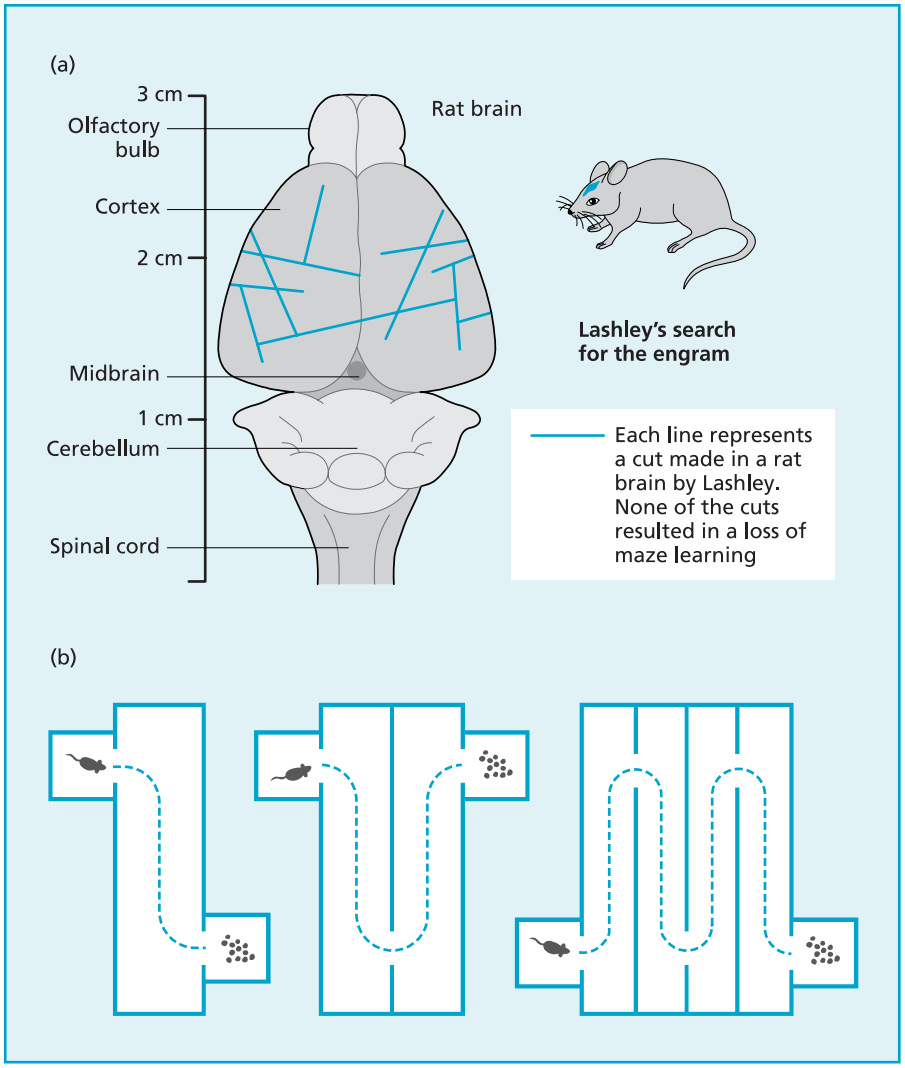


FIG. 1.4 Lashley's lesions and one of his mazes. (a) The anatomical location of some of the lesions performed by Lashley. (b) The types of maze used by Lashley in his search for the engram in rodents' brains.

lesioned different parts of cortex, he might have interfered with the animal's tactile skills or sense of smell, while leaving other functions intact. The animal could still learn the maze using the "localised" functions that remained, but perhaps not as quickly as before.

INTERIM COMMENT

In fact, sound experimental support for Lashley's ideas has been hard to come by, and it is probably helpful to know that most neuropsychologists continue to favour some form of localisation. Indeed, at present the main questions in this area are less to do with *whether or not* the human cortex is organised locally,

than the *extent* to which localisation of function applies, and whether it applies equally on both the left and right sides of the brain (an issue we consider in Chapter 3). There is, additionally, a very important lesson for neuropsychologists embedded in the alternative explanation of Lashley's findings. This concerns the interpretation of results about "recovery of function" in brain-damaged individuals, and we will return to it later in the book.

THE (RE)EMERGENCE OF NEUROPSYCHOLOGY

Historians seem unsure why, after such a promising start in the late 19th century, neuropsychology seemed to go into a form of hibernation until after World War II. In reality a combination of factors was responsible, notably the increased interest shown by mainstream psychology in behaviourism and **psychoanalysis**, rivals perhaps, but both understandable without direct reference to the brain. During this period there was also a distinct lack of progress in understanding basic brain physiology. Cajal and Golgi engaged in a protracted argument about whether the brain was, in effect, a single complex nerve field (as Golgi thought), or comprised individual structurally distinct units (neurons) as Cajal believed. Moreover, the discovery of chemically mediated **synapses** was made only in the 1930s by Otto Loewi, and even then there was a further delay of several years before the chemical that Loewi had found in his classic experiment was identified as acetylcholine (see Box 1.1).

Box 1.1 Brain discoveries in the early 20th century

Early in the 20th centrury Camillo Golgi, a neuroanatomist working in a small university in northern Italy, discovered that a silver salt could be used to stain brain tissue. For reasons that are still not fully understood, some tissue absorbed the stain giving it a distinct black appearance, and it could then be examined more closely under the light microscope. Golgi's stain highlighted individual neurons, but he was convinced that he was actually staining small regions of a continuous mass of relatively undifferentiated tissue. Santiago Ramon y Cajal (1913, 1937), a Spanish neuroanatomist, used Golgi's method to show that the regions of stained tissue were, indeed, individual neurons and, moreover, that they carried electrical information (we would now identify this as volleys of action potentials) in one direction only, from the cell body (or more specifically the axon hillock) to the end of the axon (see Appendix). Despite jointly receiving the Nobel prize in 1906, the two men remained fierce rivals, Golgi in particular rebuffing Cajal's ideas—although time has shown that Cajal, rather than Golgi, was right.

By the time Otto Loewi discovered chemically mediated synaptic transmission in 1931, most researchers accepted the "neuron" hypothesis (the direct conclusion from Cajal's work) but assumed that "contacts" between neurons were electrically mediated. Loewi is reputed to have come up with the idea for his "frog-heart" perfusion experiment following a dream. He was aware that a frog's heart could be slowed down by electrical stimulation of its vagus nerve, but he did not know what actually caused this effect. He repeated his experiment on a live frog, stimulating its vagus nerve while bathing the exposed heart with water. The "run-off" fluid was collected then trickled over the exposed heart of a second

KEY TERMS

Psychoanalysis: The school of psychology initiated by Freud that emphasises the role(s) of unresolved subconscious conflicts in psychological disorder.

Synapses: The tiny fluid-filled gaps between neurons where synaptic transmission (see below) may occur. Typically 20–30 nanometres (millionths of a millimetre) wide.

frog, which slowed down. This showed that some chemical in the perfused water from the first frog mediated the effect seen following vagus nerve stimulation. Some 8 years after this study, the chemical in question was identified as acetylcholine (ACh), now recognised as one of the most widespread neurotransmitter substances. Among its many vital functions in our own nervous system, ACh is a key neurotransmitter at neuromuscular synapses, and also plays many critical roles in the brain.

CONNECTIONISM TO MODULARITY

As we have already suggested, the 1950s and 1960s were marked by a gradual increase (or perhaps re-emergence) of interest in both physiological and cognitive psychology, each making important contributions to the subject matter that we now consider under the heading of neuropsychology. Meanwhile, the concepts of mass-action and equipotentiality gained little support from the new wave of brain research, and interest in them dwindled. New understanding about the connectivity of the brain, on the other hand, prompted a revival of interest in "connectionist models" of brain function. Such models had first appeared almost a century earlier as explanations of how, for instance, the various aphasic conditions might be related to one another, and how they in turn might be linked to pathology in different but interconnected left-sided brain regions (Lichtheim, 1885). Similar types of model were also proposed to explain **agnosia(s)** (loss of ability to recognise visually presented commonplace objects; Lissauer, 1890) and **apraxia(s)** (inability to perform or copy gestures on demand; Liepmann, 1905). However, in each case, a combination of problems with the original conceptualisation of the model (for instance, the identification of cases whose profile did not conform to the stereotypic disorder) coupled with the rise in 20th-century (non-brain) psychology worked to marginalise them, and connectionist models fell out of favour with researchers.

In neuropsychology, their re-emergence in the 1960s as "neural wiring diagrams" was an attempt to clarify the different cortical regions that might be responsible for particular psychological processes. One of the most influential was Geschwind's neo-associationist model of language and aphasia (Geschwind, 1965), considered in Chapter 6. That the model itself contained a number of flaws is not now, some 40 years later, seen as being as important as the impetus it gave to neuropsychological thinking at a critical time in the subject's re-emergence. Most neuropsychologists now think that the human brain coordinates mental processes through the collaboration of (and interconnections between) multiple brain regions. It thus follows that circumscribed deficits in higher brain function should be attributable to (1) loss through damage or disease of some specialised cortical function, or (2) loss through damage or disease to connecting pathways, or (3) both. At present the first alternative is better understood, mainly because of the continuing difficulty in establishing functional connections within the brain, but new "in-vivo" pathway-tracing techniques such as diffusion tensor imaging (DTI) are likely to lead to rapid developments in this area (see Chapter 2)

The circuits comprising areas of specialised cortical function and their interconnections are sometimes called "distributed control networks". Although this sounds rather complicated, think of it as meaning that psychological

Key Terms
Agnosia: Loss of ability to recognise objects, persons, sounds, shapes, or smells in spite of intact sensory function.
Apraxia: The inability to carry out certain motor acts on instruction without evident loss of muscle tone (acts may be performed spontaneously, for example).

functions (such as language or movement) depend on the activity of, and connections between, several (many) different but specific locations. Clearly this is a different idea from the "strict" localisation of function concept mentioned earlier, because it implies that no one region has sole responsibility for a particular psychological function (or faculty in Gall's terms). However, it is also quite distinct from Lashley's ideas of mass-action and equipotentiality, because it suggests that some regions of cortex are fundamentally involved in particular psychological processes while others are not.

In a way, the concept of distributed control is a compromise between the two approaches, because it implies cortical specialisation (localisation of function) but also suggests that several (perhaps many) interconnected but anatomically distributed centres may be involved in the overall process. As Kosslyn and Anderson (1992) have commented, the problem for the strict localisationists was of thinking that psychological processes like memory, attention, or language were equivalent to Gall's faculties, and therefore could be localised to one particular brain region. In reality, such processes are complex and multi-tiered, involving the collaborative efforts of many underlying mechanisms. These subsidiary elements could, of course, be "localised" to very specific cortical regions, but the network as a whole may nonetheless actually "engage" broad swathes of cortex when the subsidiary elements interact to serve the particular psychological process.

For some neuropsychologists, Jerry Fodor captured the essence of this emerging view in his influential book *The modularity of mind* (1983). He argued that it was necessary to distinguish between two classes of cognitive processes: central systems and **modules**. The former are non-specific in the sense of operating across cognitive domains: attention, thinking, and memory have been suggested as examples. Modules, on the other hand, are domain specific in that they only process very particular types of input information: colour, shape, movement, faces, and so on. In Fodor's view, modules are likely to be hard-wired (immutable), autonomous, and localised. Critically, they can process information rapidly, and without reference to other modules; something that Fodor called "informational encapsulation".

It must be said at this point that debating the relative merits of different conceptual models of brain functioning takes us into "difficult" territory, certainly beyond the scope of this introductory text. However, we can say that Fodor's model (presented, by the way, without detailed reference to particular brain structures) had at least one advantage over Geschwind's. It allowed for, and indeed presumed that, the brain used **parallel information processing**, at least at the lower "modular" level, so different modules could become simultaneously active, whereas Geschwind's was essentially a serial processing model.

As for the distinction between localised modules and non-localised higher-order cognition, here we must tread very carefully. Certainly there is good evidence for modularity within perceptual systems: Zeki et al. (1991) have described over 30 "modules" in the mammalian visual system for example. But as for non-localised higher-order cognitive processes, current thinking envisages these as mediated by networks of multiple specialised cortical areas, connected through parallel, bi-directional pathways. Thus it could be argued that even processes such as attention and memory, though not localisable to singular specific locations (modules), are nevertheless localisable to networks (or is this a contradiction in terms?). The extent to which components in networks are then dedicated to particular higher-order cognitive functions, or shared between several, is another current

Key Terms
Module: A core unit in an integral modular system.
Parallel information processing: The idea that the brain processes two sources of information simultaneously.

matter of debate. (See Box 1.2 for further consideration of this complicated issue, and Chapter 9 for an introduction to the concept of the global workspace model of consciousness.)

Box 1.2 The precuneus: Trying to make sense of its many connections and behavioural correlates

In this focus box we hope to illustrate how our understanding of brain–behaviour relationships has advanced beyond the early connectionist models described in the text, as in-vivo imaging procedures, coupled with ingenious psychological challenges, have been refined. The precuneus (BA [**Brodmann area**] 7) is located medially (in the longitudinal fissure) above the occipital lobe, forming part of the posterior parietal cortex (see Figure 1.5). You actually have both a right and a left precuneus (one in the right hemisphere and another in the left). The precuneus has reciprocal cortical connections (inputs to and outputs from) with other parietal regions: parts of the frontal and temporal lobes and the anterior cingulate gyrus. It has reciprocal subcortical connections with the **thalamus**, and sends outputs to the **striatum** and several **brainstem** areas.

Functional investigations have identified at least four roles for this hitherto poorly understood region. A series of PET and fMRI studies suggest that the precuneus is part of a network (also involving other parietal areas and the supplementary motor region of the frontal lobes) concerned with visuospatial processing and imagery, particularly self-referential imagery such as imagining reaching or pointing, or planning of movements in environments with lots of obstacles that have to be avoided (Malouin et al., 2003). Second, the precuneus has been strongly implicated (along with the prefrontal and anterior cingulate regions) in imagery components of episodic memory retrieval (memory for previously experienced events sequenced in time, in which, presumably, one might use imagery to run through the sequence of events to be recalled) and was labelled by Fletcher et al. (1995) as "the mind's eye". Closer investigation has indicated that the anterior part may be particularly involved in imagery, while the posterior region is associated with successful retrieval in general. A third important observation about the precuneus is that it is more active in tasks related to self—"seeing" things from one's own as opposed to another person's perspective. This network also includes other medial and lateral parietal regions, and a lateral frontal region known as the insula. Fourth, and most intriguing of all, it appears that the precuneus (in combination with posterior cingulate and medial prefrontal regions) is more metabolically active during conscious resting states (such as during meditation) than during goal-directed active tasks. The opposite side of this coin is that it becomes markedly inactive during altered conscious states including slow-wave sleep, hypnosis, and anaesthesia. This preliminary evidence has been marshalled to suggest that the precuneus may be an important node in the neural network mediating consciousness.

Taken together, these findings suggested to Cavanna and Trimble (2006) that: "the precuneus may be involved in the integration of multiple neural systems producing a conscious self-percept" (p. 579). A somewhat more modest interpretation might be that it plays a key role in the modulation of conscious processes, perhaps supporting mental representations of "self".

Key Terms

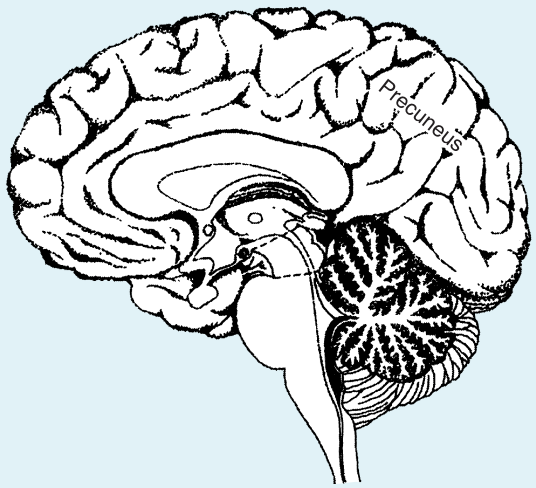
Brodmann area: A region of the cortex defined on the basis of cytoarchitecture.

Thalamus: A multi-functional subcortical brain region.

Striatum: A collective name for the caudate and putamen; key input regions in the basal ganglia.

Brainstem: The lower part of the brain, adjoining and structurally continuous with the spinal cord.

Cognitive neuropsychologists have also made extensive use of diagrams and models to identify both the component processing units (modules) and the way they collaborate to enable psychological processes such as memory, object recognition, or attention to operate. In certain respects, however, the cognitive neuropsychology approach and methodology is quite distinct from that of clinical neuropsychology (as exemplified by Geschwind). Whereas clinical neuropsychologists develop models that are anatomically referenced to specific cortical regions, cognitive neuropsychologists generate hypothetical models that more closely resemble "box and arrow" flow diagrams, and may make little or no reference to possible underlying brain regions (see, for example, Riddoch & Humphreys' 2001 model of visual object recognition, introduced in Chapter 8 and illustrated in Figure 1.6). Such models serve as templates (hypotheses) that attempt to account for *known* cases—of a neuropsychological deficit such as prosopagnosia (difficulty in recognising faces), or amnesia (loss of some aspect of memory) for example—but which must be amended if other cases come to light that do not fit. Cognitive neuropsychologists therefore put great weight on detailed case study of individuals with particular disorders, eschewing research based on groups of individuals, on the grounds that brain damage is infinitely variable and it therefore makes little sense (they would say) to



(b)

CORTICAL CONNECTIONS:

Medial parietal cortex:
posterior cingulate cortex
retrosplenial cortex

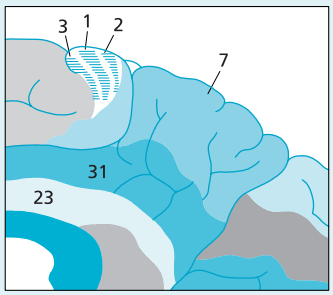
Lateral parietal cortex:
inferior parietal lobule
superior parietal lobule
lateral intraparietal cortex
medial intraparietal cortex
caudal parietal operculum

Frontal cortex:
mid-dorsolateral prefrontal cortex
dorsal premotor area
supplementary motor area

Other association cortices:
anterior cingulate cortex

medial prestriate cortex
superior temporal sulcus

PRECUNEUS



SUBCORTICAL CONNECTIONS:

Thalamus:
posterior complex
central intralaminar complex
lateral posterior nucleus
ventrolateral nucleus
pulvinar (mainly lateral)

anterior intralaminar nuclei

Striatum:
caudate nucleus and putamen

Claustrum:

Brainstem:
zona incerta
pregeniculate nucleus
pretectal nuclei
superior colliculus
nucleus reticularis tegmenti points
dorsolateral pontine nucleus

FIG. 1.5 The location and connections of the precuneus. (a) The precuneus forms part of the medial parietal lobe. It is hidden in the posterior part of the longitudinal fissure [after Critchley, M. (1953). *The parietal lobes*. London: Edward Arnold]. (b) Cortical and subcortical connections of the precuneus. [Adapted from Cavanna, A. E. & Trimble, M. R. (2006). The precuneus: A review of its functional anatomy and behavioural correlates. *Brain*, *129*, 564–583. Reproduced with permission.]

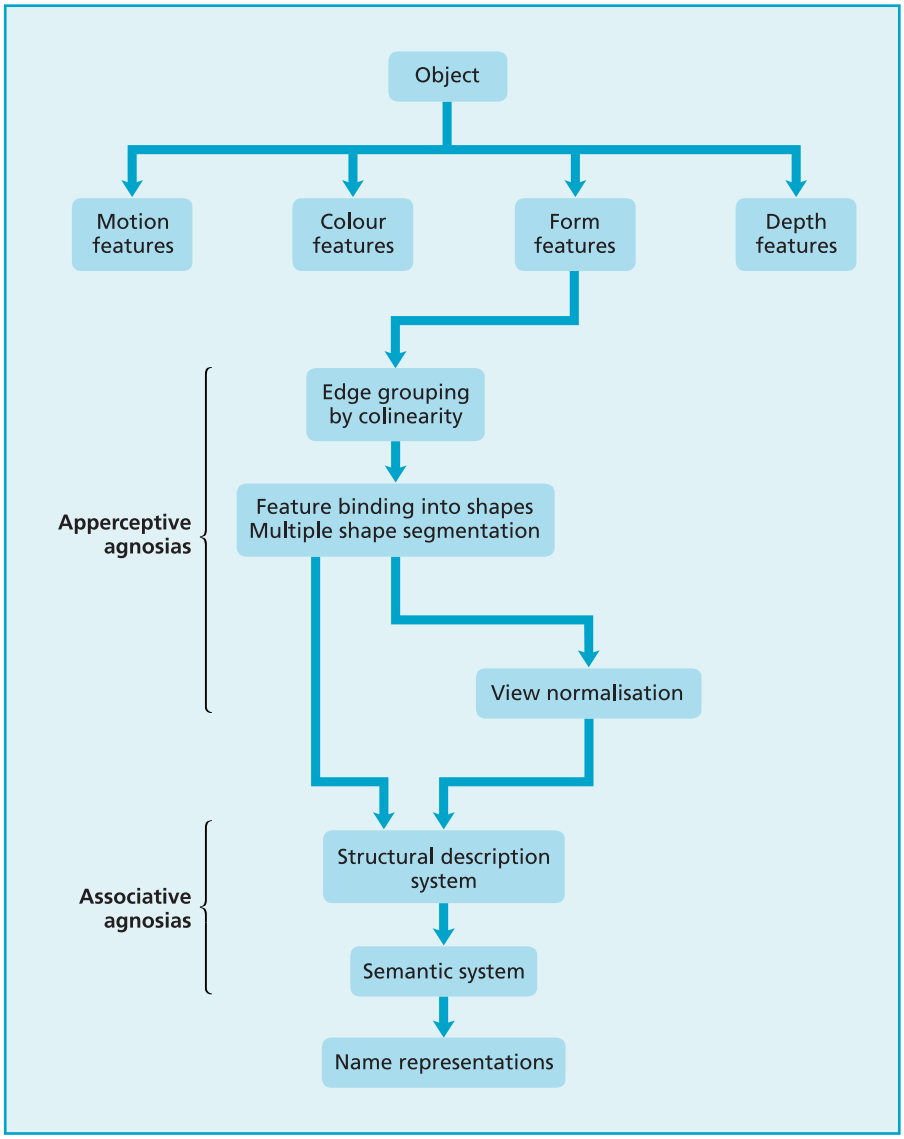


FIG. 1.6 Riddoch and Humphreys' (2001) model of visual object recognition. Typical of the cognitive neuropsychological approach, the model describes the component processes (and their connections) assumed to underpin normal and faulty object recognition. We describe this model in more detail in Chapter 8. [Adapted from Riddoch & Humphreys (2001) in B. Rapp (Ed.), *Handbook of cognitive neuropsychology*. Hove, UK: Psychology Press. Reproduced with permission.]

group individuals together simply because they may have vaguely overlapping areas of damage. Coltheart et al.'s (1998) review of the case of AC (neuropsychological cases are often identified by initials in this way) provides a typical illustration of this approach which we have summarised in Box 1.3.

According to Coltheart (2001), cognitive neuropsychology attempts to interpret cognitive disorders in terms of selective impairments of functional architectures. (Note his use of the term "*functional* architectures" referring to

"box and arrow" diagrams, rather than reference to brain regions or "*structural* architectures", i.e., anatomically referenced neural networks, loops, or circuits.) The approach is premised on four key assumptions:

- *Functional modularity*: simply stated, this means that cognitive systems are actually configurations of modules, each of which has quite specific functions (see our earlier reference to "modularity of mind").
- *Anatomical modularity*: meaning that such modules probably occupy rather specific anatomical locations.
- *Uniform functional architecture*: meaning that the above relationship is consistent from one person to the next.
- *Subtractivity*: meaning that damage may impair or "knock out" a module or connection in a system (or architecture), but not replace it with a new one.

Are these assumptions legitimate? According to Coltheart if they were not, cognitive-neuropsychological research would have run into severe difficulties by now, whereas in fact the approach continues to be very informative. However, this is a rather glib answer, and a more prudent approach may be to consider these not as "key assumptions underlying cognitive neuropsychology" but simply as working hypotheses about brain functionality. So, as with any other hypotheses, the scientist retains them until the evidence dictates that they should be rejected (Popper, 1934).

Box 1.3 The case of AC (Coltheart et al., 1998)

AC, a 67-year-old male, had recently suffered a major stroke, creating an area of damage on the left side of his brain. A CT scan additionally indicated evidence of earlier cerebrovascular incidents (probably minor strokes) in both hemispheres. Not surprisingly in view of the left-hemisphere damage, AC's language ability was severely compromised, both in terms of reading and writing and in relation to verbal expression, where it was apparent that although he knew what he wanted to say, he struggled to find the appropriate words to say it. However, careful examination of his cognitive impairments revealed an additional specific problem with his knowledge of objects, suggesting a profound semantic impairment. When asked how many legs an oyster had, he replied "a few", and for a seagull, "four". Yet he had a 95% success rate in classifying animals as dangerous (or not), and a 96% success rate in determining whether or not an animal would be considered "edible". In other words, he certainly retained considerable semantic information about animals despite not knowing how many legs they had. Further testing indicated that AC's deficit was, in fact, related to loss of knowledge about the *appearance* of objects including animals, as he also struggled to identify those with tails, or indeed their general shape.

From a cognitive neuropsychological perspective, the implication of these findings is that there must be separate independent systems of knowledge about the properties of objects and their visual appearances. Of course there may, in fact, be separate systems of perceptual knowledge (about objects) for each of our senses, in addition to a system for non-perceptual object knowledge.

INTERIM COMMENT

Although the cognitive neuropsychology approach has been useful in certain domains such as language (see Chapter 6) and object recognition (see Chapter 8), its reliance on case study rather than group comparisons and its indifference towards brain structures have not been to everyone's taste. Small *N* research makes for problems of generalisability in any discipline, and neuropsychology cannot be excepted. As for the inclination to marginalise, or even ignore, matters of brain neuroanatomy, it should be noted that the continuing development of in-vivo techniques (see Chapter 2) means that data about functional activation in the brains of people both with and without damage as they undertake various psychological challenges are now readily accessible, and this is likely to mean that cognitive neuropsychologists will, in the future, have to take more notice of the brain. A concise account of the key events in the history and development of neuropsychology is offered by Selnes (2001).

CHAPTER SUMMARY

Scientific interest in the relationship between brain structure and function can be traced back to the work of the 19th-century European neurologists. In the intervening years, researchers have debated the extent to which the brain operates on the basis of localisation of function or according to the principles of equipotentiality and mass-action. Although still a matter of considerable debate, most modern-day researchers favour some form of localisation, albeit one involving specialised distributed networks, as providing the best account for our understanding of how the brain actually operates. Equipotentiality and mass-action currently have few advocates among brain scientists.

In this chapter we have traced the development of scientific brain research, and introduced some of the theories that have surfaced as our understanding of these relationships has developed. A promising start in the 19th century gave way to a period in the first half of the 20th when psychology was dominated by theories and ideas that made only passing reference to the brain. Renewed interest in physiological psychology in the second half of the 20th century, along with greater interest in cognitive processes within psychology, set the scene for the birth (rebirth?) of the discipline we recognise today as neuropsychology. Although it is not an entirely unified enterprise, its cognitive and clinical strands complement one another in many respects. The rapid increase in access to, and consequent use of, in-vivo imaging procedures (which brings into the equation both clinical and non-brain-damaged cases) is likely to lead to greater convergence. These techniques also provide exciting new insights into the functions of particular cortical regions, and the precuneus is an excellent example of this.

CHAPTER 2

CONTENTS

2

Methods in neuropsychology

INTRODUCTION

In this chapter we introduce some of the methods that are used in neuropsychology to explore the relationship between brain structure and function. In Chapter 1 we described neuropsychology as a "bridging discipline" and consequently there are a wide range of methodologies involved—from neuroanatomical procedures at one end of the spectrum, through to experimental psychology assessments at the other. The advent of in-vivo neuroimaging techniques over the last 20 years has revolutionised neuropsychology, providing research opportunities that were previously unthinkable. In-vivo imaging has, for example, confirmed some of the long-suspected roles of particular brain regions in certain psychological processes (e.g., the role of **anterior cingulate** cortex in attention; see Chapter 9). Imaging techniques have also revealed the complexity inherent in functions that traditional neuropsychology had previously oversimplified. Imaging of language processes is an example of this, as discussed in Chapter 6.

While imaging techniques have undoubtedly provided a wealth of new information, it is important to be aware that they are not without limitations. Older techniques have therefore remained valuable, in spite of predictions of their demise. In fact imaging and traditional neuropsychology techniques provide complementary methodologies, generating more information when used in conjunction than either could do alone. A key element of imaging studies in neuropsychology is the vital importance of good experimental design aimed at testing specific hypotheses. In the excitement of newly available techniques, it is important to remember that they are simply techniques to answer interesting questions—neuroimaging is a means not an end.

An important though sometimes unspoken concept in neuropsychological methodology is that of **converging operations**. Human neuropsychology is inevitably constrained by many practical and ethical concerns: for example, repeating Lashley's research with human subjects would be impossible. Putting this another way, definitive, theory-changing experiments are actually few and far between in neuropsychology. Rather, researchers develop ideas (and ultimately theories) about different aspects of neuropsychology by "being receptive" to

KEY TERMS

Anterior cingulate: A midline frontal lobe structure implicated in attention, response inhibition, and emotional response (especially to pain).

Converging operations: The use of several research methods to solve a single problem so that the strengths of one method balance out the weaknesses of the others.

research findings derived from quite distinct approaches. For example, as discussed in Chapter 3, current ideas about the differing responsibilities of the left and right sides of the brain derive from:

- case studies of individuals with localised brain damage;
- individuals who have been surgically operated on;
- experimental psychological studies of healthy individuals;
- imaging studies of both healthy and brain-damaged individuals.

All these data should additionally be "evaluated" in relation to both basic neuroanatomical observations of similarities and differences between the two sides of the brain, and (we suggest) broader comparative/evolutionary perspectives. Using all this information to generate neuropsychological theories would, in effect, be to endorse the concept of converging operations—something that the authors of this text are, with certain caveats, happy to do. However, it is important to know that this approach is not to everyone's liking, and most neuropsychological methods have their critics (see, for example, Caramazza's objections to studying groups of individuals with similar brain damage: Caramazza, 1986).

Interestingly, a "new take" on converging operations derives from combining methods in a single study (as we hinted earlier), and we review this potentially fruitful line of inquiry towards the end of this chapter. However, we start with a brief review of classic techniques that are, for the most part, neuroanatomical in origin. We then consider the use of electrical stimulation and electrical recording in the brain. Then we review the in-vivo neuroimaging procedures that have been increasingly used to characterise brain structure and function. Lastly we review the neuropsychological approach. Where possible, we try to refer readers to specific examples of the use of these techniques described elsewhere in this book.

INVASIVE TECHNIQUES FOR MEASURING BRAIN STRUCTURE AND FUNCTION

EXAMINING TISSUE

Until quite recently, the only options for measurement of brain structure were post-mortem investigation or, very occasionally, **biopsy**. The latter technique involves the removal and examination of small (but irreplaceable) samples of brain tissue from the brain region in question. Biopsy is essentially somewhat "hit and miss" and also causes inevitable damage to the brain. It is therefore hardly ever used in humans. Post-mortem analysis by contrast, has a long and sometimes colourful history in medicine. It does, of course, require the subject to be dead, and therefore early signs of disease are typically masked by changes that have occurred as the disease process has progressed.

Sometimes the damage that is revealed in post-mortem is blatantly obvious. In one of neuropsychology's classic cases, Broca observed the brain of his aphasic patient "Tan". His very superficial post-mortem revealed clear damage to the left frontal cortex (in the region still referred to as "Broca's area"). The brain of a patient who has died due to **Alzheimer's disease** or **Huntington's disease** will look abnormal even to the naked eye. It will appear shrunken, with deflated gyri (surface bumps) and widened sulci (surface grooves). These changes are, however,

KEY TERMS

Biopsy: The removal of tissue (in a living individual) for analysis.

Alzheimer's disease: A form of dementia involving progressive loss of psychological functions as a result of widespread loss of cortical and subcortical neurons.

Huntington's disease: A rare, genetically determined, neurological disorder causing dementia and death due to progressive loss of neurons in the striatum.

probably of less interest to researchers than the more subtle brain changes that occurred at the start of the disease, or even before clinical symptoms of the disease were noted. Since the patient would still have been alive at this point, post-mortem investigation would not have been an option.

In other cases, a brain can appear externally normal at post-mortem, and it is only on closer inspection of internal structures and tissues that damage or disease becomes apparent. Brain tissue looks solid to the naked eye, so such closer inspection depended on two crucial developments. The first was the invention and gradual refinement of light microscopy: Van Leeuwenhoek first used a microscope to examine biological tissue in 1674, and since then improvements in lens manufacture have led to the technique becoming ever more effective. Light microscopes can now magnify by a factor of several hundred. The newer technique of electron microscopy provides magnification by a factor of several thousand. It is now possible to view images of individual synapses or even individual **receptor sites** for **neurotransmitters**.

The second crucial development for post-mortem analysis was the discovery of staining techniques that can be used to "highlight" particular component structures of tissue. Staining was pioneered by Golgi in the late 19th century and his silver-staining method ("Golgi staining") is still used today to highlight neurons. Other staining techniques, such as horseradish peroxidase (HRP), have been developed to enable the tracing of connections between neurons. This stain is absorbed by the **distal** (remote) parts of neurons but is carried back to the cell bodies, thus revealing the path that the axons take. A combination of these staining techniques in post-mortem tissue provides evidence of functional connectivity between brain regions, such as the innervation of the striatum by the **substantia nigra**, which deteriorates progressively in **Parkinson's disease** (see Chapter 5).

At the start of the 20th century, Brodmann used a combination of microscopy and staining to map the cytoarchitecture of the human cortex. His research revealed that different cortical locations are characterised by structurally distinct cell types. His comprehensive map, which is still used today (with minor modifications) for reference and anatomical location, identified 52 numbered regions (Brodmann, 1909). For example, the primary visual cortex is known as Brodmann's area 17 (BA 17), while Broca's area spans Brodmann's areas (BA) 44 and 45 in the left hemisphere (see Figure 2.1).

Key Terms

Receptor sites: Molecular structures on (or in) the membranes of neurons that neurotransmitter substances (and hormones) can "influence" when they occupy them, usually by making the neuron more or less excited.

Neurotransmitters: A heterogeneous group of chemical messengers usually manufactured by, stored in, and released by neurons that can influence the excitability of other neurons (or muscles).

Distal: Far away; as opposed to proximal, meaning near to.

Substantia nigra: Another component of the basal ganglia. Neurons originating in the substantia nigra terminate in the striatum, where they release the neurotransmitter dopamine.

Parkinson's disease: A neurological disorder in which movements become slowed or are lost altogether. Rigidity and tremor are also found. Associated with loss of cells in and around the basal ganglia.

Epilepsy: The term for a group of neurological disorders characterised by synchronised but excessive neuronal activity.

LESION AND ABLATION

Lesion (cutting) and ablation (removal) of nerve tissue are long-standing techniques in neurology. Lashley, whose work we introduced in Chapter 1, put forward the theory of mass-action based on lesion studies in animals. For obvious reasons, these procedures are not used experimentally in humans. However, brain tissue is sometimes ablated for medical reasons (e.g., the removal of a tumour). Surgical lesioning is also occasionally undertaken. For example, lesioning the corpus callosum has been used as a treatment for **epilepsy**, which will be discussed further in Chapter 3. Sometimes lesions or ablations may occur as the result of accidents. A famous case is that of Phineas Gage, who had an accident involving an iron rod and some dynamite that resulted in extensive damage to his prefrontal cortex. Another less famous case is NA, who developed amnesia after an accident with a fencing foil (see Chapters 7, 10, and 11).

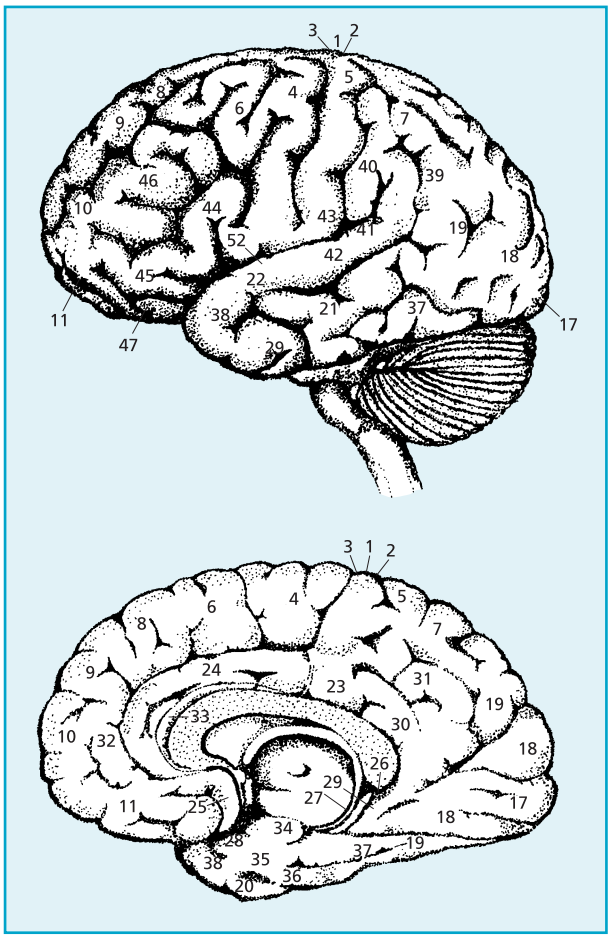


FIG. 2.1 Brodmann's cortical areas revisited. Brodmann identified 52 cortical areas on the basis of the type and density of neurons present.

Lesions can also be induced through the use of chemicals or drugs. The **Wada test** (Wada & Rasmussen, 1960) involves the administration of a fast-acting barbiturate via the carotid artery to one hemisphere at a time. This causes a temporary lesion lasting a matter of minutes, and has historically been used to establish hemispheric dominance for language prior to brain surgery. Other chemicals may induce permanent lesions via toxic influence. The substance MPTP, a toxin that was inadvertently mixed with synthetic heroin by recreational drug users in 1980s California, irreversibly destroys **dopamine** neurons in the substantia nigra, resulting in a very severe form of induced Parkinsonism. (We review the case of the "frozen addicts" in Chapter 5.)

"VIRTUAL LESIONS": TRANSCRANIAL MAGNETIC STIMULATION

Transcranial magnetic stimulation (TMS) was originally investigated as a possible treatment in various therapeutic settings, however it also provides a potential tool for neuropsychologists because it can be used to induce a "virtual lesion". TMS uses strong pulses of magnetisation that can be focally administered via a hand-held coil (see Figure 2.2). Thus, different areas of cortex can be stimulated depending on the positioning of the coil. Single pulses of TMS or brief trains of repetitive TMS at higher frequencies typically increase neuronal excitability. However, continuous stimulation at lower frequencies suppresses neuronal excitability, an effect that can last several minutes after TMS is stopped (Hoffman & Cavus, 2002). Essentially, it is this low-frequency TMS that induces the "virtual lesion". The potential value of this technique is highlighted by a study by Hilgetag et al. (2001) who reproduced the classic neurological symptom of **spatial neglect** (see Chapter 8) by stimulating the parietal cortex in normal subjects.

TMS can also be used in conjunction with structural neuroimaging to investigate the effects of virtual lesions in anatomically localised brain regions. Various studies have shown the utility of the technique in diverse areas of perception and cognition. However, despite its obvious potential, the technique is not without limitations. Concerns have been raised about the safety of the procedure, particularly in subjects who may be vulnerable to developing neurological abnormalities such as epilepsy. Also, TMS is better suited for the investigation of superficial brain regions (the cortex for example) than for probing less accessible regions and deeper structures.

KEY TERMS
Wada test: A test that involves the administration of a fast-acting barbiturate (via the carotid artery) to one hemisphere at a time, to determine, among other things, the hemisphere that is dominant for language.
Dopamine: A catecholamine neurotransmitter found in the brain.
Spatial neglect: A condition in which damage to one side of the brain causes a deficit in attention to the opposite side of space.

ELECTRICAL PROCEDURES

ELECTRICAL STIMULATION

The neurosurgeon Wilder Penfield was responsible for much of the pioneering work on mapping primary somatosensory and motor cortex. His subjects were patients who required surgery for life-threatening conditions, typically the removal of tumours or blood clots. He asked these patients whether during the course of surgery he could apply mild electrical stimulation to the surface of their brains. Brain surgery is typically carried out with the patient awake, due in part to the lack of pain receptors in the brain, and resultant pain insensitivity. Therefore Penfield was able to talk to his patients about their sensory impressions and motor responses as he stimulated specific regions. Penfield was the first researcher to discover the amazing topographic representation of body parts in the primary motor and somatosensory cortex (which we describe in Chapters 4 and 5). (See Penfield & Rasmussen, 1950.)

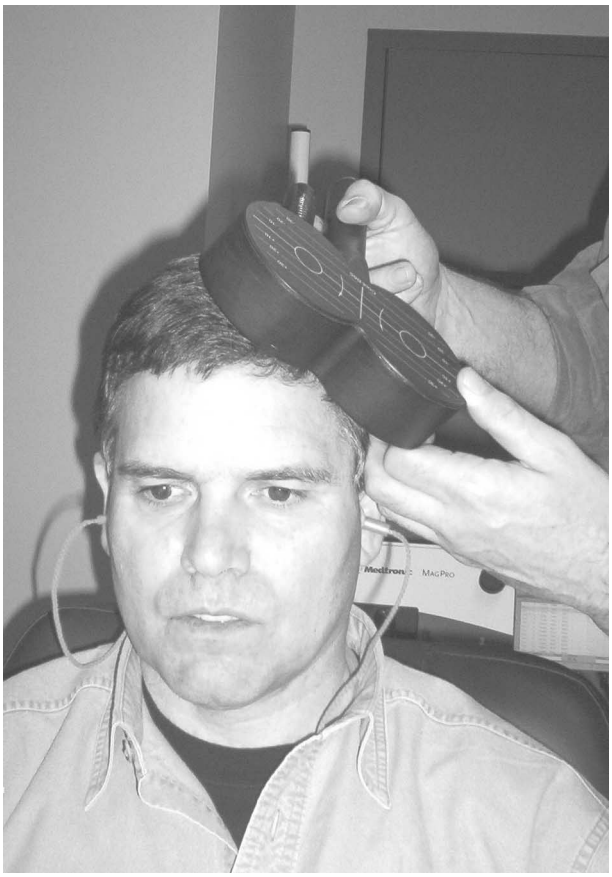


FIG. 2.2 Transcranial magnetic stimulation. A subject receiving stimulation with a typical "figure of eight" TMS stimulator.

ELECTRICAL RECORDING

We can also learn about brain function by recording its electrical activity. In electroencephalography (EEG) and the closely related procedure of event-related potential (ERP) recording, this involves attaching electrodes to the scalp. The underlying activity is detected and amplified, and usually displayed on a chart recorder or computer screen. Surface recording is possible because electrical activity in the brain is conducted passively through the **meninges** (protective membranes surrounding the brain) and the skull to the scalp. Of course, voltages recorded represent the sum of activity from millions of neurons in the area of brain closest to the recording electrode. So, in order to get an idea about the spatial distribution of activity, several separate channels of EEG corresponding to electrodes in different positions on the head can be recorded simultaneously. This procedure has been widely used in research and also has clinical relevance, having proved invaluable in the diagnosis of epilepsy and in the identification of sleep-related disorders (see Figure 2.3).

In a research study with ERPs, a series of stimuli such as tones or light flashes are presented to a participant. The raw EEG for a precise 1- or 2-second period following each stimulus is recorded and fed into a computer where it is summed and averaged. There will be a response (or "event-related potential") in the brain to each separate stimulus but this will be small (millionths of a volt) in comparison with the background EEG (thousandths of a volt). By summing all the EEGs and averaging them, the more-or-less random EEG averages to zero, to leave an ERP that has a characteristic waveform when shown on the computer screen. Abnormalities in this waveform have been linked to clinical disorders, for example

KEY TERM
Meninges: The system of membranes that enclose the central nervous system.

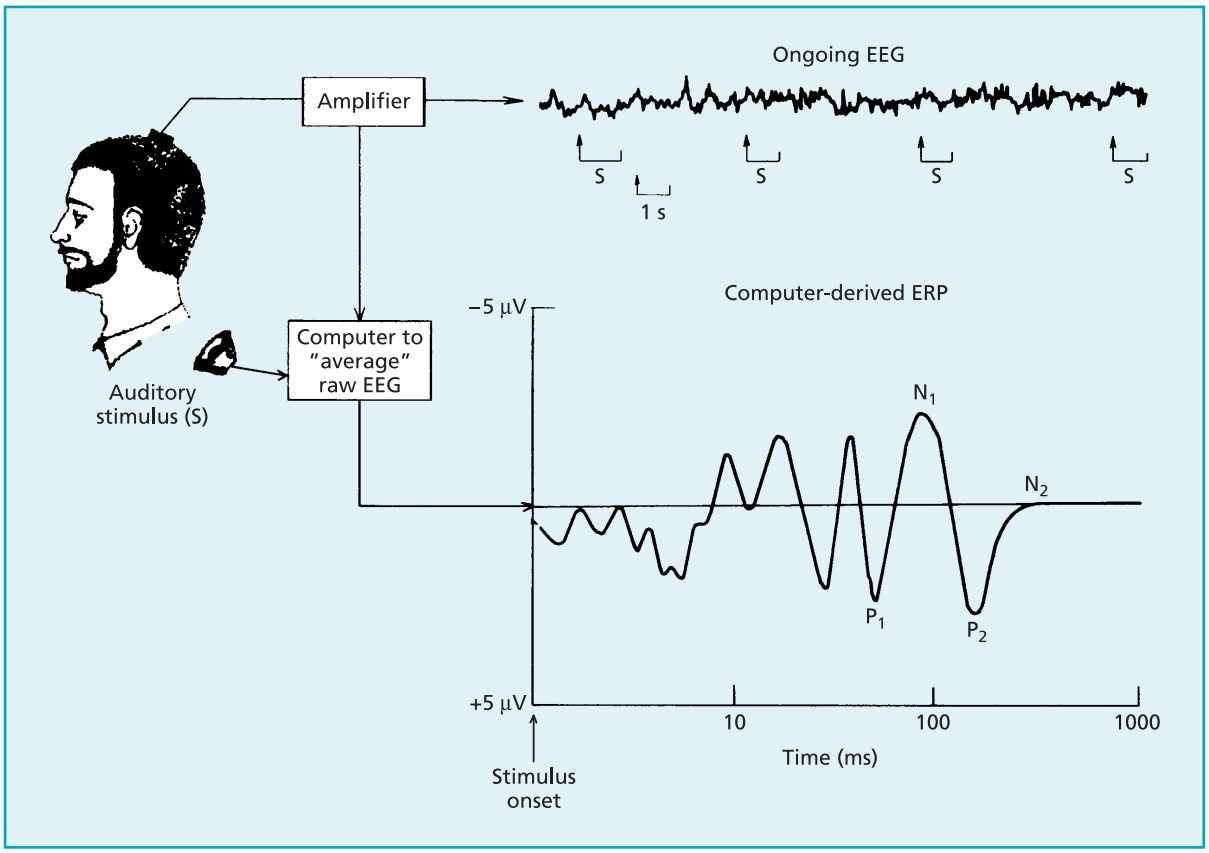


FIG. 2.3 Recording of EEGs and ERPs. Raw EEG can be recorded from surface electrodes on the scalp. If a series of stimuli are presented to the respondent there will be a small but characteristic response to each stimulus but this will be "hidden" in the EEG. ERPs are obtained by feeding brief "epochs" of the EEG (typically 500 to 1000 ms following each stimulus) into a computer that averages them. The random background EEG tends to average to zero, leaving the characteristic ERP waveform.

a predisposition to alcoholism or schizophrenia. The ERP technique has also been useful as a tool to explore the mechanisms of attention, and we describe some of this research in Chapter 9.

Recently, a variant of ERP known as magnetoencephalography (MEG) has been developed. (Mogilner et al.'s 1993 study of remapping in the cortex described in Chapter 4 employs this procedure.) MEG involves upwards of 60 electrodes attached to the participant's scalp, and takes advantage of the fact that when neurons are active they generate tiny magnetic fields. Event-related fields (ERFs) can be detected by an MEG analyser in much the same way as ERPs, but they provide a more accurate means of identifying the origin of particular signals. MEG can therefore locate the source of maximum magnetic field activity in response to stimuli and, if required, map these areas three-dimensionally and in real time. This technique has been of use in identifying the precise focal origins of epileptic seizures and, as hinted above, it has also been used to map areas of the somatosensory cortex. Perhaps surprisingly, MEG had not, until recently, become a widely used research technique. Although it has superior spatial resolution compared to EEG, both techniques are constrained by the fact that they are only

suitable for looking at surface structures of the brain. The MEG technology was developed at the same time as the spatially superior in-vivo imaging techniques discussed below, and historically relatively few research groups have chosen to invest in MEG. However, this appears to be changing, as more groups recognise the advantages of combining MRI and MEG technologies. Many leading research centres are opting for MEG technology and the technique is likely to become increasingly influential over the next few years.

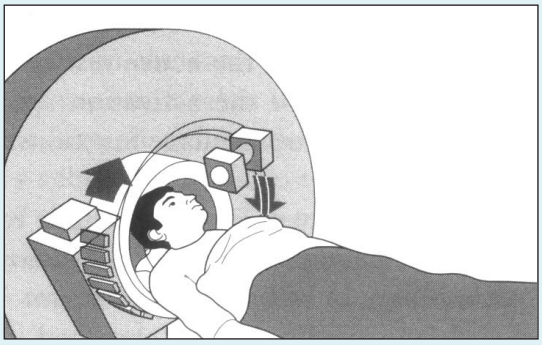
IN-VIVO IMAGING

The first of the in-vivo imaging techniques was computerised tomography (CT, or sometimes CAT) scanning, which came on stream in the early 1970s. As technologies developed, and the value of scanning became clearer, it was soon followed by other procedures including PET (positron emission tomography), rCBF imaging (regional cerebral blood flow), and MRI (magnetic resonance imaging). The common feature of these procedures is that researchers can produce images of the structure or functional activity of the brains of *living* people (see Figure 2.4).

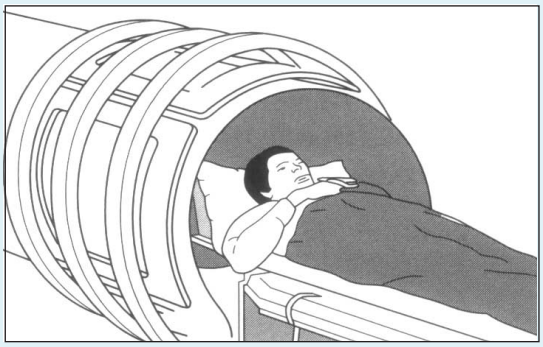
STRUCTURAL IMAGING

Computerised tomography (CT, but also known as computerised axial tomography or CAT) provides structural images of the brain. To generate brain scans, low levels of X radiation are passed through an individual's head at a series of different angles (through 180°). A computer analyses each "image" and generates what is, effectively, a compound X-ray. It can produce a "slice-by-slice" picture of the entire brain, or other parts of the nervous system such as the spinal cord. A drawback of CT scanning is that the contrast between more and less dense tissue is not particularly good, although this can be improved by the administration of a dye (injected into the bloodstream just before the scan is taken). CT scans cannot measure functional activity but they have provided valuable information about *structural* changes seen in the brains of some people with dementia, and about the effects and location of brain damage in general.

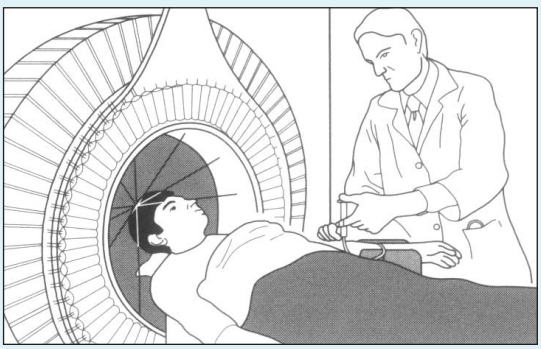
Magnetic resonance imaging (MRI) is a more recent development and the technique is very



(a) Computerised tomography (CT)



(b) Magnetic resonance imaging (MRI)



(c) Positron emission tomography (PET)

FIG. 2.4 CT, MRI, and PET scanning. CT scans provide reasonably well-defined images of brain structure. PET scans generate images of functional activity, although structure is only poorly defined. MRI can generate "photographic"-quality images of brain structure, and functional MRI (see Figures 2.5 and 2.6) can produce integrated structural and functional images. Source: Rosenzweig et al. (1999). *Biological psychology*. Sunderland, MA: Sinauer Associates Inc. Reproduced by permission of Sinauer Associates Inc.

complex. In summary, it depends on the fact that protons in tissue act as little bar magnets that spin. When a strong magnetic field is applied externally by the MRI scanner, these spinning protons interact with the external field in a way that produces small but detectable changes in magnetic signal that the scanner can measure. Different types of (brain) tissue have different concentrations of protons and different chemical environments which influence the magnetic properties. Thus different tissues produce different signals and the scan data can be computer-processed to generate images that clearly show, in remarkable detail, the structures of the brain. The entire brain can be imaged in successive slices, which can be produced in **sagittal** (side), **coronal** (front), or horizontal transverse planes. Structural MRI has significant advantages over CT; for example, the images are much higher resolution and do not involve exposing people to X radiation.

FUNCTIONAL IMAGING

PET scanning was the first widely used functional imaging technique and provides images of a person's brain that show which regions are activated as they undertake different sorts of task, such as reading words, solving mental arithmetic, and listening to music. There are different types of PET scanning. One of the commonly used techniques involves injecting subjects with water that has been labelled with the short-lived radio-isotope oxygen 15. When a region of the brain is more active, blood flow to that region increases and therefore more radio-labelled water will be carried to active areas. As the oxygen 15 decays, with a half-life of around 2 minutes, gamma rays are emitted that can be detected by the PET scanner. The scanner can determine whereabouts in the brain the gamma rays were produced, and thus provide a picture of regions where blood flow is increased, indirectly determining areas of enhanced neural activity.

Another PET technique uses radio-labelled glucose rather than water. More active regions of the brain need more glucose (as a fuel), so again the radiotracer becomes concentrated in the more active regions and this can be detected as it decays. It is also possible to use PET to look at neurotransmitter function by manufacturing more complex radiotracers. For example, raclopride is a molecule that binds to dopamine receptors in the brain. A radio-labelled form of raclopride can be prepared that uses the isotope carbon 13. If this tracer is used, it will bind directly to dopamine receptors, in competition with endogenous dopamine, and therefore provides information about dopamine function. This technique has been used to study reward systems in the brain (Koepp et al., 1998; and see Chapter 10).

PET is thus a powerful means of assessing *functional* brain activity, although it does not directly measure neuronal events. Rather, it indicates relative levels of (or changes in) activity under different conditions. To do this, "image subtraction" is often employed, meaning that activity during a control condition is (literally) subtracted by computer from activity during the active test condition, and the remaining PET activity taken as an index of the activation specific to the test condition (see Box 2.1 below). Two other variants of the PET technique that you may read about are regional cerebral blood flow (rCBF) and single photon emission computerised tomography (SPECT). In rCBF, the participant inhales a small amount of a radioactive gas such as xenon, which is absorbed into the bloodstream and thus transported around the body. The participant sits in a piece of apparatus that looks a little like a dryer seen in old-fashioned hair-salons. This has a series of sensors that detect the radioactivity from the transported xenon,

KEY TERMS
Sagittal: Sideways, as in sagittal brain scans taken from the side of the head.
Coronal: (As in section) the orientation of a brain slice if you were looking "face on" and the brain was sliced vertically.

Box 2.1 Cognitive subtraction, conjunction, and factorial designs

Many early neuroimaging experiments used a technique called "cognitive subtraction". This is based on the idea that a complex process involves a number of stages, and if you are interested in a particular stage you need an active task that involves that stage and a control task that involves all other stages but for the critical one. By subtracting brain activity in the control task from brain activity in the active task, you isolate brain activity associated with the process of interest. For example, if we are interested in object naming we might have an active task involving naming pictures of objects and a control task involving passively viewing the same pictures. On the face of it, the critical difference is that the object is only named in the active condition. One obvious problem with this is that there may well be incidental naming in the passive condition. It is likely that participants instructed to view pictures of objects passively will nevertheless find themselves mentally naming the objects. Many experiments using the cognitive subtraction approach have used "serial subtraction" where they attempt to isolate a series of stages in processing. So in our object-naming experiment we might also include a condition of viewing meaningless shapes. Subtracting this from the passive viewing condition might identify regions involved in object recognition. The serial subtraction approach makes the assumption of "pure insertion"; that is, it assumes that each process of interest is independent. In fact, many cases are likely to involve a degree of interaction between component processes, such that adding (or subtracting) a cognitive component may affect the other components.

To overcome these limitations, many of the best functional imaging experiments use "cognitive conjunction" or "factorial designs". The logic of cognitive conjunction is to select several tasks that activate the same process of interest, each with an appropriate control. By considering *common* activations across these tasks, we can be confident that we are identifying the core process of interest. Factorial designs explicitly tackle the issue of interactions between processes. This type of design can best be illustrated using an example. Imagine we are still interested in object recognition and naming. We develop a task with four conditions:

1. Naming pictures of objects (naming and object recognition both present).
2. Naming colour of a meaningless design (naming present, object recognition absent).
3. Viewing pictures of objects (object recognition present, naming absent).
4. Viewing a meaningless design (naming and object recognition both absent).

Subtracting 3 and 4 from 1 and 2 will show us the main effect of naming. However we can also look at the interaction between object recognition and naming. By performing the subtraction (1-2) – (3-4), we can see whether the process of retrieving a name has an effect on object recognition, thus identifying whether or not the processes are independent. These types of designs can provide important clarification of models from cognitive neuropsychology.

and because more blood is required by "active" brain regions, a computer can build up an image of areas of greater (and lesser) activity based on the detection rates. SPECT differs from PET in certain technical respects, the upshot of which is that the clarity of the scans is less precise because they take longer to generate.

PET and its associated techniques were a major step forward in understanding brain function. However there are certain limitations with these methods. At a practical level, PET is a very time-consuming and expensive technique. It also involves exposing subjects to ionising radiation, and this precludes repeat scanning of the same person. The approach is also very limited in terms of temporal resolution—each PET image takes a matter of minutes to generate and represents activity across that period. It is therefore not possible to study activity related to brief or transient stimuli. Thus PET is being superseded by functional MRI for many applications. However, it still has a place in brain research, particularly in the area of neurochemistry. As more sophisticated **radio-ligands** are developed, it is becoming possible to use PET to ask questions about neurotransmitter function that other techniques simply cannot address. For example, Thomasius et al. (2006) have studied directly the effect of the drug ecstasy on brain serotonin function (using a PET ligand that binds to serotonin receptors), and related this to mood and cognitive function.

For many purposes, however, functional magnetic resonance imaging (fMRI) has become the imaging technique of choice. fMRI is carried out using the same scanner as structural MRI (see Figure 2.5)—in fact an advantage of the technique is that both structural and functional information can be obtained in a single scanning session. fMRI depends on a lucky chance of biology: that oxygenated and deoxygenated haemoglobin (the molecule in the blood that transports oxygen) have different magnetic properties. Changes in the relative concentrations of oxygenated and deoxygenated blood therefore produce a detectable magnetic signal. This is referred to as "BOLD (blood oxygenation level dependent) contrast". BOLD contrast provides an indirect measure of neural activity, as neuronal firing has an effect on relative concentrations of oxygenated and deoxygenated blood (see Figure 2.6). These changes are subtle and detection depends on careful "tuning" of the MRI scanner. Using more powerful magnets also improves fMRI sensitivity.

KEY TERM
Radio-ligand: A radioactive biochemical marker that binds to a specific receptor type in the brain.

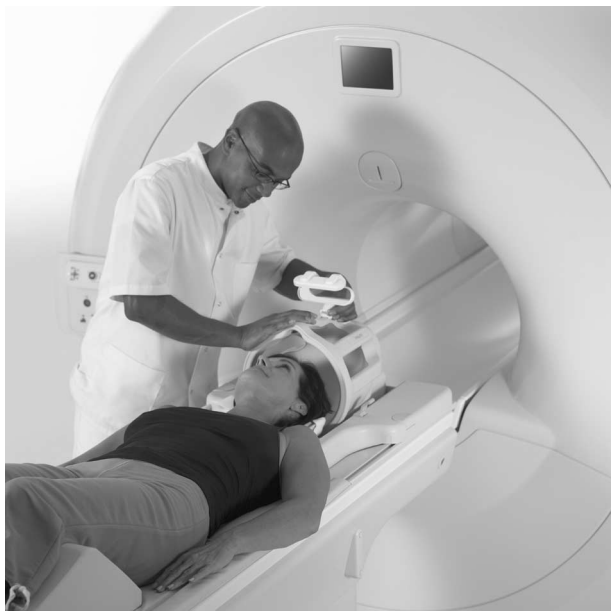


FIG. 2.5 A subject being set up in an MRI scanner. Photo courtesy of Philips Medical Systems.

fMRI has been enthusiastically embraced by neuroscience, and there has been a huge proliferation of research papers in which the technique has been used. However, fMRI is not without its limitations. Although the temporal resolution is better than that of PET, allowing neuronal responses to single events to be measured, it is still not in the league of EEG. The BOLD response occurs over a number of seconds and therefore the millisecond accuracy of EEG or MEG is not possible. It is also important to remember that fMRI measures secondary changes in haemodynamic activity and metabolism rather than directly measuring neuronal activity. This causes problems in spatial

accuracy and in quantitative measurement (although these are now being addressed to some extent; see Ugurbil, Toth, & Kim, 2003). Good fMRI studies also depend on good experimental design. Using fMRI to make inferences about cognitive processes is only possible if carefully designed, theory-driven experiments are used (see Henson, 2006; Poldrack, 2006).

In-vivo imaging continues to develop. In particular, MRI scanners are being used in new ways to explore different questions about brain structure and function. One example is diffusion tensor imaging or tractography, a technique that allows bundles of **white-matter** fibres, not identifiable using CT or conventional MRI, to be visualised. This allows the investigation of connectivity within neural networks (Minati & Aquino, 2006). Another example is magnetic resonance spectroscopy (MRS), a technique that studies the concentration of particular neurochemicals within specified regions of the brain. Both of these techniques have enormous potential for research as well as clinical applications.

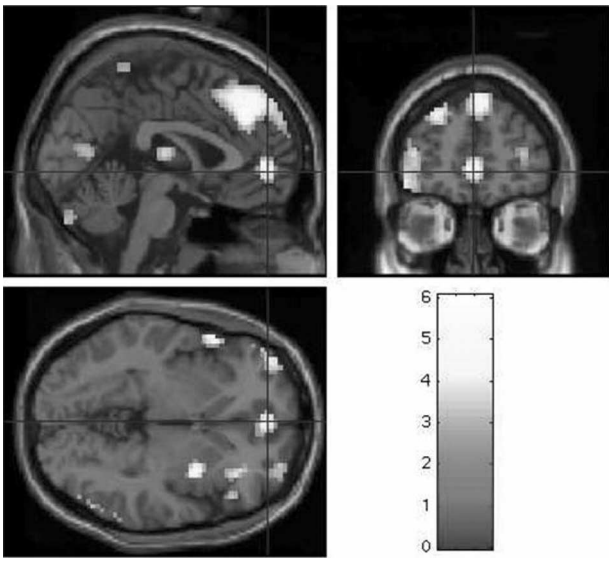


FIG. 2.6 An fMRI scan. These scans identify brain regions involved in winning money during a simple target detection task (scans obtained in the Wellcome Trust Clinical Research Facility, University of Manchester, UK).

Developments in analysis procedures are also opening up new possibilities. In particular, it is now possible to analyse patterns of connectivity between brain regions as well as region-specific activations. Thus we can determine the strength of connections between brain regions under different task conditions, and assess how these are modulated by neurological and psychiatric disease.

INTERIM COMMENT

The development of in-vivo scanning marked the beginning of a new era in brain research. For the first time scientists could examine the structure or functioning of *the living brain*. It became possible to see exactly how extensive a patient's internal brain injury or damage was, and researchers could begin to do valuable brain research in individuals with "intact" brains. By using special "labelling" techniques it even became possible to observe for the first time where in the brain drugs were acting.

Despite the scientific advances that have been made as a result of the wider availability of CT, PET, and MRI, there are drawbacks to each technique, as discussed. One additional practical drawback is worth remembering. All scanning techniques currently require the respondent to lie in a scanner. Not only can this be uncomfortable and, in the case of MRI, very noisy, but it also places significant constraints on the sorts of psychological investigation that can be conducted. Additionally, it raises questions about whether we are imaging the "normal" function of the brain. In drawing inferences from scanning results, we implicitly assume that the brain would act in the same way if a person was going about their day-to-day life as it does when they are lying in a strange scanning environment. That assumption is obviously questionable.

KEY TERM
White matter: Parts of the brain comprising axons of nerve cells, mainly responsible for neuronal transmission rather than information processing.

NEUROPSYCHOLOGICAL ASSESSMENT

The neuropsychological approach relies on using tests designed to reflect, usually in a relatively specific way, different aspects of cognitive function. Poor performance on a test may indicate focal (localised) brain damage. Poor performance on a series of tests may, on the other hand, reflect diffuse (widespread) damage. Neuropsychological assessment serves several purposes. First, it can give a "neurocognitive" profile of an individual, identifying both strengths and weaknesses in cognitive performance. For example, an individual's initial assessment may highlight a specific problem with spatial memory set against a background of above average IQ. Since many tests are "standardised", a person's performance can be readily compared with scores generated by other age- and/or sex-matched respondents (a process known as norm-referencing). Second, repeated testing over time can give an insight into changes in cognitive functioning that may relate either to recovery after accident/injury or to the progression of a neurological illness.

STANDARD AND CUSTOMISED TEST BATTERIES

In a typical neuropsychological assessment, a series of tests (called a test battery) will be given. One widely used battery is the Halstead-Reitan, which includes measures of verbal and non-verbal intelligence, language, tactile and manipulative skills, auditory sensitivity, and so on (Reitan & Wolfson, 1993). Some of the tests are very straightforward: for example, the tapping test, which assesses motor function, requires nothing more than for the respondent to tap as quickly as possible with each of his/her fingers for a fixed time period on a touch-sensitive pad. The Corsi block-tapping test measures spatial memory using a series of strategically placed wooden blocks on a tray (see Figure 2.7a). A third test measures memory span for sets of digits. Another example of a test battery is the Luria-Nebraska (Luria, 1966; see also Christensen, 1979), an even more exhaustive procedure that takes about 3 hours to administer and includes over 250 test items. Today, this battery is regarded as somewhat unwieldy, poorly standardised, and biased towards sensory, verbal, and motor functions—away from core cognitive domains of current interest such as attention, memory, and executive functioning. The battery is probably of more use as a clinical tool.

The administration of a standard lengthy test battery may be unsuitable for some individuals (such as demented or psychiatric patients) who simply do not have the requisite attention span. In such instances a customised battery may be more appropriate. Such assessments typically include some overall index of intelligence: the comprehensively norm-referenced WAIS-R (the revised Wechsler Adult Intelligence Scale; Wechsler, 1981) is still commonly used (though see below). In addition, specific measures may be adopted to test particular hypotheses about an individual. For example, if the person has received brain damage to his/her frontal lobes, tests might be selected that are known to be especially sensitive to frontal damage. The Wisconsin card sort test (see Figure 2.7b), the trails test (in which respondents have to join up numbered dots on a page according to particular rules), and verbal fluency (generating words starting with a particular letter or belonging to a specific category) are typical examples.

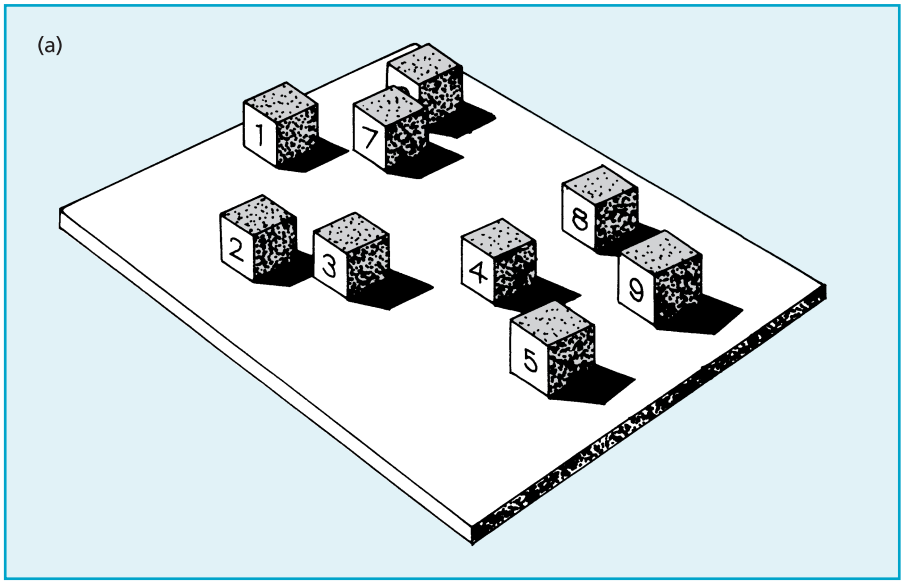


FIG. 2.7 (a) Corsi's block tapping task and (b) the Wisconsin card sort test. Corsi's test assesses spatial memory. The tester taps out progressively longer sequences of blocks to establish spatial memory "span". The respondent cannot see the numbers, so must memorise the correct sequence using spatial memory. In the Wisconsin test, the respondent sorts cards into four piles according to an "unspoken" rule: by colour, shape, or number. The only feedback received from the tester is whether or not a particular card has been correctly sorted. The respondent must use this feedback to guide future card sorts. Every so often the tester changes the sorting rule and the respondent must try to adjust to it. Source of 2.7(b): Gazzaniga et al. (1998). *Cognitive neuroscience: The biology of the mind* (Figure 11.5). © 1998 by W. W. Norton & Company, Inc. Reproduced by permission of W. W. Norton & Company, Inc.

The CANTAB (Cambridge Automated Neuropsychological Assessment battery; Robbins et al., 1994) has been developed as a battery of some 12–14 tests administered via a touch-sensitive screen. Many of the tests resemble computer games in certain respects, and are essentially computerised versions of standard pen and paper neuropsychological tests. For example the "stockings of Cambridge test" is analogous to the Tower of Hanoi test (see Figure 2.8), and the "intra/extra dimensional shift" test is based on the Wisconsin card sort test. Test norms are built into the CANTAB software, so that a particular respondent's performance on any given test can be interpreted in relation to age- and sex-matched peers (norms). The majority of the CANTAB tests are non-verbal—predominantly aimed at assessing

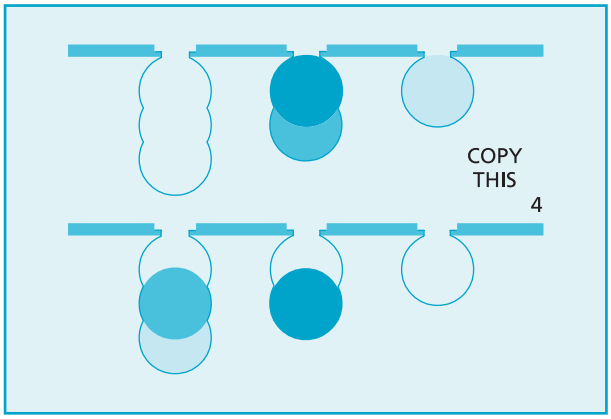


FIG. 2.8 Stockings of Cambridge test from the CANTAB battery. This is a test of executive function from the widely used CANTAB battery of neuropsychological tests. This particular image shows a four-move problem; respondents must try to copy the template pattern in four moves. Image kindly provided by Cambridge Cognition (© 2007 Cambridge Cognition Limited. All rights reserved. Reproduced in 2-colour from coloured original with permission).

executive and memory functions. This fully computerised battery has quickly become particularly popular with researchers and, at time of writing, has formed at least part of the neuropsychological assessment of participants in over 400 published studies. While the CANTAB battery is widely used, other computerised test batteries have also been developed in recent years and different neuropsychological research centres advocate different batteries.

Poor across-the-board performance on test batteries may indicate generalised damage, while poor performance on a particular test may signal possible localised damage or dysfunction. (In general, non-specific deficits across tests are relatively less interesting than more specific problems.) A patient with advanced dementia may perform poorly on all tests, commensurate with the widespread brain damage seen in severely demented individuals. But the neuropsychologist needs to be aware that apparent generalised deficits might alternatively represent a fundamental problem with concentration or motivation. If a person simply can't or won't make the effort to perform tests, they will typically do badly on all measures; this is sometimes seen in psychiatric patients. There are various strategies neuropsychologists can use to get round this problem, for example offering incentives or performing testing over a number of very short sessions. However, in some cases, it may remain a significant concern.

Where a subject has very selective deficits, neuropsychological test batteries can be extremely informative and allow inferences to be drawn about the location of brain damage. For example, inability to recognise objects by touch (**astereognosis**) may be a sign of damage to a fairly specific region in the **parietal lobe** (see Chapter 4). A poor verbal test score (compared with a normal non-verbal test score) may indicate generalised left hemisphere damage (see Chapter 3). In a patient with very early Alzheimer's disease, selective deficits on certain learning and memory tasks are seen, which has contributed to understanding how the pathology of the disease develops.

ASSESSING GENERAL COGNITIVE FUNCTIONING

The WAIS-R, referred to earlier, has been particularly useful for studying selective deficits because the 11 component subtests address a wide range of psychological functions. Moreover, it is possible to derive separate verbal and non-verbal estimates of IQ by amalgamating scores on the six verbal and five non-verbal subtests. Norms for each of these were derived from a sample of almost 2000 (US) respondents. The WAIS III was launched in 1997 as an updated and extended battery. Now comprising 14 subtests (the original 11 plus 3 new ones), with updated norms and the removal of items deemed to be culturally biased, subtest scores can be used to calculate verbal, performance, and general IQ as before. But additionally, four so-called "index" scores (of verbal comprehension,

KEY TERMS
Astereognosis: An agnosic condition in which objects cannot be recognised by touch alone.
Parietal lobe: Region of cortex behind the frontal lobes and above the occipital lobes. It plays key roles in spatial function and attention.

perceptual organisation, working memory, and processing speed) can be derived, which are said to better reflect the underlying factor structure of cognitive function than the older binary distinction.

On the minus side, it should be remembered that all three of the Wechsler intelligence scales were devised primarily to assess cognitive function in non-pathological groups, although they have in fact been extensively used with both psychiatric and neurological patients. None has proper parallel versions, and this makes retesting of individuals (who may be of interest to neuropsychologists wishing to plot change in function over time) complicated by carry-over—that is, residual learning from the first exposure to the tests. Perhaps with this problem in mind, the WASI (Wechsler Abbreviated Scale of Intelligence (Wechsler, 1999) was developed *with* parallel versions to facilitate retesting, and has quickly become an important tool for neuropsychologists. It comprises alternate versions of the most-informative four tests from the WAIS III: block design, matrix reasoning, vocabulary, and similarities. In fact a reliable assessment of general IQ can, the author claims, be derived in less than 15 minutes from just the vocabulary and matrix reasoning subtests.

An even briefer measure of IQ is the National Adult Reading Test (NART; Nelson, 1982). This allows the researcher to obtain an estimate of an individual's IQ prior to damage or disease onset. This may be useful if a neuropsychologist is making an initial assessment of a person who has been brain damaged/ill for some time. The NART rather cunningly comprises 50 words that sound different from their spelling (such as yacht, ache, and thought). The respondent reads through the list until they begin to make pronunciation errors. Such words were almost certainly learned before the onset of illness or brain damage, and because this test has been referenced against the WAIS, the cut-off point can be used to estimate IQ prior to illness, disease, or accident.

COMBINING IN-VIVO IMAGING TECHNIQUES WITH NEUROPSYCHOLOGICAL CHALLENGES

The use of neuropsychological tests in combination with in-vivo techniques promises to be one of the most informative research approaches. If a test is known to draw on the capacity of a particular brain region, it could be given to a person while he or she is being scanned. This combined technique was used by Smith and Jonides (1994) to examine the role(s) of the frontal lobes in **working memory**. They selected various neuropsychological tests of verbal and non-verbal working memory, and recorded PET scans of normal people as they completed them. The results showed a clear division of labour: non-verbal working memory led to increased right frontal activation, whereas verbal working memory caused greater activation in the left frontal (and parietal) regions (see Chapter 7 for a further discussion of Smith and Jonides' findings). Many other examples of combining neuropsychological challenge with functional imaging are discussed in subsequent chapters. For instance, see Chapter 11 for a discussion of how neuroimaging has informed our understanding of executive function using classic tests such as the Tower of London.

A slightly different way of combining neuropsychology and imaging is to perform detailed neuropsychological testing outside the scanner and then scan the people during performance of specific tasks. One area where this approach is

Key Term
Working memory: A form of short-term memory, first characterised by Alan Baddeley, which allows a person to hold "on-line" (and manipulate) a certain amount of information for a few seconds after it has been presented. For example, keeping a phone number in mind until you have dialled it.

proving particularly useful is in studying the early stages of dementia. Mild cognitive impairment (MCI) is relatively common in elderly populations, but in some cases MCI can progress to Alzheimer's disease. Early diagnosis of Alzheimer's disease is very important for optimal treatment and care, however it is not always easy. Recent research that combines focal neuropsychological assessment and functional imaging has suggested that this combined approach facilitates early detection. Cabranes et al. (2004) showed that lower test scores and lower left frontal blood flow predicted progression from MCI to Alzheimer's disease with high sensitivity and specificity. Similarly, Elgh et al. (2003) found that people at high risk for developing Alzheimer's disease showed poorer scores on episodic memory tasks and reduced prefrontal activation during cognitive challenge fMRI. Thus the combined neuropsychology and neuroimaging approach has clinical implications as well as furthering our theoretical understanding of how the brain works.

INTERIM COMMENT

Neuropsychological testing has gained considerable respect in recent years. However, it would be wrong to think that a battery of neuropsychological tests alone could somehow provide the researcher or clinician with a complete map of brain functioning. At best they give an indication of underlying problems. Two further concerns also merit consideration. First, an apparently normal performance on neuropsychological tests can be deceptive. We know that, as individuals recover from brain damage, they often develop alternative strategies or techniques to overcome remaining deficits—see, for example, the case study of the brain-damaged architecture student (Clarke, Assal, & DeTribolet, 1993) which we present in Chapter 4. Second, although neuropsychological and in-vivo assessments usually agree about what regions of brain are dysfunctional or damaged, they do not always do so and the reasons for this are usually unclear.

A further concern about neuropsychological testing that has received attention recently is the ecological validity of tests. A puzzling conundrum for neuropsychologists is that patients' performance on neuropsychological tests can, in fact, be inconsistent with their performance in everyday life (Wilson, 1993). Ideally, test performance should predict this, but ecological validity actually varies from test to test. For example, Chaytor, Schmitter-Edgecombe, and Burr (2006) have studied the ecological validity of executive function measures and found some standard tests "wanting" in this regard. Some researchers are now starting to develop more ecologically valid tests that aim to mimic real-life scenarios (see Burgess et al., 2006). Obviously, the test situation is likely to be different from everyday life, but the continuing challenge for researchers is to develop tests that capture everyday performance as well as possible. We return to this issue in Chapter 11.

DISSOCIATIONS AND DOUBLE DISSOCIATIONS

Neuropsychologists typically try to design studies that provide evidence of the differential performance of brain-damaged and control participants because such

studies can inform structure–function relationships. Consider the following example: The right frontal lobe is thought to be important for memorising designs. To test this hypothesis, a researcher assesses memory for designs (MemD) and memory for words (MemW) in a group of people with known right frontal damage and a second group of non-brain-damaged controls.

Hypothetical results from this study are shown in Table 2.1a. At first glance they seem to support the hypothesis, because the right frontal participants appear to be selectively impaired on the MemD condition. Many neuropsychological investigations employ this sort of design, and might use the evidence of a (*single*) *dissociation* between groups in the MemD but not the MemW conditions as support for the hypothesis under investigation. However, there is a design problem with single dissociation studies stemming from the assumption that the two conditions are equally "sensitive" to differences between the two groups of participants (which may or may not be the case). For example, it could be that right frontal participants have poor attention, which happens to affect the MemD task more than the MemW task.

A much "stronger" design is one with the potential to show a *double dissociation*. For example, if we also thought that left frontal damage impaired MemW but not MemD, we could recruit two groups of patients—one with left and the other with right frontal damage—plus a control group—and test all participants on both measures. Hypothetical results from this design are shown in Table 2.1b. They indicate that one group of patients is good at one test but not the other, and the reverse pattern is true for the second group of patients. In other words, we have evidence of a double dissociation (similar to the one found by Smith and Jonides and described earlier), which suggests to neuropsychologists that the two tasks involve non-overlapping component operations that may be anatomically separable too.

TABLE 2.1 A SINGLE AND A DOUBLE DISSOCIATION EXPERIMENT (% CORRECT)

(a) Single dissociation experiment

Group	MemD	MemW
Right frontal	70%	90%
Control	95%	95%

(b) A double dissociation experiment

Group	MemD	MemW
Right frontal	70%	90%
Left frontal	93%	60%
Control	95%	95%

In the single dissociation experiment, frontal patients appear worse on the MemD task than controls, and about the same on the MemW task. However, this result might be due to poor attention (or some other extraneous variable) which happens to affect the patients on this test. In the double dissociation experiment, the "opposite" performance of right and left frontal patients suggests that damage to the different brain regions has a specific and selective effect on the two memory tests.

CHAPTER SUMMARY

Researchers interested in understanding brain function and its relations to psychological function can now draw on a wide range of investigative techniques. In

this chapter we have introduced lesion and ablation, electrical/magnetic stimulation and recording, and the structural and functional in-vivo imaging procedures. Consideration is also given to the widespread use of neuropsychological testing. Researchers have moved rapidly from an era in which analysis of brain structure could usually only be assessed post-mortem to an era in which the various in-vivo imaging techniques are quickly becoming almost as commonplace as X-radiography. Their use, in combination with neuropsychological procedures, is a particularly promising research area. Imaging techniques are still evolving and the next few years hold further promise of more exciting developments in this approach to understanding brain function.

CHAPTER 3

CONTENTS

3

Lateralisation

INTRODUCTION

We should not be surprised that Gall regarded the cortical hemispheres as "mirror image duplicates" of one another, with the same mental faculties located **homotopically** (at the same relative location) in each—after all, the brain, like most other components of the nervous system, is superficially symmetrical along the **midline**. But closer inspection reveals many differences in structure, and behavioural studies suggest intriguing differences in function too.

The reason for these so-called asymmetries is unclear although, as the blueprint for the basic structure (and functioning) of our nervous system is under genetic control, asymmetries too are assumed to depend on the action of genes. Some researchers have suggested that they are particularly linked to the "arrival" of *Homo sapiens* as a species, an event that is thought to have occurred between 100,000 and 150,000 years ago, coincidental with the development of a sophisticated language system (Mitchell & Crow, 2005). Others have argued that the asymmetries pre-dated the appearance of language and are related to tool use, gesture, and hand preference. Corballis (1991, 2003), among others, has suggested that language skills, being analytical and sequential in nature, emerged as left hemisphere functions because this hemisphere had already been operating preferentially in this way for hundreds of thousands of years to mediate gestural (i.e., non-verbal) language and dominant hand use more generally.

Humans are not the only animals to show hemispheric specialisation (see Box 3.1) although it is undoubtedly more marked and consistent in humans than any other species. This observation alone points to an ancient evolutionary origin of laterality as being more likely. But whatever the cause or causes of asymmetry, hemispheric differences in psychological functions encompass many areas in addition to language. In this chapter we consider the various ways that scientists have examined lateralisation/hemispheric specialisation/asymmetry—the terms are sometimes used interchangeably although asymmetry in particular carries connotations about structure (see next section) as well as function—and the conclusions that they have drawn from their research.

KEY TERMS

Homotopical: Occurring at the same relative location.

Midline: Anatomically, in mammals, the imaginary line separating the left from the right side.

Box 3.1 Asymmetries in non-humans

Song birds, chickens, rodents, cats, and primates all show evidence of functional asymmetry. Nottebohm (1980), for example, has illustrated convincingly that song production in canaries depends on left brain structures, and can be disrupted by lesions here, but not by equivalent lesions in the right hemisphere. Rose (1992) showed that imprinting (the formation of early attachments and thus a form of memory) could be impaired in newborn chicks following left brain (but not right brain) lesions. Chickens appear to have right foot preference for scratching the ground when searching for food, and cats too show preferential paw use when reaching for food (Warren, Abplanalp, & Warren, 1967).

Several primate species show structural as well as functional asymmetries similar to those seen in humans: for example, old-world monkeys show both asymmetry of the Sylvian fissure and cortical torque (forward expansion; see above) of the right hemisphere, although how these relate to function remains unclear. At an individual level, non-human primates may show a preference for using one particular hand, but collectively they do not display predominant right-handedness. However, rhesus monkeys, like humans, are better able to make tactile discriminations with their left than their right hand (Hatta & Koike, 1991), whereas fine motor skills are better performed by the right than the left hand (Morris, Hopkins, & Bolser-Gilmore, 1993).

In sum, while both functional and structural asymmetries are apparent in other species, these are somewhat inconsistent, and certainly less pronounced than for humans. Some authors conclude that hemispheric specialisation is an adaptive general design principle which has simply evolved further in humans than other animals.

STRUCTURAL DIFFERENCES

Despite their superficial similarity, the two hemispheres of the human brain consistently differ in a number of characteristic ways that are summarised in Table 3.1.

TABLE 3.1 ANATOMICAL HEMISPHERIC ASYMMETRIES

- Viewed from the top of the head, the right frontal lobe extends several millimetres further forward, and the left occipital lobe further back (known as cortical torque).
- The Sylvian fissure, which is the dividing line between the frontal and temporal lobes, is less sloped on the left side than on the right.
- A region of the temporal lobe known as the planum temporale, which is adjacent to the Sylvian fissure and encompasses Wernicke's area, is significantly larger on the left than on the right.
- Cells in the region of the left frontal lobe that we now call Broca's area have many more synapses (contacts with other neurons) than the equivalent region on the right side.
- The angular gyrus (located in the posterior parietal lobe), which may be important in reading and semantic aspects of language, is larger on the left than on the right side.
- The parietal area on the right side (just behind the location of the angular gyrus on the left) is larger and has more synaptic contacts. This region is linked with visual perception and spatial processing.

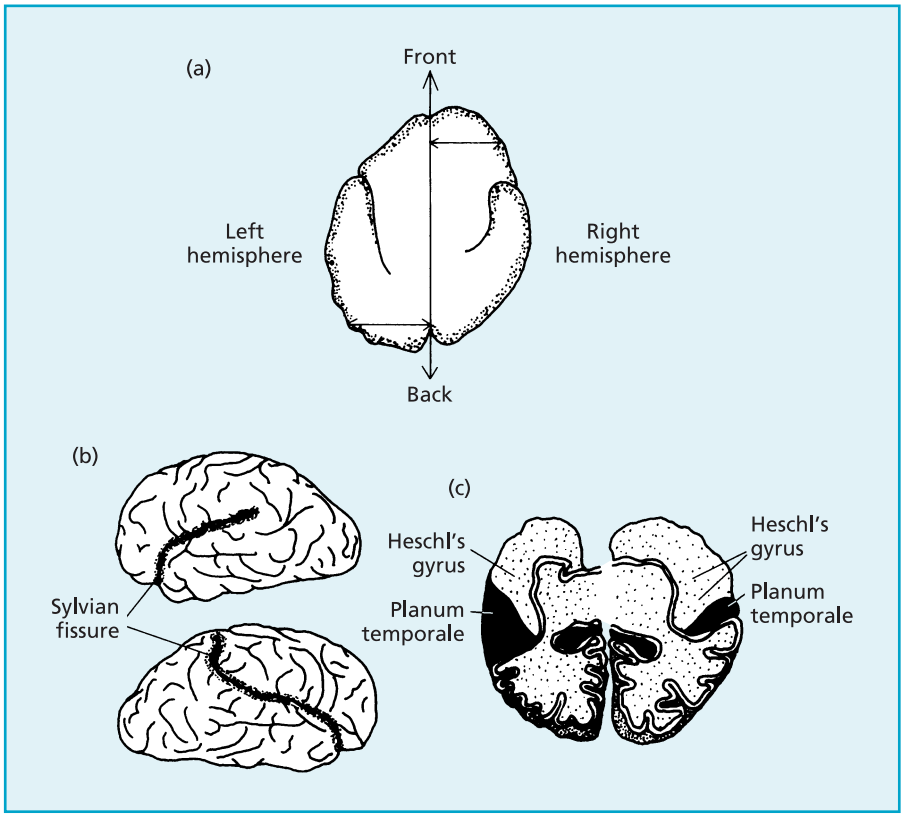


FIG. 3.1 Externally visible structural asymmetries of the human brain. (a) The right frontal region typically projects further forward and is wider than the left frontal region. The reverse pattern is seen in the occipital lobes. (Adapted from Hellige, 1990.) (b) The Sylvian fissure extends further back horizontally on the left side than the right (where it takes a more upward course). (Adapted from Kolb & Whishaw, 1996.) (c) The planum temporale is larger on the left side than on the right.

(Externally visible asymmetries are also shown in Figure 3.1.) Some of these are, so to speak, visible to the naked eye (assuming the brain is exposed), whereas others are only detectable using a microscope. Even at this relatively coarse level of analysis there are tantalising glimpses of the possible links between structure and function, with the left hemisphere's language responsibilities (function) corresponding to more complex cellular connectivity (structure) here. For example, Hutsler, Galuske, and Ralf (2003) have recently confirmed that the columnar structure (and the neuronal connections within columns) in the auditory cortex of the left hemisphere are distinct from the homotopic regions on the right. However, despite the appeal of these observations, Hutsler et al. themselves point out that actually relating structure to function, especially at this level of complexity, is notoriously problematic (see Chapter 2) and must remain, for the moment, speculative.

UNILATERAL NEUROLOGICAL DAMAGE

We cannot manipulate brain damage experimentally in humans but we can assess function in individuals whose brains have been damaged or have become diseased. However, it is important to bear in mind that the degree and extent of damage is variable and idiosyncratic, and it is difficult to generalise on the basis of case studies alone. Nevertheless, damage to the left hemisphere seems to result in a greater impairment to language-related skills than to spatial (or non-linguistic) skills, whereas the reverse is true for right hemisphere damage. A stroke affecting the left hemisphere frequently leads to aphasia (think of Broca's "Tan" for instance), whereas right hemisphere damage can lead to deficits in spatial skills such as mental rotation, map reading, orientation, and, in the most severe cases, spatial neglect, but rarely aphasia (although more subtle language deficits such as impaired prosody may arise; see Chapter 6).

More control is possible when tissue must be surgically removed for medical reasons. An early report by Taylor (1969) described two patients who underwent temporal lobectomies (ablation of temporal lobe) to remove brain tumours. Each patient completed a battery of neuropsychological and IQ tests both before and after surgery. For the patient whose left temporal lobe was removed, a significant decline in performance on tasks with a verbal component was noted, but there was little change in non-verbal function. For the patient who underwent a right temporal **lobectomy**, the exact reverse pattern of outcome was observed. Verbal skills were preserved, but spatial performance dipped markedly.

You may recall from Chapter 2 that this pattern of distinct/opposite impairment is referred to by neuropsychologists as a double dissociation, and it is also observed in patients with left and right frontal and parietal lesions. Once again (in general terms) left-sided damage tends to impact more on verbally based skills, and right-sided damage on non-verbally based skills. For example, surgical removal of tissue from the left frontal lobe may lead to a decline in verbal fluency ("*Think of as many words beginning with the letter S as possible*"), but not to design fluency ("*Draw as many patterns made of four lines as possible*"), and vice versa for right frontal ablation. Removal of tissue on the right side has additionally been associated with impairments in a wide range of psychological skills, including spatial orientation, discrimination of auditory tones, and face recognition (see also Chapter 8).

Very occasionally, and usually only in young children, it is deemed necessary to surgically ablate an entire hemisphere, or most of it (van Empelen et al., 2004). This is usually because the hemisphere has become irreparably damaged, perhaps following vascular pathology (an extensive stroke for example), or following encephalitis, or even in order to remove a widely invasive tumour. Such unfortunate cases nevertheless present fascinating opportunities for researchers to examine what functions are lost post-surgery, and more intriguingly, which ones recover. In very general terms, such individuals often show a marked recovery of function after surgery, but nevertheless remain impaired in comparison with age-matched controls. Following left hemisphere removal, a number of children have gone on to develop near-normal language function, which *must* be mediated by their right hemisphere.

KEY TERM
Lobectomy: Surgical removal of all or part of a cortical lobe (as in temporal lobectomy for removal of the temporal lobe).

The willingness of the opposite hemisphere to take over the work of the ablated one is often attributed to the remarkable degree of neuronal plasticity that is apparent in the "developing" mammalian nervous system (Isaacs et al., 1996).

Curiously however, if the lesion is localised, say to Broca's area in the left hemisphere, the recovery of language function post-surgery appears to be mediated by undamaged tissue adjacent to the lesioned site but still in the left hemisphere, suggesting a "reluctance" to relocate to the opposite hemisphere if it can be avoided—still evidence of remarkable plasticity, but not quite to the extent seen in complete hemispherectomy (Liégeois et al., 2004).

There have been no comparable studies of the effects of complete right hemispherectomy on spatial functioning, although a recent report by Backlund et al. (2005) of four hemispherectomised children (three right hemisphere) indicated "recovered" (normal) touch sensitivity for a static stimulus on the side of the body opposite to the ablation, but a failure to "recover" sensitivity to the direction of a moving tactile stimulus on the contralateral side.

These data can arguably be interpreted in two ways depending on one's viewpoint: either they can be taken as evidence of the fantastic inherent plasticity of the developing brain and the "irrelevance" of pre-determined hemispheric specialisation under these circumstances; or, more prudently perhaps, they can be viewed as evidence of the "desire" of the developing brain to adhere to the preferred blueprint if possible, and an inability to completely overcome wholesale early damage. Whatever your view, it must be said that the degree of neuronal plasticity apparent in young children is rarely seen in individuals who incur similar damage as adults.

INTERIM COMMENT

Notwithstanding the previous discussion, neuropsychologists are rightly cautious about oversimplifying the structure–function relationship (left hemisphere (language); right hemisphere (spatial functions)) to the extent that some writers, working in applied settings such as education and business, have (see Kaminski da Rosa, 1984, for an illustration of this). This is because a slightly more detailed analysis of the lesion/surgical data indicates that although left-sided damage *is* more likely to be associated with some loss of language function, other non-language functions may also be affected. For example, certain forms of apraxia (disorders of purposeful movement, introduced in Chapter 5) are linked to left-sided damage. Moreover, failure to detect emotional intonation in verbal messages, or to impart language with emotional tone (known as aprosody), both clearly para-linguistic skills, are common features of right-sided damage (see above and Chapter 6). The simplistic analysis is also complicated by both sex and handedness, and we return to these issues later in this chapter. A slightly more detailed synopsis of asymmetries is offered in Figure 3.2.

THE SPLIT-BRAIN SYNDROME

Fifty years ago, anti-convulsants (drugs for epilepsy) were not as effective as those available today, and for some people even the highest safe levels of medication could not prevent regular seizures. As these could occur 10 or even 15 times each day, normal life could be profoundly compromised by epilepsy. Scientists were also beginning to realise that the seizures themselves could cause progressive

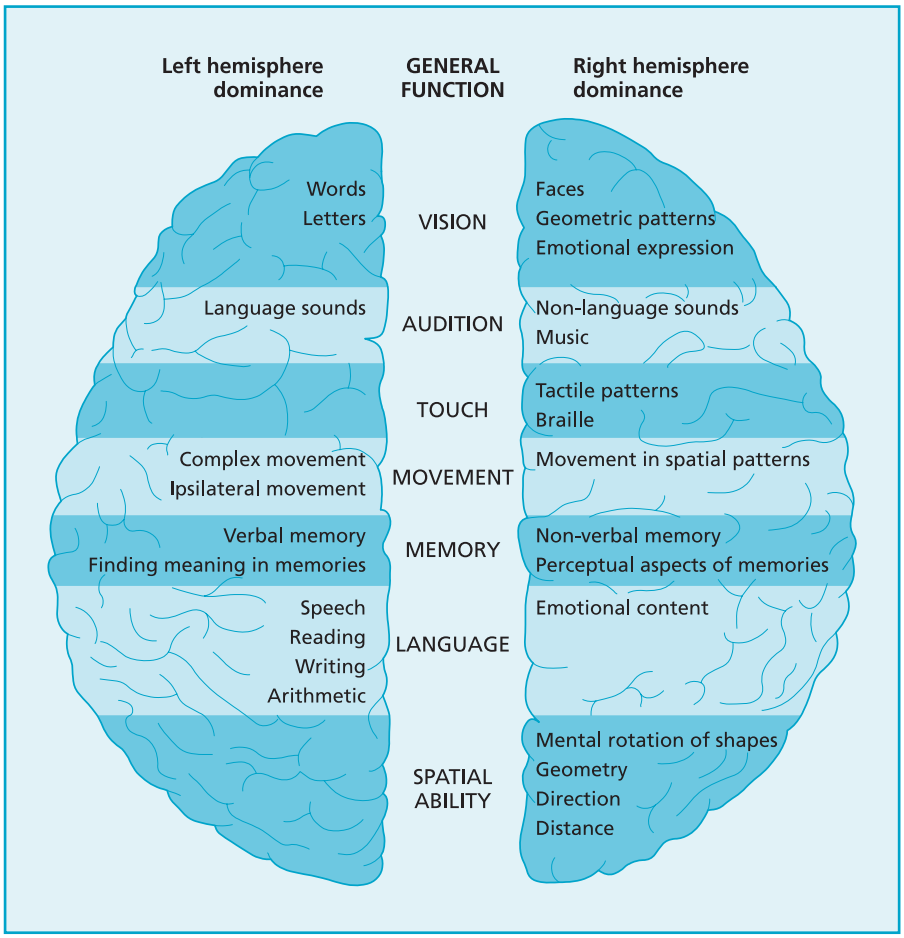


FIG. 3.2 Functional asymmetries in the adult brain. A simplified summary of the "specialisms" of the two cerebral hemispheres. Source: (Adapted from) Pinel (2006). Published by Allyn & Bacon, Boston, MA. Copyright © 2006 by Pearson Education. Reprinted by permission of the publisher.

cumulative damage to the brain, so there were two imperatives for the development of new epilepsy treatments.

Seizures usually originate in a particular location known as the **ictal focus**, but may then spread (rather like ink on a blotter) to affect adjacent cortical regions. Sometimes, they pass via the corpus callosum (see Box. 3.2) to the opposite hemisphere to bring about a bilateral seizure. Having exhausted other treatments, two Californian surgeons, Bogen and Vogel, decided to try to contain seizure activity to just one hemisphere by lesioning the corpus callosa of their patients. Although this sounds drastic, remember that at the time (in the 1950s) scientists did not fully understand what the corpus callosum did, and they knew that animals given this surgical procedure seemed to suffer no lasting ill effects (see Figure 3.3).

KEY TERM
Ictal focus: The point of origin of epileptic activity, often a discrete region of damaged cortical tissue.

Over a period of several years about 100 people underwent "sectioning" of the corpus callosum. In some cases the lesion was partial; just the anterior (front) or posterior (rear) region would be cut. For some patients, however, complete sectioning was performed, rendering the two hemispheres anatomically almost

completely isolated from one another. Many individuals were assessed on batteries of psychological tests both before and after their operations, and at first glance the procedure appeared remarkably effective. Post-surgery, some patients were initially hemiplegic, mute, and confused, but after a period of recovery these features abated, and both the intensity and frequency of epileptic activity were almost always reduced, with some patients no longer experiencing major seizures at all. Moreover, patients' IQ scores and scores on many other tests often improved and, perhaps because of reduced seizure activity, most people claimed to feel better too. These preliminary data presented a paradox: How could a surgical procedure that involved lesioning the major inter-hemispheric pathway not have a significant effect on psychological functioning? To address this question, a group of researchers led by Sperry, Myers, and Gazzaniga developed a series of tests that were designed to shed more light on the true nature of the split-brain syndrome (see Gazzaniga & Sperry, 1967, for an early account of this work).

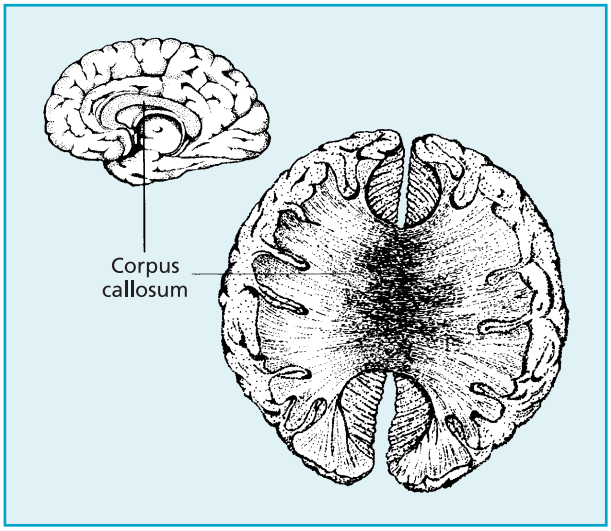


FIG. 3.3 The corpus callosum is (by far) the largest pathway linking the two sides of the brain. In adult humans it comprises several hundred million myelinated axons carrying information from the left to the right hemisphere and vice versa.

Box 3.2 The corpus callosum

This is the largest of the four nerve tracts bridging the hemispheres (the others being the anterior, thalamic, and hippocampal commissures). It develops slowly during childhood, reaching full maturity only in late adolescence, and much of this maturation process actually involves the progressive deposition of myelin, so that by early adulthood the human corpus callosum comprises between 200 and 800 million myelinated axons running transversely from one hemisphere to the other. At this stage, the structure is about 10 cm in length and more than 1 cm deep in places. The anterior section bends under and back on itself—the bend is known as the genu (knee). The mid section comprises the anterior and posterior mid-bodies and isthmus, and the most posterior "bulbous" section is known as the splenium.

The majority of callosal fibres appear to "course" from particular regions in one hemisphere to homologous (homotopic) regions in the other, although connections to non-homologous regions are also seen. Moreover, the left and right frontal lobes communicate via the anterior body, whereas the occipital lobes exchange information via the splenium. Similar precise mapping of temporal and parietal exchanges is apparent in the mid-body regions. This detail is important because it is now clear that when surgeons lesioned this structure to restrict the spread of seizure activity, their procedures were sometimes imprecise, and thus incomplete. (This has been established by MRI scanning of split-brain patients many years post-surgery.) Additionally, in other cases, surgeons deliberately

sought to spare anterior or posterior regions, reasoning, in view of a patient's ictal focus, that complete sectioning would serve no additional purpose.

Individual differences in the size of the corpus callosum are of interest: for example, it has been reported that men have a larger anterior corpus callosum, whereas in women, both the isthmus and splenium are larger. However, these findings have not always been replicated and thus remain controversial (see Witelson, 1985; see also Holloway & Lacoste, 1986). Similarly, Witelson reported that individuals with mixed handedness had larger corpus callosa than right-handed individuals, but this too has been questioned by other researchers. A recent study by Chung, Dalton, and Davidson (2004) has reported that the corpus callosa of a group of autistic individuals were smaller than normal. Intriguing though this is, the significance of the finding remains, for the moment, a matter of debate.

EXPERIMENTAL STUDIES

To fully understand the experimental procedures that Sperry, Gazzaniga, and others developed it is important to realise that in higher mammals, including humans, most visual information from the right visual field (that is, everything to your right if you look straight ahead) travels from both eyes, via the visual pathways, to the *left* occipital lobe. Similarly, most information from the left visual field travels to the *right* hemisphere. Auditory and **somatosensory** input is also predominantly, though not completely, "crossed", so the left ear sends most of its sensory input to the right auditory cortex, and the left hand is controlled by, and sends sensory information back to, the right hemisphere, and vice versa for the right hand (see Figure 3.4). Sperry and colleagues were interested to know what would happen if information was presented to the split-brain patient *one hemisphere at a time*. Using a **tachistoscope**, they presented visual stimuli very briefly to either the left or right of a central fixation point on a screen in front of the patient. (A presentation duration of under 200 ms allowed for accurate recognition while ensuring that the participant did not have time to move their eyes towards the stimulus, which would have meant that the image went to both hemispheres.) After each presentation the participant had to say what (if anything) they had seen. Sometimes, they were also given the opportunity to reach behind a screen to feel items (with either their left or right hand) that might be related to the stimuli presented via the tachistoscope. On other occasions, they were invited to draw (again with either their left or right hand) images of the presented material.

KEY TERMS
Somatosensory: Sensation relating to the body's superficial and deep parts, as contrasted to specialised senses such as sight.
Tachistoscope: An item of psychological equipment with which visual material can be presented to respondents for very brief exposure times (these days often replaced by digital computers).

With these procedures the true nature of the split-brain syndrome was revealed. Consider, for example, the results of an early study reported by Sperry (1968). If a picture of a car was flashed to the right of the fixation point, the patient reported seeing a car. This would be expected because the image travelled to the left (talking) hemisphere so the patient could say what they saw. If the same picture was flashed to the left of the fixation point, the patient usually reported seeing nothing: now the image went to the "non-speaking" right hemisphere. However, if the patient was allowed to reach behind a screen with their left hand, they could usually select a model car from among other out-of-sight objects. (Remember that the left hand connects to the right hemisphere.) Similarly, if the patient was allowed to "doodle" with their left hand, a drawing of

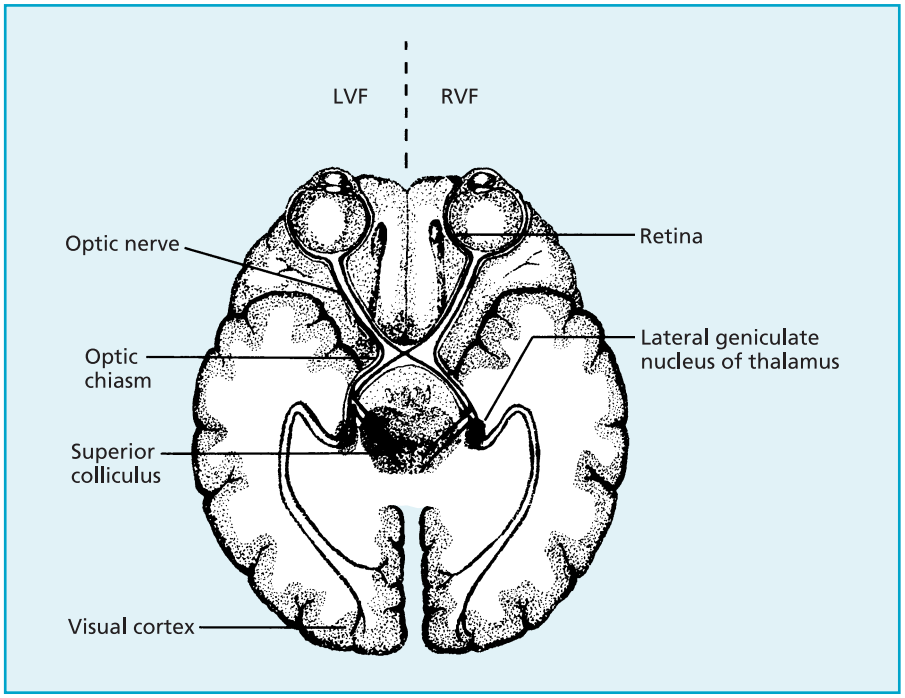


FIG. 3.4 Visual pathways from eye to brain: the route from retina to occipital cortex via the lateral geniculate nuclei of the thalamus. Note that information from the right visual field (everything to the right as you look straight ahead) entering *both* eyes will be channelled to the left occipital lobe. Visual input from the left visual field will be fed to the right occipital lobe.

a car often appeared! Even more amazingly, when asked why they had drawn a car, patients usually expressed surprise and were unable to give the right answer (see Figure 3.5a). We return briefly to consider the significance of this last observation for recent ideas about consciousness in Chapter 9.

THE SPLIT-BRAIN SYNDROME AND LANGUAGE

The results of these early split-brain studies supported the view that for almost all right-handers, and the majority of left-handers, control of speech was localised to the left hemisphere. Did this mean that the right hemisphere was devoid of all language functions? How, for example, would spilt-brain patients deal with letters or words presented to the right hemisphere? The results of such studies are not quite as clear-cut as we might expect. Gazzaniga and Hillyard (1971) reported that when words were briefly presented to the left visual field (right hemisphere) they could not be read aloud, but split-brain patients could often select related items with their left hand from behind a screen. This and other similar observations soon led to the counter-claim that the right hemisphere also possessed language skills but was simply mute (see Figure 3.5b).

This view was partly supported by Zaidel (1978) who developed a lens system (as an alternative to the tachistoscope) as a means of selectively presenting visual input to just one hemisphere. This apparatus comprised a contact lens with one visual field occluded (blacked out). A stalk attached to the lens held a display area at the other end, thus ensuring that any eye movements would cause

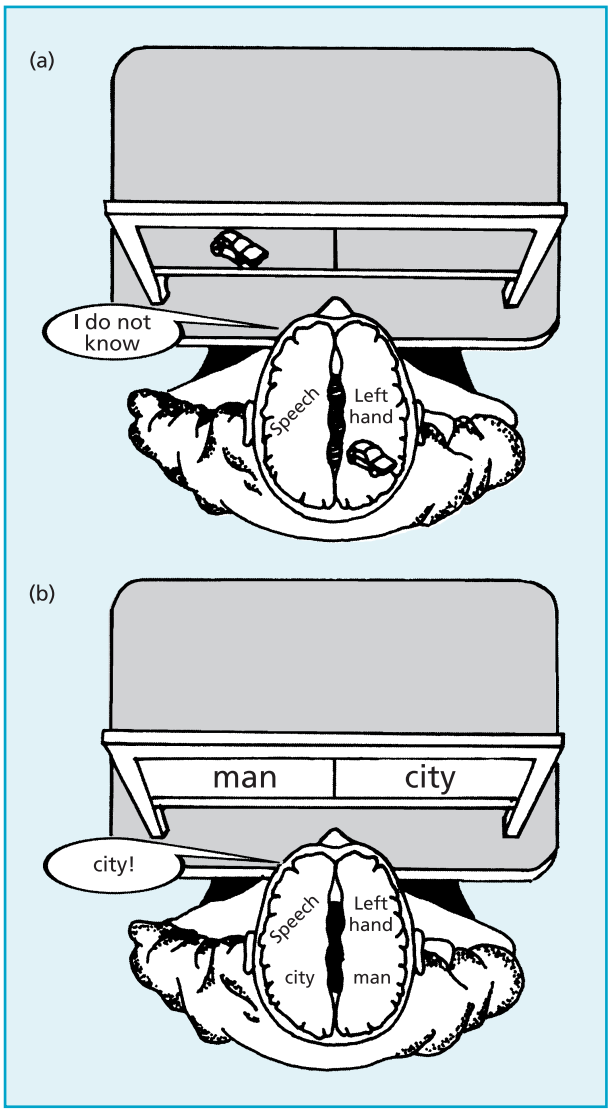


FIG. 3.5 A typical split-brain experiment with objects and words. In (a) the respondent is unable to "say" what image has been briefly projected to the non-speaking right hemisphere. In (b) the respondent reports only the word appearing in the right visual field which projects to the "speaking" left hemisphere. (Adapted from Temple, 1993.)

corresponding display movements. This, along with the occluded visual field, ensured that whatever was shown on the display would only register in one hemisphere. Because Zaidel's system was not restricted to brief presentations he could present longer words. Alternatively, he could present linguistic material aurally (and thus bilaterally), but require participants to make response selections unilaterally from a choice of alternatives presented to just one or other visual field via his lens. Using this method, and working in depth with two spilt-brain patients, Zaidel reported that the right hemisphere had an extensive **lexicon** (vocabulary) equivalent to that of a normal 10-year-old. A schematic diagram of Zaidel's lens system is shown in Figure 3.6.

Clearly then, the right hemisphere was not devoid of all language functions. However, notwithstanding the discovery of a right hemisphere lexicon in a small number of split-brain patients, Zaidel found little evidence of right hemisphere **syntax**. This was apparent, for example, from his participants' difficulties in completing the Token Test (DeRenzi & Vignolo, 1962) in which respondents have to follow a set of simple verbal instructions, such as "*Place the yellow circle above the blue square*". Zaidel's participants performed at about the same level as patients with severe aphasia. In other words, despite an extensive vocabulary, the right hemisphere's ability to extract meaning from sentences was clearly limited.

The debate about the extent of right hemisphere language function has nevertheless rumbled on. Critics have pointed out that only a small proportion of the split-brain cohort (probably no more than six right-handed cases) have shown any notable right hemisphere linguistic skills, and that even for these individuals there was no evidence of right hemisphere "generative syntax" (the ability to produce grammatically structured word strings assessed by left-handed writing: see Gazzaniga, 2000).

Indeed, the integrity of lexical organisation (the way in which words are assumed to be stored in terms of sound, meaning, physical properties, and so on) in the right hemisphere has now also been questioned in view of the absence of a "priming effect" for letters presented to the left visual field of split-brain patients. This effect is apparent in intact individuals by dint of faster reaction times to upper-case single letters that are preceded by lower-case identical letters, compared with non-identical ones. In one intensely researched patient (JW) priming was apparent only for stimuli presented to the right visual field. This patient also

KEY TERMS
Lexicon: Loosely equates to stored vocabulary: that is, one's long-term memory of native-tongue words (estimated to be about 50,000 for English speakers).
Syntax: The rules governing the structure of sentences.

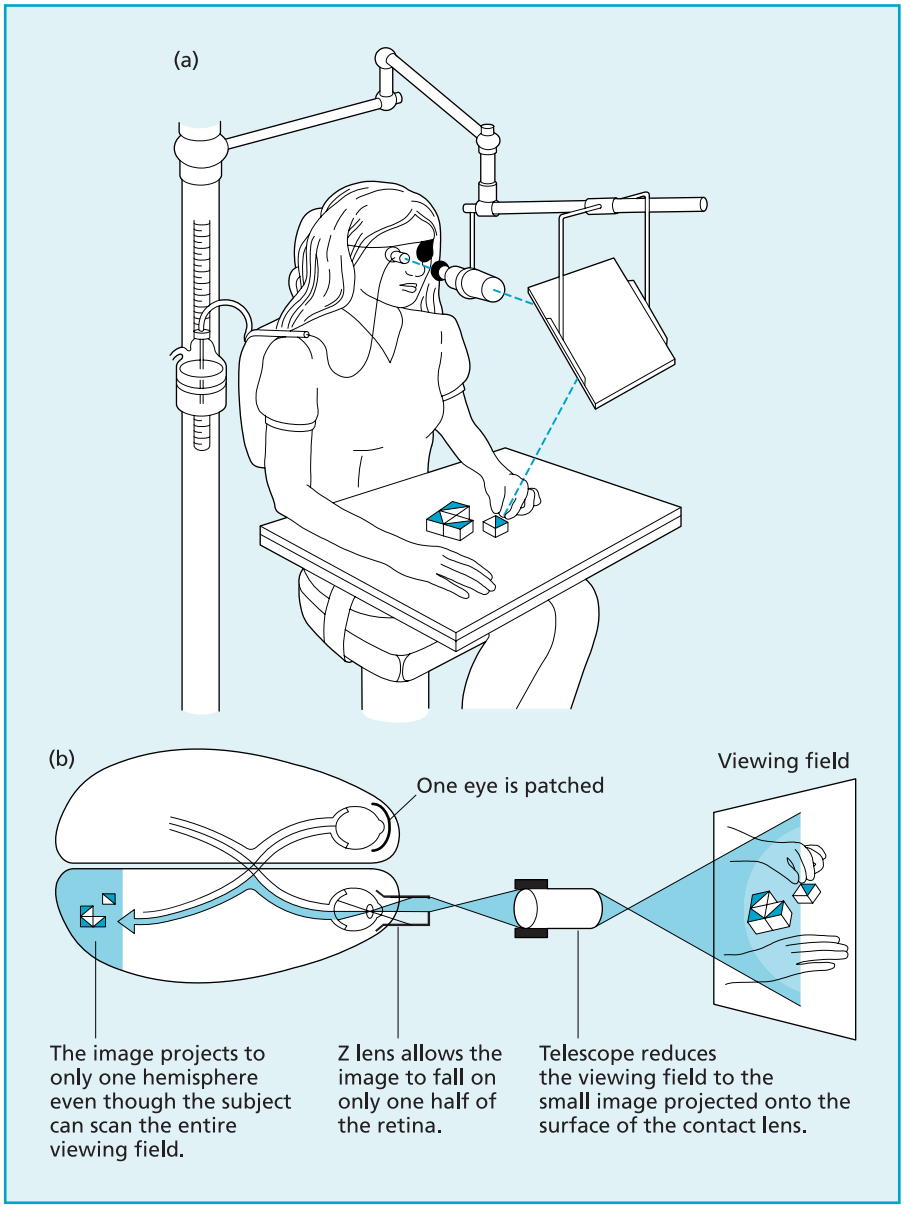


FIG. 3.6 Zaidel's lens system. One eye is patched, and the split-brain patient wears a special contact lens on the other eye to circumvent eye movements (the lens moves with the eye). Visual images are projected to just one half of the lens, enabling Zaidel to present material to just one hemisphere for extended periods of time. Source: Adapted from Zaidel (1978) in Caramazza & Zurif (Eds.) *Language acquisition and language breakdown* (p. 233) © 1978 The Johns Hopkins University Press. Adapted with permission of The Johns Hopkins University Press.

had difficulties in judging which of two words presented to the right hemisphere was sub/superordinate (e.g., animal–rabbit) or in deciding whether two words were antonyms (semantic opposites) of each another. These findings suggest that the right hemisphere is unable to access so-called parallel processing mechanisms, and relies instead on less efficient serial ones.

Nevertheless, on rare occasions, right-handed split-brain patients may develop the ability to speak single words with their right hemisphere! For patient JW, referred to above, speech only developed 13 years after surgery. This is an astonishing finding, although there are parallels in the neurology literature which includes several reports of adults who, having lost their left hemisphere (through accident or surgery), subsequently developed rudimentary right hemisphere language skills. Recovery of function is, of course, much more likely in children, as discussed earlier.

THE SPLIT-BRAIN SYNDROME AND OTHER PSYCHOLOGICAL FUNCTIONS

The split-brain studies support the idea of a key role for the left hemisphere in linguistic skills, but do they tell us anything about the particular roles and responsibilities of the right hemisphere? Franco and Sperry (1977) reported a study in which right-handed split-brain patients were tested using both their right and left hands on a range of visuospatial tasks including route finding and solving jigsaw puzzles. These patients consistently performed better with their non-preferred left hand than with their right hand. This finding is similar to that reported by Sperry, Gazzaniga, and Bogen (1969) in which split-brain patients were tested using a version of the block design test (see Chapter 8 for an example). In this test, geometric visual patterns must be "built" using individual coloured blocks. Right-handed split-brain patients could do this spatial construction test much more effectively with their non-preferred left hand (which is connected to the right hemisphere) than with their dominant hand.

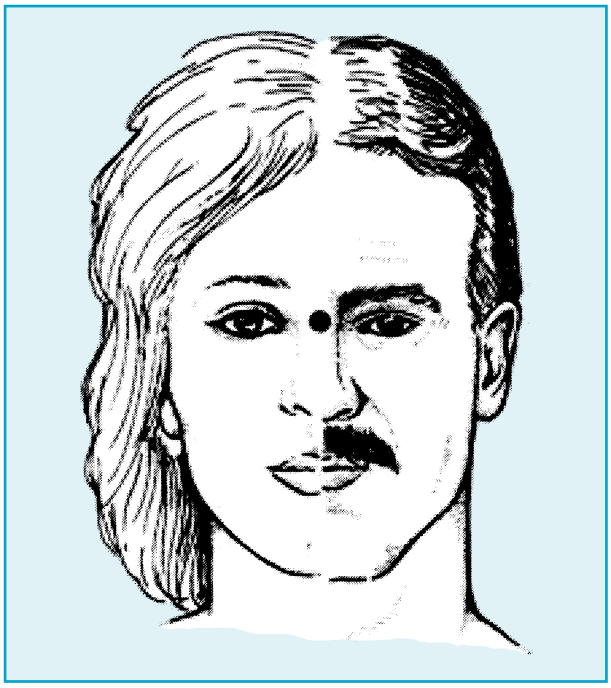


FIG. 3.7 Example of a chimeric image showing fixation point.

Levy, Trevarthen, and Sperry (1972) presented data consistent with the view that face processing may also be dealt with preferentially in the right hemisphere. Split-brain patients were shown images of pairs of half-faces via a tachistoscope. These "chimeric" images might, for example, comprise half the face of a girl on the left side, and half the face of a man on the right (see Figure 3.7). The fixation point was exactly on the joint at the bridge of the nose. When a participant was asked to say what they had seen, they usually reported seeing an intact (i.e., complete) picture of a man. We might have predicted this, because this half-image went to the left/talking hemisphere. However, when asked to select what they had seen from a set of complete pictures, the same split-brain patient invariably chose the picture of the girl, which had gone to their right hemisphere (see Figure 3.8). It is important to note that we have referred to this as evidence of a *preferential* effect, because further work has confirmed that both hemispheres can "recognise" faces (Gazzaniga, 1989). Indeed, the left hemisphere may be better than the right at processing familiar faces, whereas

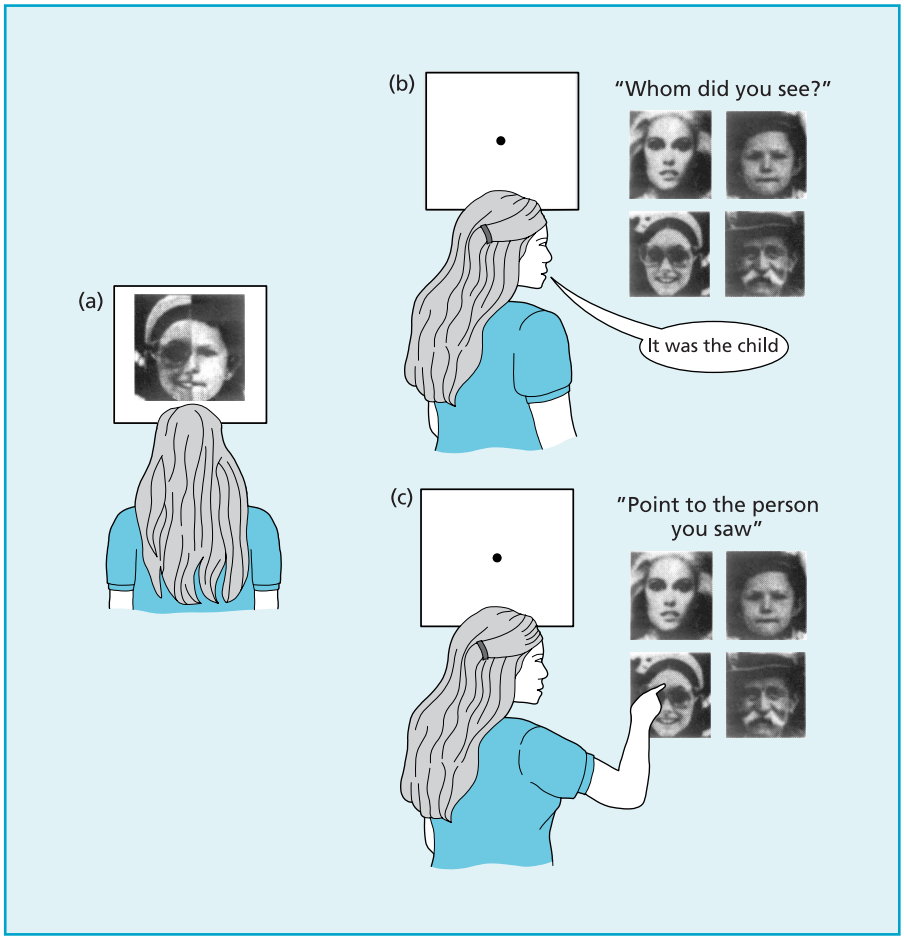


FIG. 3.8 Summary of Levy et al.'s (1972) split-brain study. The split-brain patient views chimeric figures (a). When she is asked to say what she saw (b), she describes the whole image of the half chimeric figure from her right visual field (the child). When asked to "select" what she saw, the right hemisphere tends to dominate (c) and she chooses the whole image of the half chimeric figure from her left visual field that projected to her right hemisphere (the woman wearing glasses). Source: Levy, J., Trevarthen, C. W., & Sperry, R. W. (1972). Perception of bilateral chimeric figures following hemispheric deconnection. *Brain*, *95*, 61–78. Reproduced with permission.

the right hemisphere seems specialised for dealing with unfamiliar or novel faces (Gazzaniga & Smylie, 1983).

In fact, right hemisphere advantages equivalent to the left hemisphere advantage for generative syntax (and other language functions) are hard to come by in split-brain research. However, one illustration is seen in the work of Corballis, Funnell, and Gazzaniga (1999) on perceptual grouping using figures derived from the Kanizsa illusion. Figures similar to those used by Corballis are illustrated in Figure 3.9. In one condition, split-brain and control respondents had to judge whether the illusory rectangle (formed by the four segmented circles) was fat or thin. With the versions on the left in Figure 3.9, although patients were not as good in general at this discrimination as controls, there was no laterality effect: left and right hemispheres were equally proficient. But when outlines were added to the segmented circles (versions on the right in Figure 3.9) in the so-called amodal

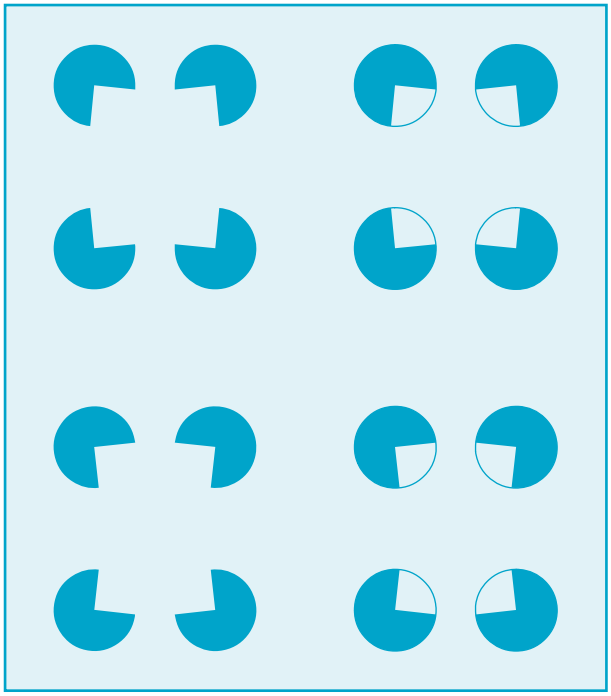


FIG. 3.9 The Kanizsa illusion explored by Corballis (1999). Both hemispheres can decide whether the illusory shapes (left) are "fat" or "thin". When outlines are added so that shapes can only be perceived by amodal completion (right), a more difficult task, only the right hemisphere can still tell the difference. Adapted from Corballis, P. M., Funnell, M. G., and Gazzaniga, M. S. (1999). A dissociation between spatial and identity matching in callosotomy patients. *Neuroreport*, *10*, 2183–2187. Reproduced with permission of Lippincott Williams & Wilkins.

completion condition (which is generally thought to be harder), a clear laterality effect emerged, with the right hemisphere significantly out-performing the left. This finding has been interpreted in a number of different ways, but one explanation is that the right hemisphere has an inherently more "holistic" processing style attuned to the **gestalt** nature of this task, which becomes particularly apparent in the harder amodal condition. We will return to the question of differential processing styles later in this chapter.

The surgery that brings about the split-brain syndrome effectively disconnects the two hemispheres. The amazing thing is that it has so little effect on routine daily activities for the patients themselves. Just occasionally, however, anecdotal accounts from individuals suggest that in particular situations there may be some disagreement between hemispheres (a phenomenon known as hemispheric rivalry). One female split-brain patient complained that as she went to select a dress from her wardrobe with her right hand, she found her left hand reaching for a different one. On another occasion the right hand turned the heating up, only for the left hand to turn it down again! Experimentally, this apparent absence of inter-hemispheric collaboration is best illustrated by the general failure of split-brain patients to combine (in any meaningful sense) potentially linkable information sent simultaneously to separate hemispheres. For example, tachistoscopic presentation of the words "sky" and "scraper" briefly to the two hemispheres failed to generate any drawings of skyscrapers. Instead, patients drew images depicting clouds in the sky and scraper-like tools (Kingstone & Gazzaniga, 1995).

That these examples of rivalry or absence of collaboration are few and far between is probably because in ordinary day-to-day activities visual, auditory, and most other sensory information actually finds its way into both hemispheres. (It takes a group of cunning researchers to think of situations in which input is restricted to just one.) Patients additionally develop strategies to try to ensure that sensory information gets to both hemispheres. The use of exaggerated head movements is one trick. Another is to make more use of "cross-cueing", essentially converting the sensory input into a different modality that will be available to both hemispheres, as illustrated by the following example: a split-brain patient trying to identify a comb by touch alone might tweak the teeth, which will make sounds that travel to both ears, and hence to both hemispheres. It is additionally likely that some "recovery" of inter-hemispheric communication may be achieved through the "recruitment" either of spared corpus callosum tissue (tissue that was not lesioned in the original surgery) or by increased use of one or more of the other non-lesioned commissures.

KEY TERM
Gestalt: A collection of physical, biological, psychological, or symbolic entities that creates a unified concept, configuration, or pattern.

INTERIM COMMENT

Despite the wealth of findings to have emerged from more than 40 years of research into the split-brain syndrome, caution is required in evaluating it. First, the individuals who underwent the surgery could not be regarded as a normal or random sample. They were, in reality, a very atypical group of individuals who had suffered from intractable epilepsy and, in the process, had usually been treated with a range of powerful drugs for many years. Second, it is likely that the cumulative effects of seizure activity will have led to discrete areas of damage and the possibility of shifts in lateralisation prior to any surgery. Third, background information about IQ or other basic cognitive abilities such as memory or attention is missing from some split-brain cases. Fourth, the extent of callosal lesion described in a patient's medical notes has not always been confirmed by later scan (although not all split-brain patients have subsequently been scanned). Finally, most of the published work on the syndrome has actually been based on intensive research with just a small proportion of the entire cohort of cases. Overall, it is probably best to regard the evidence from individuals who have had spilt-brain surgery as just one strand of a comprehensive research quest (applying the principle of converging operations, so to speak) to establish the true nature of the different psychological specialisms of the cerebral hemispheres.

CALLOSAL AGENESIS

The split-brain procedure was, of course, usually carried out on adults who had been born with an intact corpus callosum. However, a small number of people are born with a grossly malformed or entirely missing corpus callosum (see Figures 3.10a and b). Callosal agenesis, as the condition is known, is a very rare disorder

(a) (b)

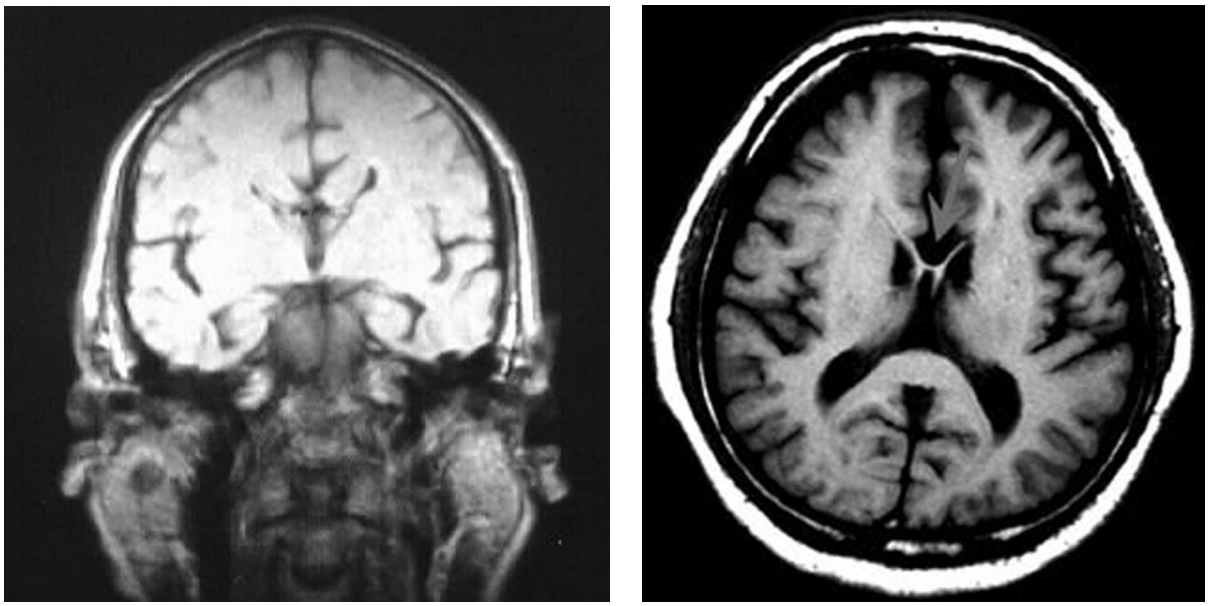


FIG. 3.10 Callosal agenesis. (a) Coronal MRI of complete agenesis. (b) Horizontal MRI of partial agenesis; the splenium is spared. The arrow depicts the intact optic chiasm (the point where about half the axons of the optic nerve from each eye cross to the other side).

of unknown cause, and is often associated with other structural anomalies. In particular, there are more pathways linking the front and back of each hemisphere, and pathways between the hemispheres other than the corpus callosum (notably the anterior commissure and/or the hippocampal commissure) are sometimes more fully developed. Other congenital abnormalities are often apparent, including various brain malformations and ventricular enlargement/displacement. In view of these structural anomalies we might expect acallosal children to have multiple handicaps, and in reality the majority (perhaps four out of five) do. But some do not, and these children are of particular interest because, in principle, they offer an opportunity to examine the role of the corpus callosum during development. If these individuals show the "usual" pattern of asymmetry, this would suggest that lateralisation is determined very early on in life and that the corpus callosum is not necessary for its development. If, on the other hand, lateralisation is partly a developmental process that depends on the corpus callosum, we should find abnormalities of lateralisation in acallosal cases. It is also of interest to compare such individuals with split-brain cases (Geffen & Butterworth, 1992).

In general, research on acallosal children has indicated that they too have language skills lateralised to the left hemisphere, and spatial skills lateralised to the right—findings that tend to support the first hypothesis that lateralisation is not gradually acquired during childhood. However, people with callosal agenesis do have certain difficulties with aspects of *both* language *and* spatial processing. In language tasks, difficulties are frequently reported when the "sound" of a word (testing the integrity of the phonological processing) is important. This becomes apparent in rhyming tasks or when the participant is asked to generate words that sound alike (Jeeves & Temple, 1987). Adding to this picture, acallosal people also have difficulties with spatial tasks such as jigsaws, copying drawings, puzzles, depth perception, and so on (Temple & Ilsley, 1993). The reasons for these deficits are not known but it is likely that, as with other tasks, these are ordinarily best dealt with by a collaborative brain effort involving networks of neurons spanning both hemispheres, which, of course, would be compromised in acallosal people. A recent illustration of the subtle "higher-order" psychological deficits resulting from this "mis-wiring" is provided by Brown et al. (2005). They reported that a group of acallosal adults struggled to understand narrative jokes that depended on verbal nuance, double meanings, and so on, even after controlling for verbal IQ. Anecdotal reports from relatives of acallosal individuals also attest to subtle psychosocial impairments linked to over-literal interpretation, superficiality, and impaired performance on tests that address "**theory of mind**" skills (similar deficits to those observed in autistic individuals; see Chapter 10).

Nevertheless, the most consistent and obvious deficits seen in callosal agenesis relate directly to the general problem of inter-hemispheric transfer. Indeed, a strong hint about the role of the corpus callosum in cortical functioning comes from the observation that acallosal children and adults are very clumsy in tasks that require bimanual cooperation. Examples include playing a musical instrument, doing certain sports, or even tying shoelaces. In certain respects, acallosal adults are rather like normal young children whose corpus callosum is immature. Its presence seems less involved in the process of shaping asymmetry than in promoting interaction between the hemispheres.

KEY TERM
Theory of mind: The ability to attribute mental states to others and to understand that others have beliefs that are different from one's own.

INTERIM COMMENT

In many cases of callosal agenesis other brain abnormalities are also apparent, so it is difficult for neuropsychologists to identify with any confidence those behavioural disturbances that have resulted specifically from the absence of a corpus callosum. In cases where meaningful data have been collected, asymmetries occur regardless, indicating that the corpus callosum is not necessary for lateralisation to develop.

Actually, some inter-hemispheric transfer is still apparent in acallosal people, who can, for example, sometimes tell whether two objects held in the left and right hand (but out of sight) are the same or different, although response speeds are invariably slower than for "intact" controls. It is widely presumed that this occurs via one or more of the remaining intact transverse pathways, illustrating once again the brain's ability to adapt in order to overcome adversity. However, the general clumsiness and lack of two-handed coordination seen in acallosal individuals are reminders of the importance of rapid inter-hemispheric exchange of information (via the corpus callosum) for normal behaviour.

ASYMMETRIES IN NORMAL INDIVIDUALS

A variety of experimental procedures permit investigation of lateralisation in normal individuals. Dichotic listening tasks take advantage of the fact that most auditory input to the right ear is relayed to the opposite auditory cortex for detailed processing, and vice versa for the left ear. Different auditory stimuli can thus be presented simultaneously to both ears (via stereo headphones) and participants can be asked to report what is heard. Most research of this kind shows a small but consistent right ear advantage for linguistic material (Kimura, 1973). This is thought to occur because words heard by the right ear are processed directly by the left hemisphere, whereas words heard by the left ear are initially processed by the right hemisphere, before being relayed to the left hemisphere for fuller analysis.

Of course, it could be argued that these findings simply illustrate a superiority of the right ear for auditory materials, but Bartholomeus (1974) established a double dissociation using dichotic presentation of letter strings sung to well-known tunes (for example, the letters p-g-t-v-l-m-d to the tune of "Twinkle, twinkle, little star"). In a subsequent recognition test, respondents showed a right ear advantage for letter recognition and a left ear advantage for tune recognition. Brancucci et al. (2005) have recently additionally confirmed a left ear (right hemisphere) advantage for discrimination of "intensity" for dichotically presented auditory tones and speech sounds.

The same general pattern of left hemisphere advantage for verbal material and right hemisphere advantage for non-verbal material appears to hold in other modalities too. Normal participants can recognise words more quickly when they are presented briefly (using a tachistoscope or computer) to the right visual field, and faces more efficiently when presented to the left visual field (Levine, Banich, & Koch-Weser, 1988). Asymmetry can also be seen in relation to movement. While most humans are right-handed, a motor skill performed with the right hand is

more likely to be interfered with by a concurrent language task than the same skill performed by the left hand. You can illustrate this in a very simple experiment. Ask a friend to balance a stick on the end of the first finger of either their left or right hand. When they have mastered this task, ask them to shadow (i.e., repeat as soon as they hear it) a paragraph of text that you read aloud. The concurrent verbal task will usually affect right-hand balance sooner than left-hand balance.

WHAT IS LATERALISED?

Despite our previous reservations about oversimplistic interpretations of data, the accumulating evidence from brain-damaged, split-brain, acallosal, and normal individuals reviewed so far does suggest a general division of labour along the lines of language (left hemisphere) and non-language (right hemisphere), and it is easy to see why this model has been the dominant one until quite recently. However, in recent years a somewhat different explanation of laterality effects has grown in popularity. The "processing styles" approach (Levy & Trevarthen, 1976) suggests that the main functional difference between the hemispheres is not so much "what" they process, but "how" they process it. According to this view, the left hemisphere is specialised to process information in an "analytical-sequential" way, whereas the right hemisphere adopts a more "holistic-parallel" mode of processing. In other words, the left hemisphere's modus operandi is to break tasks down into smaller elements that are dealt with one by one, whereas the right hemisphere tends to ignore the fine detail, paying more attention to the "whole image".

One advantage of this approach is that it allows for the possibility that *both* hemispheres will be involved in linguistic *and* spatial tasks (as strongly suggested by the deficits apparent in acallosal individuals), but that they will differ in the type of processing that is undertaken. For example, the right hemisphere is better at judging whether two photographs are of the same person. Face recognition is a holistic skill in the sense that it involves putting together "the facial image" from its individual elements. However, the left hemisphere is better at identifying individual facial features that may distinguish between two otherwise identical faces. This is an analytic skill, because it requires the "whole" to be broken down into its constituent parts. Language is both sequential and analytical—sequential because word order is critical for meaning; analytical because the meaning of (spoken) language depends on breaking up what is, in effect, a continuous stream of verbal sounds in order to identify words and understand the message. It is thus dealt with mainly by the left hemisphere, whereas facial recognition requires a holistic analysis and is thus dealt with more effectively by the right hemisphere.

The different processing styles of the two hemispheres were very clearly illustrated in a study by Sergent (1982). She used stimuli (similar to those developed by Navon, 1977) that were large capital letters, made up of small letters that were either the same as, or different from, the capital letter. The stimuli were shown briefly via a tachistoscope to either the left or right visual fields of normal participants who had to indicate whether or not particular target letters were present. On some trials participants were directed to attend to the large capital letters and at other times to the small letters (that made up the capitals). Sergent found that the left hemisphere (right visual field presentation) was better at detecting the small letters, and the right hemisphere (left visual field presentation) was better for the large letters. The left hemisphere focused on the fine detail, while

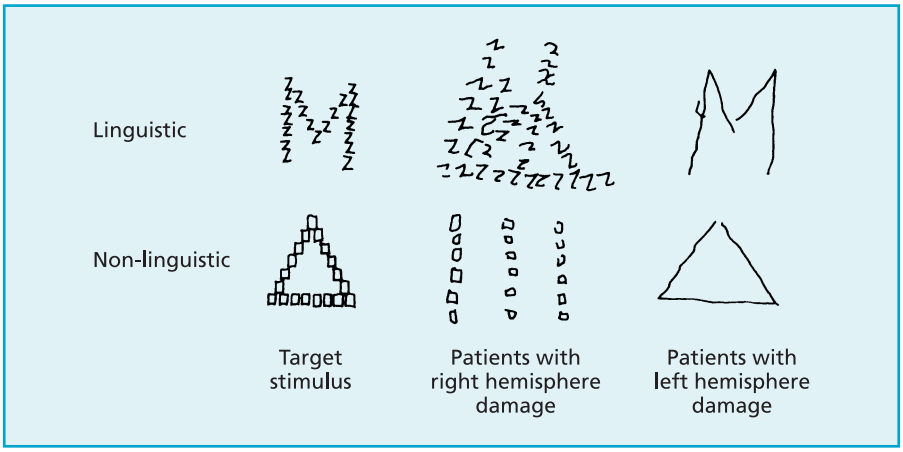


FIG. 3.11 Figures similar to those used by Delis et al. (1986) which comprise large images made up of smaller, different components. Patients with left-sided damage tend to make identification or memory errors relating to the fine detail. Those with right-sided damage are more likely to make "holistic" errors.

the right hemisphere attended to the "big picture". Similar findings have been reported by Delis, Robertson, and Efron (1986) in their study of memory impairment in unilaterally damaged individuals (see Figure 3.11).

INTERIM COMMENT

These studies show us that rather than having absolute and exclusive responsibilities, the cortical hemispheres may have complementary processing roles: The right hemisphere preferentially sees (so to speak) the forest, while the left hemisphere sees the trees. The right hemisphere preferentially processes information at a coarser level than the left, which deals with information at a more detailed and local level. Analytical and sequential aspects of language are thus dealt with predominantly (but not exclusively) by the left hemisphere, whereas more holistic aspects of language such as emotional intonation or interpretation are dealt with by the right. Likewise, spatial tasks, which usually involve integrative rather than analytic skills, are handled more efficiently by the right hemisphere. This model of hemispheric specialisation, with its emphasis on processing style rather than psychological function, arguably makes better sense of the laterality research data than the traditional left brain (language), right brain (spatial skills) model, and is becoming widely accepted by neuropsychologists. However, it is important to remember that with the possible exception of fluent speech production, *both* hemispheres can actually mediate *most* skills; so what we have is a preferential (or more efficient) processing style for one or other hemisphere rather than an absolute division of labour.

INTER-HEMISPHERIC TRANSFER VIA THE CORPUS CALLOSUM

Despite its heuristic appeal, the processing styles approach still doesn't entirely explain the "seamless" nature of psychological functioning. People intuitively

"feel" they have a single brain in their heads, not two separate processors set to operate at different levels of analysis. Moreover, we also tend to respond serially; humans actually have difficulty doing two different things at once. You will probably be aware of the playground prank in which a child tries to pat their head and rub their stomach at the same time! This phenomenon can be examined experimentally by asking respondents to draw shapes simultaneously with both hands. Intact individuals can do this with simple shapes that are either identical or mirror images of one another, but not (easily) for shapes where one is rotated 90° in relation to the other. Split-brain patients, however, can do this easily. This suggests that the spatial representations of movements remain independent for split-brain patients, but not for healthy controls . . . and this leads to their impaired performance (Franz, Ivry, & Gazzaniga, 1996). On the other hand, in a study by Sergent (1990), split-brain patients had difficulty deciding whether (or not) pairs of photographs presented briefly and simultaneously to right and left visual fields were of the same or different people. As we mentioned earlier, normal people can usually complete this task without error, even when the photographs are taken from a variety of different angles and perspectives. Both these observations illustrate the importance of the corpus callosum for integrating the activity of the two hemispheres. Although other pathways connecting the two sides of the brain exist, the corpus callosum is the largest commissure, and it enables the two hemispheres of the cortex to relay information backwards and forwards almost instantaneously: ERP recording has shown that inter-hemispheric transfer takes no more than 20 ms. When this pathway is absent from the outset (as in callosal agenesis) other pathways may take on some of the work normally done by it, but they generally fail to work as efficiently or as quickly in the cause of inter-hemispheric transfer, hence the slower response speeds seen on tasks requiring inter-hemispheric comparisons. From the first example however, it is clear that inter-hemispheric transfer does not always facilitate "cooperation" between the hemispheres, and several scientists have argued that a significant proportion of callosal transfer actually involves inhibition rather than facilitation of the "rival" hemisphere (Ringo et al., 1994). As we shall see (in Chapter 9), others, most notably Gazzaniga (cf. Gazzaniga, 2002), have argued that at the highest level of conscious cognitive control, it is the left hemisphere that wins this particular rivalry.

INDIVIDUAL DIFFERENCES IN BRAIN ORGANISATION

The evidence we have considered thus far indicates that both structural and functional asymmetries are intrinsic features of nervous system development. However, it is also of interest to know whether (or not) the degree of lateralisation described above varies between people, and if so, why. Two areas where these questions seem particularly relevant (and controversial) are handedness and gender.

HANDEDNESS

Neuropsychologists are now sure that handedness is something you are born with rather than something you acquire with experience, although researchers continue to debate whether it is genetic in origin as Annett (1985) has argued, or related to

intrauterine factors such as the position of the foetus in the womb (Previc, 1991). In fact, the two accounts may not be mutually exclusive, and it is interesting to note that researchers using **ultrasound** have reported that hand preference is already apparent in foetuses at 15 weeks of gestation, judging by their preference for sucking either left or right hand digits (Hepper, Shalidullah, & White, 1991). A recent follow-up of this cohort (now aged 10–12 yrs) has, incidentally, confirmed that early thumb preference is an excellent predictor of later handedness, especially for right-handers (Hepper, Wells, & Lynch, 2005). Hepper, McCartney, and Alyson (1998) also reported a strong preference for right (over left) arm movements in 10-week-old foetuses. This is a fascinating finding because this laterality preference pre-dates, by several weeks, any overt indications of asymmetry in the developing brain.

About one in ten humans is left-handed according to Annett (1985), although *degree* of left- or right-handedness certainly varies. Left-handedness has, historically, been frowned on and, at one time, it was common practice for "natural" left-handers to be forced to use their non-dominant right hands both at school and at home. Interestingly, as this practice has faded the proportion of left-handers has increased, but only to the figure cited above.

For many years it was more or less assumed by psychologists that the organisation of the left-hander's brain was the mirror image of that of the right-hander. However, data from the Wada test (see Chapter 2) put paid to this idea (Rasmussen & Milner, 1977). As expected, results indicated a pattern of left-lateralised language for almost all right-handed individuals. But for left-handers a different result emerged. About two-thirds have the same arrangement as right-handers. Of the remainder, about half show the opposite pattern (reversed asymmetry) and half show language and non-language skills both distributed in each hemisphere (bilateral distribution). Nevertheless, combining these figures, about 96.5% of the population has left hemisphere specialisation for language generation. These data have recently been broadly confirmed by Knecht et al. (2000a; 2000b) using "functional transcranial Doppler sonography". This new procedure can measure speed of blood flow independently in each hemisphere, indicating which is more active during verbal tasks and, by implication, dominant for language.

HANDEDNESS AND COGNITIVE FUNCTION

What, if any, then, are the psychological consequences of left- or right-handedness? Researchers have tried to answer this question by examining psychological deficits in right- and left-handed individuals who have incurred brain damage. In one of the most comprehensive reviews of such cases, Hardyck and Petrinovich (1977) found that, on average, left-handers with damage to the right hemisphere were more likely to experience language problems than right-handers with similar damage (14% versus 7%). The incidence of aphasia following left-sided damage was more or less the same for right- and left-handers. Similarly, spatial skills were more likely to be affected after right hemisphere damage in right-handers than in left-handers. Taken together, these findings suggest that left-handers as a group may be less "lateralised" than right-handers. Research on healthy left-handers using tests of both dichotic listening and divided visual attention has also led to the suggestion that left-handers show less functional asymmetry than right-handers (Springer & Deutsch, 1998). However, are these

Key Term
Ultrasound: An antenatal procedure for generating images of unborn children.

results so surprising? Remember that some left-handers show left hemisphere dominance for language, some show right hemisphere dominance, and some show mixed patterns. So, as a group, we might expect to find that left-handers were less lateralised, on average, than right-handers. The more interesting question would be to compare test performance between left-handers with left, right, and mixed dominance patterns, but at present large-scale studies of this type have yet to be undertaken.

It has long been known that left-handedness is more common among both developmental- and reading-delayed individuals. Developmental dyslexia is, for example, several times more common in left- than right-handed children (Geschwind & Behan, 1982; and see also Tonnessen et al., 1993). Is there any evidence that this relationship generalises to the "normal" population? Several research projects have set out to compare performances of normal left- and right-handers on measures that tap higher mental functions, but the results have been rather inconsistent. In Hardyck and Petrinovich's (1977) **meta-analysis** of 14 studies, left-handers did marginally worse than right-handers on some tests, and better than right-handers on others. In one study for example, left-handers were reported to have a small but consistent generalised non-verbal IQ deficit as measured by the WAIS (Levy, 1969). However, her data were drawn from a sample of just 10 left-handers and 15 right-handers, all of whom were graduate students. It would, we think, be fair to describe this as a small and unrepresentative sample.

Levy's research findings have not been well supported in follow-up studies, and where differences have been reported, they have usually been so small (Ratcliff & Newcombe, 1973) that critics have raised the possibility that they are statistical artifacts rather than genuine effects (Vogel, Bowers, & Vogel, 2003). A study unlikely to draw criticisms about sample size is that of Halpern, Haviland, and Charles (1998) who looked at the relations between handedness and intelligence in 174,547 adults who had completed the (US) Medical College Admissions Test. There was no evidence of an overall handedness effect; rather a mixed pattern of outcomes, with left-handers scoring lower overall on a writing test, and higher on a test of verbal reasoning. Frankly, we should not be surprised at the absence of effect on generalised measures of cognitive functioning. After all, as far as we know, left-handers have never actually formed either an elite or an under-class of humans (notwithstanding historic stigma for left-handedness based on religious or cultural prejudices), an observation strongly indicative of a de facto parity with right-handers.

But if generalised cognitive differences between left- and right-handers have been somewhat elusive, perhaps there are nevertheless specific cognitive domains that may distinguish the two groups. The answer to our rhetorical question, however, would seem to be that absences of difference outweigh instances of difference, unless, perhaps, one examines the extremes of the handedness distribution. For example, Coren (1992) has argued that left-handedness is over-represented among both the extraordinarily intelligent and the mentally disabled. Kopiez, Galley, and Lee (2006) have recently reported that sight-reading skills are better in left- than right-handed professional musicians, although the effect only reached statistical significance in males. Schachter and Ransil (1996) reported that left-handedness was much more common than would be expected among architects, and Coren (1995) has similarly suggested that left-handedness is more common among chess masters and mathematicians. On the other hand, Gabbard, Hart, and Gentry (1995) reported that in young children, motor performance was

Key Term
Meta-analysis: A research technique in which data from similar but separate projects are pooled into a single data set to increase statistical power.

impaired in left- (and mixed-) handers compared to right-handers, whereas Kilshaw and Annett (1983) argued that poor motor coordination was worst in extreme right-handed individuals. Finally, although Leask and Crow (2001) reported that both verbal and non-verbal cognitive abilities were more likely to be impaired in individuals with ambidexterity than in clear left- or right-handers, Francks et al. (2003) failed to replicate this finding.

In sum, the available data provide a somewhat confused picture of the relationship between cognition and handedness. While there is clear evidence that left- and right-handers may "recruit" different brain regions in order to perform cognitive tasks (see, for instance, the differential effect of left and right TMS on perception for left- and right-handers; Mevorach, Humphreys, & Shalev, 2005), the evidence of consistent differential performance is lacking. (However, see Box 3.3 for a different take of handedness effects.)

Box 3.3 Is being left-handed a health risk?

In 1988, Halpern and Coren published their analysis of the relationship between death rates and handedness based on data garnered from the 1979 Baseball Yearbook which included information about pitching/throwing and batting hand preference for over 2000 professional US baseball players. Their analysis indicated that beyond the age of 33, the proportion of surviving right-handers consistently exceeded that of left-handers, and that the former group lived, on average, 8 months longer than the latter. They argued that this effect might be caused by several factors: two suggestions were that left-handers are more susceptible to a range of illnesses relating to reduced or impaired immune function (Geschwind & Behan, 1982), and/or that left-handers are more accident prone, leading to a greater likelihood of life-threatening injuries.

Needless to say, their report caused something of a storm, and other researchers challenged Halpern and Coren's interpretation of their data: Why, for example, were mixed-handers omitted? Could the effect be related to a greater social pressure to switch from left-handedness for men born earlier in the century? Other surveys were undertaken, variously involving an updated analysis of over 5000 baseball players in the 1993 yearbook (Hicks et al., 1994), a study of death rates amongst Swedish conscripts (Persson & Allerbeck, 1994), and a study of English "first-class" cricketers (Aggleton et al., 1994; Aggleton, Kentridge, & Neave, 1993). Interestingly, none of these studies entirely undermined Halpern and Coren's original claims, and the potential role of accidental injury leading to death was actually reinforced. Both the Hicks et al. and Persson and Allerbeck studies reported an elevated accident rate amongst non-right-handers, and the study of cricketers indicated an apparent 25-month difference in longevity (right-handers living longer), although this effect disappeared when deaths due to "unusual causes" and/or warfare were removed from the analysis.

In one of the largest studies ever undertaken (Ellis & Engh, 2000), the deaths of over 5000 North Americans were considered in relation to "degree" of right- or left-handedness. One category—those described as "generally left-handed"—had statistically significantly shorter life-spans, although the reasons for this remain something of a mystery.

SEX DIFFERENCES

One of the most contentious areas of research has been the question of psychological differences between the sexes and, among other things, their relation to brain organisation. It is worth remembering that human embryos have "bipotential", meaning that for the first 6 weeks following conception they are sexually undifferentiated and could develop into either sex. Then, at this point in genetic males, hormonal actions driven by a single gene on the y chromosome throw a developmental switch that differentiates, once and for all, males from females (a so-called organising effect). Of course, if no y chromosome is present, nature's default setting of female will develop.

This may be one of the reasons why scientists have, until recently, seemed somewhat uninterested in exploring brain sex differences, although a second reason is certainly the hostility meted out by some academics towards colleagues bold enough to suggest that such differences might exist: Witness, for example, the recent acrimony between Doreen Kimura (2004) who has published extensively about the possible evolutionary origins of brain sex differences and Tone Bleie (2004) who has questioned such origins and argued that differences between the sexes depend on experiential (learned) factors. Yet there is now convincing evidence of structural differences, and additional evidence of (some) functional differences too.

Structurally, female brains are slightly lighter, but contain proportionately more grey matter (cell bodies and dendrites). Male brains have more white matter and larger ventricles. There are particular local differences in the structure of the hypothalamus, some of which are linked to hormonal differences between the sexes. Perhaps of most interest in the context of this chapter is the observation we noted earlier: that females have a larger anterior commissure and a larger splenium (the most posterior part of the corpus callosum). It has been estimated that at birth the general level of tissue development in boys is between 4 and 6 weeks behind that of girls, and they are known to be about twice as likely to be born with a range of neurodevelopmental disorders as girls. It is also well documented that cognitive developmental disorders including **autism**, **hyperactivity**, stutter, aphasia, and **dyslexia** are all four to six times more common in boys.

Turning to functional differences, Maccoby and Jacklin's (1974) text remains one of the most comprehensive reviews of sex differences and behaviour. Although their research also encompassed the study of social play and aggression, critical attention has focused on their conclusion that girls tend to do better than boys (more or less from the word go) at language-related tasks, and that boys tend to do better at visuospatial tasks. Consider, for example, language: girls begin to talk earlier, they learn to read earlier, and they develop a greater vocabulary. These differences begin to emerge almost as soon as it is possible to measure them, and they increase through childhood and adolescence: teenage girls have consistently higher scores for comprehension, fluency, and translation. Boys, on the other hand, are better at tasks of visual tracking, aiming, maze learning, mental rotation, and map reading. Clearly, we cannot rule out the possibility that some of these differences are acquired through experience: for example, male advantage at mathematics becomes more pronounced in adolescence (Hyde, Fennema, & Lamon, 1990) but boys are more likely to be studying maths courses at this stage of schooling. However, the appearance of at least some differences so early in

KEY TERMS

Autism: A developmental disorder characterised by aloofness, automaticity, and aphasia.

Hyperactivity: In neurological terms, excess functional activity. In behavioural terms, a developmental disorder marked by excess excitability, inattentiveness, restlessness, and reckless/antisocial behaviour.

Dyslexia: A specific reading difficulty found in a person with otherwise normal intelligence.

development suggests that they are, in part, a consequence of differential brain organisation.

As with the earlier debate about the functions of the left and right hemispheres, the rather simplistic conclusions drawn by early researchers (that boys are better at visuospatial skills and girls are better at linguistic skills) have required revision in light of more thorough research. For example, a maths bias favouring males is seen in reasoning tasks (*If it takes 20 workers 3 days to dig a hole 6 metres deep, how many days would it take* . . . etc.) but for females in mental arithmetic tasks. Thus the overall male advantage is smaller than was once thought and may also be reducing further with time (Friedman, 1989). Although a male visuospatial advantage is most apparent on tests of mental rotation and targeting, females outperform males on other non-verbal measures such as manual dexterity and "spot the difference" tests where subtle differences between similar figures must be found (Kimura, 2002). Most measures of language function clearly favour females, but males are better at generating verbal analogies (Halpern, 2005). Bourne (2005) has recently shown that both males and females are "right lateralised" for the interpretation of facial emotions, but males significantly more so than females. Yet Lewin and Herlitz (2002) have confirmed previous findings that females are better than males at facial recognition.

Further study of route learning, traditionally thought to favour males, has also revealed the intriguing subtlety of male–female cognitive differences: In one variant of this visuospatial task, participants were required to learn a route from point A to B depicted on a map. Boys as young as 3 years old found this task easier to do than age-matched girls (Kimura, 1992). However, once learned, girls remembered more landmarks along the route than boys. As with the earlier laterality research, these findings raise again the possibility that boys and girls employ somewhat different strategies to complete the task—boys forming a holistic plan of the relationship between points A and B, and girls negotiating the route via a series of landmarks. In support of this hypothesis Kimura (2002) reported that girls are consistently better at the party game in which they are allowed to look around a room, then blindfolded, and then, when the blindfold is later removed, asked to identify objects in the room that have been moved or taken away. Boys, on the other hand, having seen a particular room layout, are better at avoiding bumping into things when blindfolded.

The neurological literature has been cited as supporting the view that women's brains are functionally less lateralised than men's. McGlone (1980) reported on a series of case studies of people who had suffered damage to just one side of their brain. Left-sided damage was more likely to result in impaired language function in men than women. Right-sided damage was more likely to impair visuospatial function in men than women. Although these data suggest that both language and spatial abilities are more bilaterally distributed (i.e., less lateralised) in women than men, an alternative explanation is that women tend to use verbally mediated strategies to solve *both* linguistic and visuospatial problems. At present it is not possible to say which of these is more likely, but the second explanation tallies well with Kimura's theory of strategy differences between the sexes. However, in two reviews of tachistoscopic and dichotic listening studies of sex/laterality differences, Hiscock et al. (1994, 1995) concluded that the evidence in support of sex differences in degree of lateralisation was inconsistent, and at best indicative of only very small differences. In similar vein, Sommer et al. (2004) have recently

raised doubts about the assumption of greater bilateral language representation in females in a meta-analysis of functional imaging studies.

An interesting footnote to this debate comes from research that considers within-subject variability rather than differences between sexes. Although this work takes us some way from the central issue of lateralisation, it has nevertheless become apparent that cortical functioning is influenced by hormonal factors, and these in turn may affect measures of lateralisation. Kimura and Hampson (1994) have studied differences in psychological function in relation to the menstrual cycle. Immediately after ovulation (when levels of oestrogen and progesterone are relatively high) women tend to perform better at tasks involving fine motor control, thought to depend on left hemisphere function, and worse on spatial tasks that tap right hemisphere function. The opposite pattern is seen at menstruation when levels of these hormones are low. Hausmann et al. (2002) have also reported reliable within-subject changes in lexical matching ability, face discrimination, and figural comparison in relation to different stages of the menstrual cycle.

INTERIM COMMENT

The study of sex and handedness differences in relation to lateralisation continues to generate heat and light in roughly equal measure. In each domain, the results of countless investigations have been pored over in order to establish the presence/absence of meaningful group differences, and their consequences for ideas about lateralisation. In the case of handedness, we know that at least a proportion of left-handers (perhaps one in three) have a functional asymmetry that differs from the "right-hander" asymmetry, but we have no reliable data to judge whether (or not) this has consequences in terms of basic psychological functioning. As for the question about general cognitive skills in left- and right-handers, the evidence is equivocal, and a prudent interpretation would have to be that if we steer clear of the extremes of the ability range, left- and right-handers do not differ.

We are obliged to come to a slightly different conclusion in respect of sex differences: Our reading of the available literature suggests that while the early ideas of generalised superior language functions in females and superior non-language functions in males have not been supported by recent research, there are now numerous examples of sex differences relating to specific aspects of both language (e.g., verbal fluency superiority in females) and visuospatial skills (e.g., superior mental rotation skills in males). Indeed, they appear to go beyond these domains. Tranel et al. (2005) have recently reported that unilateral damage to the ventromedial prefrontal cortex influences social functioning, personality, and risk taking in males and females quite differently, right-sided damage affecting males much more than females, and left-sided damage only affecting females. Such instances of specific psychological difference are unlikely to be wholly attributable to developmental influences, and merit serious attention.

However, we do not know how these functional differences relate to more general aspects of brain organisation. A long-standing hypothesis, first mooted by Geschwind and Behan, held that the male brain is more lateralised (i.e., asymmetrical) than the female brain as a result of the inhibitory effects of testosterone on the development of the left hemisphere in males (in utero).

Although support for this model has been difficult to come by in terms of endocrinology (see Mathews et al., 2004), and patchy at best in terms of consequent functional lateralisation (see Sommer et al., 2004), the idea that males have a right hemisphere advantage and a left hemisphere disadvantage compared with females has become ingrained in popular accounts of sex differences.

Yet the issue is complicated by at least two factors not necessarily related to functional laterality differences between males and females. First, females appear to have more efficient inter-hemispheric transfer, which may or may not be related to greater bilateral functionality; at present, we just do not know. Second, males and females may use different strategies to solve identical problems (Kimura's example of landmark memory in females would be one case in point). To demonstrate unequivocally that males and females have different brain organisation, one would need to show that different brain regions are activated when both males and females are unambiguously using the *same* strategy to perform a particular task, something that, so far as we know, has yet to be demonstrated.

Thus, while there appear to be significant "pockets" of functional difference between the sexes, wholesale differences of the sort mooted 20 or 30 years ago have not been confirmed by subsequent research. How such instances of difference, where they are revealed, relate to organisational differences in the brain remains, for the time being, unknown. Further functional imaging studies (similar to Tranel et al.'s recent study) will shed light on this relationship.

LATERALISATION: A FOOTNOTE ON THE EVOLUTIONARY PERSPECTIVE

Whatever one's views about the degree of lateralisation in left- and right-handers or in males and females, the research reviewed in this chapter overwhelmingly supports the idea of hemispheric specialisations. Most researchers think it unlikely that these will all have been acquired exclusively through experience, so genetic factors come into play. Indeed, although we consider it to be beyond the remit of this text, interested readers might wish to explore two recent models on the role of genes in lateralisation by Annett (1987, 2002) and McManus (1992). But if genes are implicated—and caution is required because no one has yet found Annett's right-shift gene (which, according to the model, brings about left hemisphere dominance and right-handedness if present: if absent, chance effects determine either left or right hemispheric dominance)—this usually means that some evolutionary advantage accrues (or accrued) from its possession. According to Gazzaniga (2000), the advantage is computational: it simply makes more sense for overall control (language dominance if you will) to be in one place than to be distributed in both hemispheres. Passingham (1981) made the same point in somewhat different terms by identifying the potential problems (duplication of effort, conflict, etc.) of having bilateral control of the midline structures such as the tongue, larynx, and mouth that enable sound production, be it grunts, wails, or speech. In a sense, other asymmetries follow from this: Unilateral control of articulation frees up space on the contralateral side, to enable this region to

undertake other responsibilities such as visuospatial processing, so this hemisphere becomes dominant for non-language functions.

We began this chapter with reference to Corballis (1991), who developed an evolutionary explanation for the asymmetries in cortical function seen in humans. Initially he argued that although the overall blueprint for nervous system structure is symmetry, not asymmetry, the presence of what he called a "generative assembly device" (GAD) in just one hemisphere allows us to think and act in a "generative" manner (combining things/actions/sounds into more sophisticated entities according to set rules). Not only does this mechanism enable us to generate almost endless utterances from a pool (in English at least) of fewer than 50 phonemes (the sounds that make up spoken words), it also provides an explanation of why most humans have a preferred hand, especially when skilled actions (such as those linked to tool use) are required.

Unfortunately, the original version of this account failed to explain fully why the GAD should occupy the same left hemisphere location for almost all humans. This point has more recently been addressed by relating currently observed asymmetry of language dominance to pre-speech communication, involving hand gesture, facial expression, and non-verbal vocalisation. According to Corballis (2003), the GAD evolved for tool use, and later for language as we now know it, from asymmetries already apparent in our forebears, and perhaps even in other primates. Whatever their ultimate origin, they certainly pre-date the arrival of our species. Of course, once the genetic shift occurred, there would be "no going back" because of the advantages outlined above, although the designation of this effect to the left hemisphere was probably a chance occurrence.

CHAPTER SUMMARY

The research that we have reviewed in this chapter supports a model of hemispheric specialisation in humans. While it would be an oversimplification to call the left hemisphere the language hemisphere and the right hemisphere the spatial (or non-language) hemisphere, it is easy to see why earlier researchers jumped to this conclusion. Research conducted on people with brain damage, with surgically lesioned or absent corpus callosa, and on normal people all points to left hemisphere dominance for language. This does not mean that all language skills are, somehow, contained within this hemisphere; rather that, on balance, it "has the final say" when it comes to language, particularly its generation. Whether this is because the left hemisphere is preordained for language, or because it is innately better at analytic and sequential processing, is currently a matter of debate. Certainly, right hemisphere processing seems to be more holistic and integrative, although Corballis has suggested that this happens by default rather than because of any non-verbal equivalent of the GAD mechanism in the right hemisphere. Finally, we have seen that lateralisation can, to some extent, be modified by both handedness and sex differences.

CHAPTER 4

CONTENTS

4

Somatosensation and neuroplasticity

INTRODUCTION

We are used to hearing of *Homo sapiens'* five senses: vision, hearing, touch, smell, and taste. Yet most neuropsychologists would argue that this list underestimates our true sensory capacities. Consider, for example, balance: As bipeds, humans, above most other animals, rely on their sense of balance to teeter around on two legs, sacrificing stability for the opportunity to use their hands and arms for other purposes. How about our sensitivity to temperature? Humans might be able to survive extremes of both high and low temperature, but they are exquisitely sensitive to temperature changes of very small increments. Next, consider pain. Humans (like other mammals) have a highly evolved pain sensitivity system, and are able to differentiate between many types of pain induced by a wide range of focal or diffuse stimuli, including heat, pressure, chemical irritant, and injury. Finally, what about the experience of sensory input when clearly there should be none? We need to have a model of sensory processing that can accommodate "phantom limb" experiences of amputees too.

Our list is clearly in need of revision, but rather than extending it the solution has been to replace "touch" with "somatosensation". In this chapter, rather than offering a brief synopsis of each sense system we have chosen to describe this multi-faceted sensory system in detail. This is not altogether an accident. First, in certain respects somatosensation relies on the same sort of neural wiring as other senses, so it may serve as an approximate model for them too. Second, we know quite a lot about the neural wiring itself, which is arguably less complex than that of the visual or auditory system.

Additionally, we are beginning to realise that although the blueprint for the lay-out of the somatosensory system is, as with the rest of the central nervous system, genetically programmed, the view that it is consequently "hard-wired" and therefore immutable must now be challenged. On the contrary, the system is demonstrably capable of remarkable "plastic" changes, certainly during development, but also to a significant extent, it seems, in its mature (adult) state. An understanding of how the somatosensory system responds to damage offers an insight into the recuperative functions of the brain in other domains. We therefore examine examples of plasticity in this system, before considering neuroplasticity more generally.

To set us on our way, however, we need to review some general features of sensory systems, and familiarise ourselves with some of the confusing terminology.

GENERAL FEATURES OF SENSORY SYSTEMS

Sensory information travels from sensory receptors along afferent pathways towards the central nervous system. Some of this information gets no further than the spinal cord where, at the same segment at which it enters, there is a synapse, and output leaves the cord via motor neurons to innervate the appropriate muscles to complete what is known as the reflex arc. Most information, however, reaches the brain by a series of relays where it is interpreted in the processes of perception.

Sensory receptors may either be modified nerve endings, as is the case with pressure receptors, or separate cellular structures such as rod or cone cells in the retina. In either case, their job is to respond to particular stimulus parameters (distortion of the skin in the case of Pacinian corpuscles; light in the case of rods and cones) by a change in their own electrical "excitability". Most receptors demonstrate three further critical features. First, even within a sensory modality, they are "tuned" to be selectively most sensitive to a particular limited range of sensory input (certain cones in the retina respond maximally only to green–red colours, others to blue–yellow for example). Second, they quickly adapt, meaning their responsivity leads to fewer and fewer nerve impulses the longer the stimulus continues. A consequence of adaptation is that sensory systems are more responsive to changes in stimulation than constant stimulation. Third, there is a physical limit to their excitability, and therefore an upper limit to the number of nerve impulses that can be generated and conveyed from the receptor to other regions of the nervous system in a given period of time (about 200 per second in humans).

In the nervous system information is "conveyed" from point to point in the form of nerve impulses, so all receptors must be able to convert external energy (be it light, pressure, temperature, etc.) into nerve impulses: this process is referred to as **transduction**. (The pick-up on an electric guitar does more or less the same job, converting vibration into electric current.) If the receptor is just a modified nerve ending, as is the case for most touch receptors, we refer to this transducing process as giving rise to a receptor potential. If the receptor is a separate cell such as a rod or cone, a receptor potential (in it) gives rise to a generator potential in the sensory neuron. In either case, these potentials are graded, meaning that they are roughly proportionate to the intensity of the applied stimulus, allowing, of course, for adaptation, and a maximal rate of firing (see Figure 4.1). Thus the intensity, duration, location, variability (or other quality) of a stimulus will be relayed to the spinal cord and brain in the form of volleys of nerve impulses. As these always have the same amplitude in a given neuron (sometimes known as the all or none principle), their frequency rather than any other characteristic enables us to distinguish quiet from loud, dim from bright, or bearable from noxious.

KEY TERM
Transduction: Process by which a cell converts one kind of signal or stimulus into another.

THE SOMATOSENSORY SYSTEM

As we hinted earlier, the somatosensory system is a polymodal system, meaning it accommodates a variety of sensory inputs. First, it provides us with a constantly

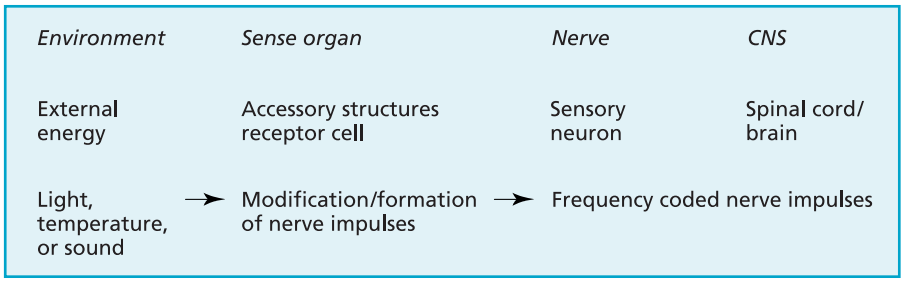


FIG. 4.1 The process of sensory transduction, which involves the conversion of one form of energy into another. In the nervous system this job is performed by sensory receptors, or by separate receptor cells. In either case they must respond to (i.e., be activated by) external stimuli (light, temperature, sounds, etc.) and convert this energy into nerve impulses. Within limits a frequency coding rule usually operates in which more intense stimuli lead to the generation of more nerve impulses.

updated picture of tactile (touch, pressure, vibration) input on the body surface (called "exteroceptive information", because it originates outside the body). Second, it provides the central nervous system (CNS) with information about the relative position of body parts, and the position of the body in space (so-called "interoceptive information", from within the body). Third, it processes information about heat and cold, and pain too.

Transduction is performed by a matrix of receptors in the skin, joints, muscles, or tendons. In humans and other mammals there are at least 20 different types of receptor dealing with information about touch, temperature, stretch, pain, and so on. In common with receptors in other sensory modalities, somatosensory receptors generate action potentials when stimulated. They also tend to be individually "tuned" to be most "responsive" to different intensities of stimulation. For example, some of the touch receptors are particularly sensitive to light touch, others to tickle, and still others to vibration, stretch, or pressure. Finally, many receptors adapt extremely quickly: hair follicle receptors only respond to movement (of the hair), and not at all even if the hair is held "out of position".

SOMATOSENSORY PATHWAYS

In the somatosensory system, receptors are modified nerve endings of sensory neurons, whose axons run from the point of stimulation towards the spinal cord. In some cases (e.g., pain receptors) the receptor is, literally, just a bare nerve ending. In other cases, the nerve ending is modified or even enveloped by an accessory structure such as a hair follicle, or a Pacinian corpuscle (a sort of multilayered structure that resembles a spring onion when viewed through a microscope, and which responds to pressure and vibration). The accessory structure simply aids in the transduction process.

Once transduction has occurred, the volleys of nerve impulses must be relayed from the receptors towards the CNS. The majority of sensory neurons carrying these impulses are myelinated, which improves the speed of conduction of action potentials dramatically: sensory neurons can convey impulses at up to 100 metres per second. On entering the spinal cord, some sensory neurons continue uninterrupted (without a synapse) up to the brainstem along pathways forming the dorsal column medial lemniscal system (so-called because they are

located medially at the back of the cord). Neurons in this pathway are all myelinated. In other cases, sensory neurons synapse as they enter the spinal cord, in a region known as the substantia gelatinosa, on to spinal neurons that then convey the information along their axons to the brain rather like a relay race. This second set of pathways are known as the spinothalamic (or anterolateral) tracts (actually comprising three separate pathways) and many axons in this pathway are unmyelinated (see Figure 4.2). The pathways can also be distinguished in terms of

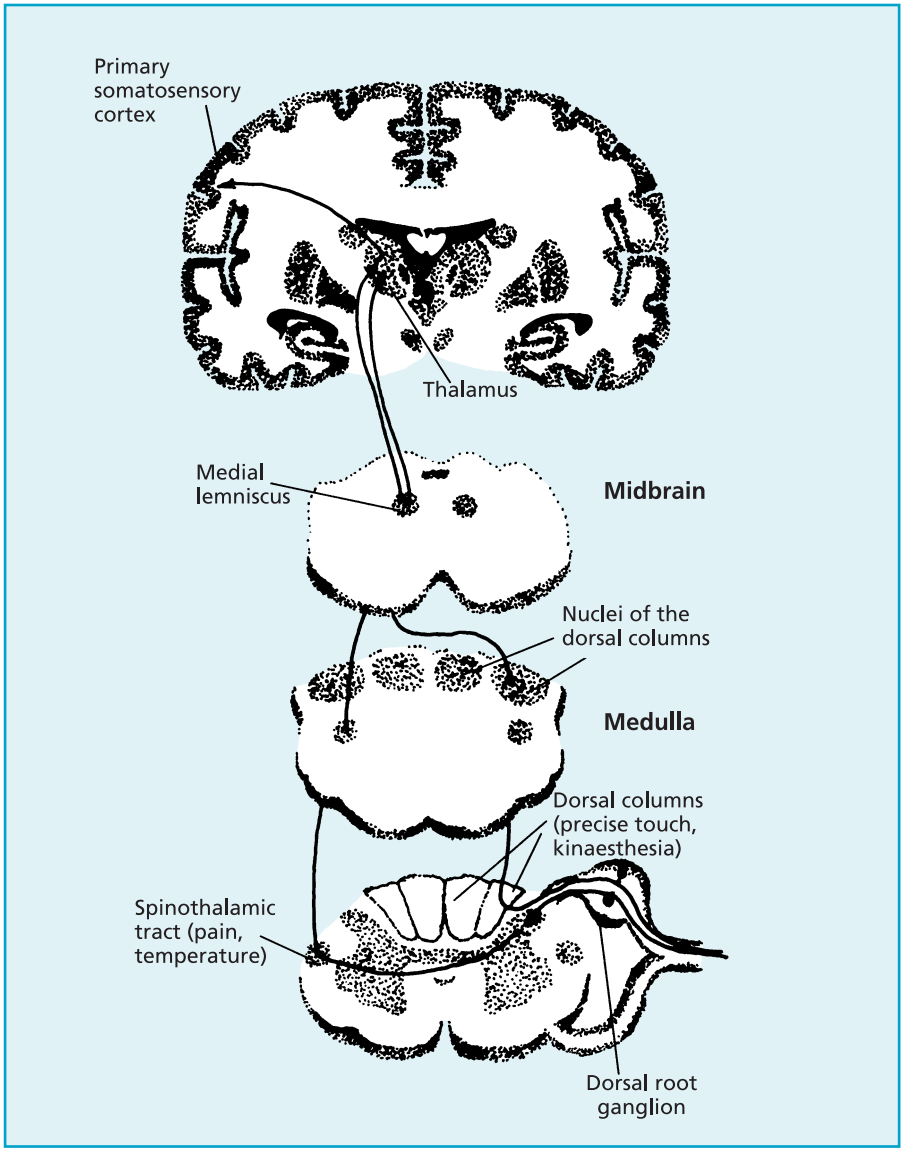


FIG. 4.2 The somatosensory pathways. There are two major sets of spinal pathways carrying somatosensory input. The dorsal columns (found at the back of the spinal cord) convey precise "fine-grain" somatosensory information. The spinothalamic tracts (at the side of the spinal cord) convey less anatomically precise somatosensory information. In each case the final destination for most of this input is the primary somatosensory cortex on the opposite side.

the information they convey. The former carries precise "fine-grained" localised information such as touch, pressure, and **kinaesthetic** information from joints: the latter carries coarser less precisely localised information to do with pain and temperature. A third important distinction between these two pathways is that in the former there is relatively little **convergence**, whereas in the latter there is a considerable amount. One obvious effect of this is that information about "localisation" is more easily retained in the dorsal column pathways than in the spinothalamic tracts.

Most somatosensory input crosses on its way to the brain from one side of the body to the other. In the dorsal columns this occurs in the medulla, whereas in the spinothalamic tracts it occurs at the segment of entry in the spinal cord after the synapse in the substantia gelatinosa. In each case, however, information from the left side of the body mostly finds its way to the right thalamus in the brain, from where it is relayed on to the cortex. In the spinothalamic system, some neurons send out collateral branches that terminate in the ascending reticular activating system (see Chapter 9) and are involved in brain arousal, and others that terminate in the tectum and are concerned with low-level (unconscious) sensory processing (also covered in Chapter 9). The route from receptor to cortex has involved relays of just two or three neurons (and one or two synapses) and the time it takes to convey information along the pathways is, typically, measured in fractions of a second (see Box 4.1 and Figure 4.2).

Box 4.1 Conduction speeds in sensory pathways

Sensory neurons carrying fine-touch information from your toes are the longest neurons in your body at up to 2 metres. Assuming a conduction speed of 100 metres per second, how long would it take for nerve impulses to get to your brain from your toe? (Answer [a] below.)

In some notable cases, speed of conduction is significantly slower. Pain information is predominantly carried along narrow unmyelinated neurons, and travels as slowly as 1 metre per second. This explains why there is sometimes a significant delay between incurring injury (say a burn to the skin) and feeling pain. How long might it take to "register" the fact that someone has trodden (painfully) on one of your toes? (Answer [b] below.)

Answers: [a] 20 ms assuming typical height. [b] 2 seconds assuming typical height.

THE SOMATOSENSORY CORTEX

Like other sensory systems the somatosensory cortex has a primary area for stimulus registration, and other areas (known as secondary and tertiary regions) for further processing, perception, and sensory integration. In humans, the primary area (known as S1) occupies a strip of cortex that runs approximately from ear to ear across the top of the brain. Strictly speaking, it is the most anterior (forward) gyrus (bump) of the parietal lobe and comprises Brodmann's areas 3 (a and b), 1, and 2. (See Figures 4.3 and 4.4.)

Key Terms
Kinaesthetic: Anything related to the sensation of body movement/location. Sensory information about the status of joints and muscles.
Convergence: In the nervous system, the process of many (converging) inputs influencing one component (for example, a neuron).

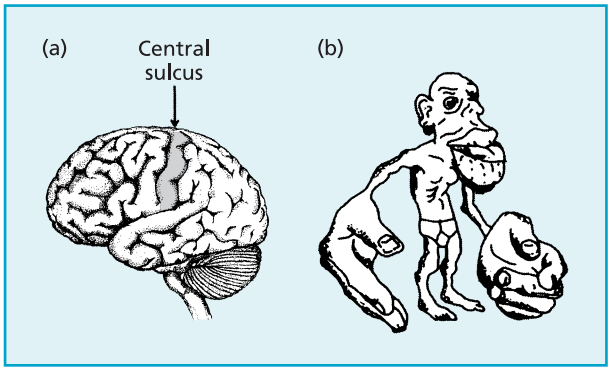


FIG. 4.3 The somatosensory cortex and sensory homunculus. (a) The primary somatosensory strip (S1) actually comprises several parallel bands of cortical neurons responsive to sensory inputs from particular body regions on the opposite side. (b) The topographic representation is precise but not proportionate, with some body regions (notably the lower face and hands) having a disproportionately large S1 representation. This disproportionate allocation is represented in the relative size of body regions in the homunculus ("little man").

A truly remarkable feature of this band of cortex is that the entire body is, in effect, mapped or "topographically represented" upside-down and left–right reversed along its length. To illustrate this, imagine you could record the activity of neurons in this band. Starting in the region of cortex located roughly behind the left ear, you would find that these neurons would only become active if there was stimulation to the right side of the tongue or jaw. A little further up, you would find neurons that were activated only to stimulation of the right cheek and forehead. Still further up, you would find neurons that respond to tactile stimulation of different parts of the right hand (with each part of each finger, and the palm, and the back of the hand represented separately), and so on. Towards the top of the left side of the brain you would find neurons that respond to tactile input from the right side of the body and the right leg. This somatotopic representation (meaning specifically that adjacent body locations are represented

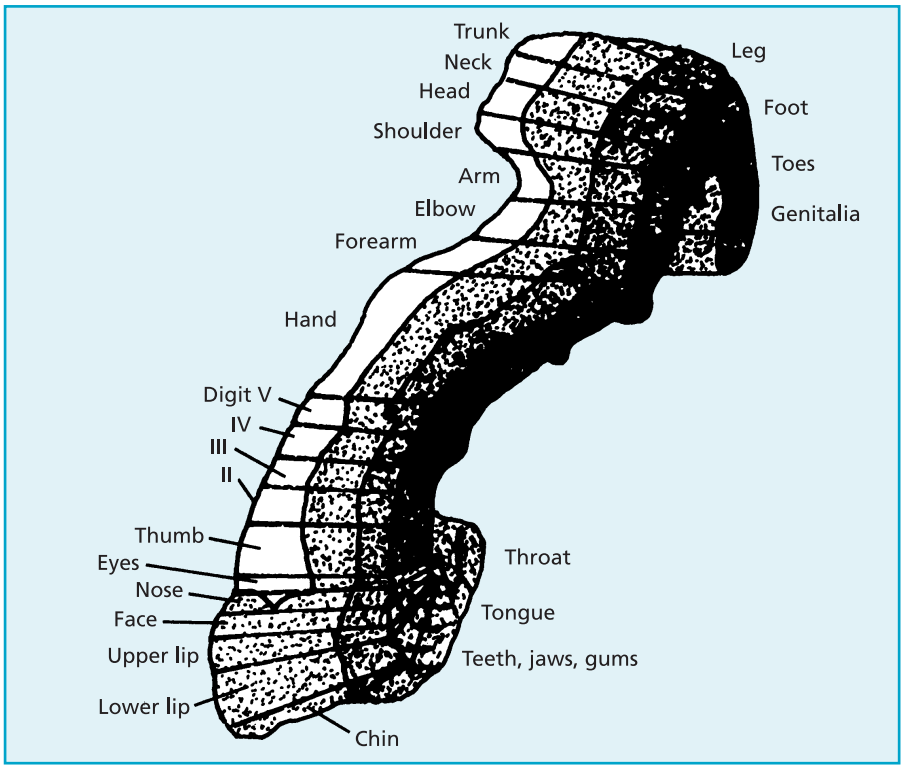


FIG. 4.4 A more detailed view of the primary somatosensory strip (S1). The figure shows how different body regions (and component parts within those regions) are "mapped" in S1. Note the disproportionate allocation (in humans) of "cortical space" for dealing with input from the hands and face. Source: Rosenzweig et al. (1999). *Biological psychology*. Sunderland, MA: Sinauer Associates Inc. Reproduced by permission of Sinauer Associates Inc.

by adjacent cortical areas) continues into the region of S1 located within the longitudinal fissure, where neurons receptive to input from the right foot and the genitals are found. The identical mirror image pattern would be apparent on the right side of S1 too. Incidentally, much of the initial work on "mapping" S1 (and the primary motor strip) was undertaken by Wilder Penfield, a Canadian neurosurgeon. He managed to persuade patients on whom he was about to operate to let him electrically stimulate areas of exposed cortex, and ask them to report what they felt (or in the case of the motor strip, to observe which body regions began to twitch!). For instance, stimulation of S1 might lead to a patient reporting that they could feel a "tingling" sensation in the palm of their hand. Moving the electrode a few millimetres along S1 might result in the same sensation now appearing to derive from their thumb.

As methods of investigation have improved, Penfield's observations have been broadly confirmed. However, it has become clear that S1 comprises not one but at least three parallel strips of neurons, each receiving distinct combinations of somatosensory input, while retaining the general pattern of topographic representation mentioned above (Kaas, 1983). The pattern of input to these parallel strips is specified in Figure 4.4. However, topographic representation in S1 is distorted. Body areas that are more sensitive, such as the hands and lips, have proportionately very much larger areas of somatosensory cortex to project to than body regions that are less sensitive, such as the upper limbs or the back of the head. The evidence suggests that for primates, including humans, about half the total number of neurons in this region receive input from either the face or hands. Researchers have illustrated this disproportionate relationship by drawing or modelling so-called homunculi (little men) whose bodies are proportionate to the area of cortex sensitive to the various body regions (see Figure 4.3b). The same relationship (of sensitivity and dedicated cortex) is also seen in other species. Mice, for example, have disproportionately large regions of somatosensory cortex dedicated to snout and whiskers, while monkeys have distinct regions dedicated to receiving input from their tails.

SECONDARY AND TERTIARY SOMATOSENSORY CORTEX

S1 is only the initial point of processing of somatosensation. While damage to it leads to reduced sensitivity for the particular body region sending inputs to it, identification of objects by touch depends on other regions of cortex. S1 projects (sends outputs) to a secondary area (S2), the role of which is to integrate input from the three (or possibly more) independent primary cortical strips, but now from both sides (i.e., bilaterally). Both of these areas project to other areas (the tertiary or association areas) of the parietal lobes behind (posterior to) the primary somatosensory strip. In fact, a significant amount of input via the anterolateral tract goes directly to S2 and tertiary regions including BA (Brodmann's areas) 5 and 7.

We can get an idea of the sort of processing that takes place in the secondary and tertiary regions by considering the effects of localised damage here. As a general rule, damage to more posterior regions affects higher-order processing while leaving basic sensitivity unimpaired. In fact, parietal damage often leads to one of the so-called agnosias, a curious and perplexing cluster of disorders that are described in more detail in Chapter 8. To give just one example here, damage to tertiary somatosensory regions can lead to a condition known as astereognosis,

in which blindfolded subjects can describe accurately the main physical features of objects that they feel, yet are unable to match them with other similar objects, or identify them by name.

INTERIM COMMENT

Somatosensory input from all over the body is relayed via the spinal cord into the brain and eventually to S1. This strip of cortex comprises neurons waiting (in effect) for input from just one particular body region. The strip maps out the entire body contralaterally and upside-down, and we refer to this relationship between body region and cortical space as topographic representation. From here, secondary and tertiary regions in the parietal lobe process the sensory input further, to enable perception and integration with other sensory modalities.

PLASTICITY IN THE SOMATOSENSORY CORTEX

The topographic representation we described in the previous section is very consistent from one person to another, which reinforces the view that the basic wiring diagram for neurons here is indeed "hard-wired". However, data from a series of studies initiated in the early 1960s (e.g., Bennett et al., 1964) had already cast some doubt on the immutability of the wiring of the brain, at least in rodents. Bennett's group showed that adult brain structure depended in part on the environment in which animals were raised from shortly after birth to maturity, a period of about 60 days. In a typical study there would be a standard (control) condition in an animal laboratory, in which several animals were housed in a cage together. There would be an impoverished condition, which was the same except that animals were caged alone, and an enriched condition in which animals had larger cages, lived in bigger social groups, and had plentiful play opportunities. In a series of experiments the researchers found not only that rats in the enriched environment developed heavier brains, but also that these had more connections between neurons (synapses) (Turner & Greenhough, 1985), and more neurotransmitter substance (Chang & Greenhough, 1982). The enriched environment rats were also quicker at problem solving and learning (Renner & Rosensweig, 1987). Although these findings were not directly related to the somatosensory cortex, they were important because they provided experimental evidence that challenged the then-current view that cortical connectivity was fixed (hard-wired) early on in development, and could not be affected by experiential factors.

The first indications that plasticity may also be observed in the somatosensory system came with the findings from Woolsey and Wann (1976). In mice there is precise topographic representation of snout whiskers contralaterally in sensory cortex. The cortical region can be mapped, with each whisker sending sensory input primarily to just one cell cluster (known as a barrel). Woolsey knew that if all whiskers (on one side) were removed in infancy, the area of cortex that would normally receive input from them fell silent. However, if a row or column of whiskers was removed, neurons in the whisker barrels that would otherwise have responded to input from these whiskers begin to respond to adjacent intact whiskers. In effect, the barrels for remaining whiskers absorb the cells from the "silent"

barrels, and become larger than normal, so that cortical space is not wasted (see Figure 4.5).

Merzenich and Kaas (1980) extended Woolsey's paradigm to primates. In the macaque monkey there is topographic representation of the hand area contralaterally in the monkey equivalent of S1 that is very similar to that in humans. In one study, Merzenich and his colleagues removed a digit from a monkey early in infancy, and later on when the monkey had matured, examined the topographic representation in S1. Like Woolsey, they found that the cortical area that would have received input from the amputated digit had, in effect, been absorbed into adjacent regions responding to other digits. In fact the cortical areas for adjacent digits were now bigger than would normally have been expected.

In subsequent research the group has shown that simply preventing or encouraging use of digits, or otherwise interfering with the sensory input from them, can influence cortical maps even in mature monkeys. In one study by Merzenich and Jenkins (1995), animals were trained to receive food only if they used particular digits to rotate a wheel, which they had to do for several hours each day. This "exercise" brought about enhanced "tactile input" from the trained digit. After just a few weeks of training, these monkeys were found to have significantly larger cortical representation areas in S1 for the trained digits. If training then ceased, the cortical mapping slowly reverted (over a period of several weeks) to its pre-training layout. In another study by Allard et al. (1991), the middle two fingers of a group of adult owl monkeys were surgically "fused" (sewn together) in order to change the somatosensory input emanating from them. Some months later, cortical mapping revealed that the usual somatotopic boundaries between digits had effectively disappeared.

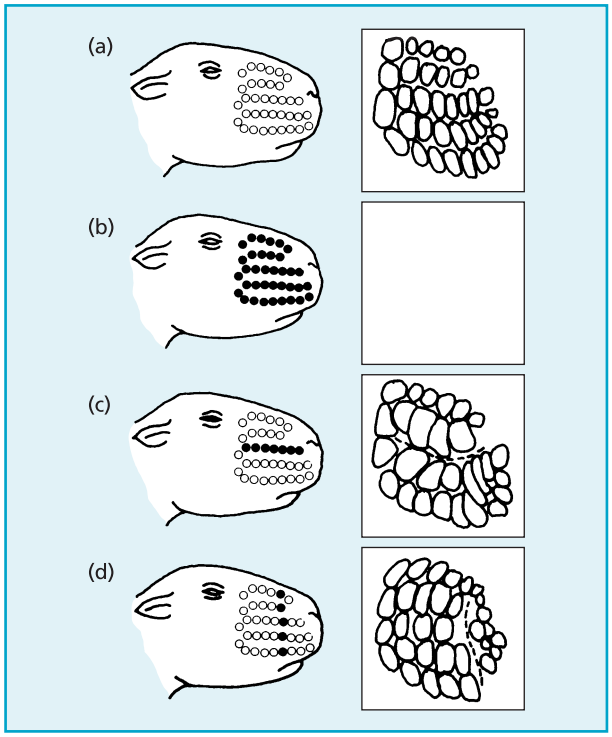


FIG. 4.5 Woolsey's whisker barrel study. (a) The usual topographic representation of snout whiskers and cortical barrels. If all the whiskers are removed (b) from one side of the snout of a new-born mouse the entire cortex that would have received sensory input from these whiskers remains silent (i.e., unused). On the other hand, if only a row (c) or column (d) of whiskers is removed, the whisker barrels (areas of S1) receiving inputs from adjacent whiskers grow, effectively absorbing much of the "silent" cortex, which now responds to the remaining adjacent whiskers. Source: Woolsey & Wann (1976); © 1976 Wiley-Liss, Inc. Reprinted with permission of Wiley-Liss, Inc., a subsidiary of John Wiley & Sons, Inc.

Can similar effects be seen in humans? Obviously, scientists cannot go around removing babies' fingers (or sewing them together) and waiting to see how this will influence adult cortical representations. However, Mogilner et al. (1993) have reported on a small number of individuals with syndactyly, a congenital disorder in which the fingers are malformed and fused together. Such individuals can have their fingers surgically separated. The researchers used magnetoencephalography (MEG) (see Chapter 2) to record activity in the "hand" region of the primary somatosensory cortex of these patients before, and again after, surgery to "free" their fused fingers. Prior to surgery, the cortical mapping of the hand region in each case was quite distinct and unusual in comparison with the controls. In particular, presurgical digit representation was displaced within S1. Moreover, the relevant cortical areas were unusually close to one another, and partly

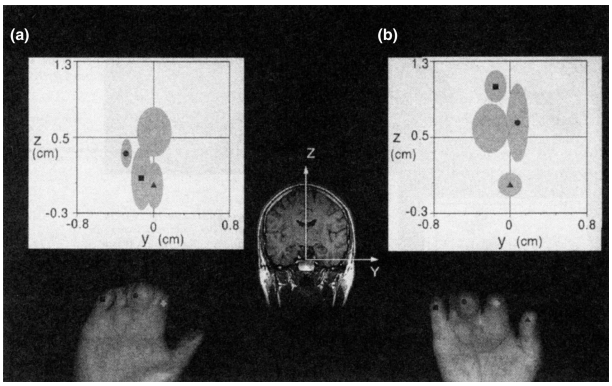


FIG. 4.6 Mogilner et al.'s (1993) syndactyly surgery study. The representation of the hand in the somatosensory cortex changes following surgical correction for syndactyly of digits two to five. (a) A pre-operative map shows that the cortical representation of the thumb, index, middle, and little fingers is abnormal and lacks any somatotopic organisation. For example, the distance between sites of representation of the thumb and little finger is significantly smaller than normal. (b) Twenty-six days after surgical separation of the digits the organisation of the hand area is somatotopic, and the distance between the sites of representation of the thumb and little finger has increased to 1.06 cm. Source: Mogilner et al. (1993). Somatosensory cortical plasticity in adult humans revealed by magnetoencephalography. *Proceedings of the National Academy of Sciences, 90*, 3593–3597. Copyright (1993) National Academy of Sciences, USA. Reproduced with permission.

overlapping. In comparison post-surgery, MEG maps indicated marked reorganisation in the cortical hand area in both cases. The resulting arrangement now more closely resembled the cortical maps of controls, and there was no longer overlap. Astonishingly, these changes were apparent within 1 week, and further MEGs recorded 3 and 6 weeks later indicated relatively little additional change. The remapping appeared to occur over distances of between 5 and 10 mm (see Figure 4.6). Readers will probably recognise the fact that Mogilner et al.'s study is, in effect, the obverse of Allard et al.'s. Together they show that, far from being hard-wired, the mammalian cortex is a dynamic place capable of undergoing remarkable functional plastic change.

As if to underline the effects of experience (as opposed to surgical intervention) on cortical representation in humans, Pascual-Leone and Torres (1993) used MEG to map the changes in cortical representations of (blind) adults who were learning to use Braille. Results indicated an expansion of the cortical representation for the single digit (usually the right or left index finger) that Braille readers used, and a corresponding reduction in the representation of hand regions not used.

INTERIM COMMENT

Mogilner et al.'s (1993) study was the first to illustrate that functional remapping is possible (albeit in rather dramatic circumstances) in the human adult somatosensory cortex, and that this region is not, as was once believed, "hard-wired". The more surprising finding was that areas of cortex responsive to input from individual fingers "appear" to move within a few days of surgery. Clearly, the cortex does not actually move, but new regions several millimetres away from the original site began to respond to sensory input from the newly freed fingers. It is important to remember that Mogilner et al.'s study was based on individuals who had the abnormality (syndactyly) from birth. However, in certain respects this makes the speed of change all the more remarkable, and scientists are now trying to identify the mechanisms that permit such remapping to occur. Further studies have now confirmed that drastic surgical interventions are not necessary for remapping to occur: experiental change (over time) is just as likely to bring it about.

THE PHANTOM LIMB SYNDROME

The observation that experience alone can influence cortical mapping in S1 is important for researchers interested in trying to understand the neurobiological correlates of "practice" (for skill acquisition) and physiotherapy to aid recovery, and we return to consider these issues later in this chapter. Before that however, we want to introduce one further line of research that bears on our understanding of plasticity in the somatosensory system.

A sense of residual (and often painful) feeling emanating from an amputated body region (referred to as phantom limb experience) is felt, at least intermittently, by between 50% and 80% of amputees (Ehde, Czerneicki, & Smith, 2000). The experience is graded, usually being most pronounced soon after surgery, and gradually reducing ("shrinking back") over time (Melzak, 1992). However, some phantom limb feelings can persist for many years. It is important to emphasise that phantom limb experiences are not "made up". Indeed, a remarkable feature of them for the amputee is their realistic nature. Sometimes, the experience will be so real that the individual might forget that their leg has been amputated, and try to stand up, or may start to reach for something with their "amputated" arm.

Until recently, little was known about the physiology of the phantom limb phenomenon, and it was generally assumed that phantom experiences were caused by residual neuronal activity from nerves in the stump. Painful phantom limb experiences can sometimes be so severe that further surgery is conducted (often at the behest of the amputee) to try to eliminate the pain. Unfortunately, this is rarely very effective and scientists now think that the phantom limb experience is, effectively, "recreated" in the brain.

An insight into the possible mechanisms that are involved has been offered by Ramachandran (1994). He reported the case of a young man who had lost his lower left arm in a traffic accident. Four weeks later, the subject reported a series of sensations in his (amputated) arm and hand whenever the left side of his face was "gently stimulated" (Ramachandran used a cotton bud/q-tip to do this). In fact, different regions of the face elicited "sensations" in different parts of the phantom hand. Touching his cheek evoked feelings in his first finger, whereas touching his lower jaw evoked sensations in his little finger, and so on (see Figure 4.7). Ramachandran collected several similar anecdotal reports of phantom experiences being evoked during stimulation of intact body regions. In one case, a woman who had had her foot amputated experienced phantom feelings in it whenever she had sexual intercourse!

Ramachandran explained these observations by proposing that the cortical region that should have received input from the missing limb was now receiving stimulation from the region that evoked the phantom experience—the face in the case of the traffic accident victim and the genitals in the case of the woman. Ramachandran put forward his theory after considering the layout of the somatosensory homunculus. He knew that this was very consistent from one person to another, and he also knew that the evocation of the phantom experience could be achieved by stimulating body regions whose cortical receptive fields were close to the region attendant on input from the amputated limb. For example, you may recall that the hand area is adjacent to the face area, and reference to Figure 4.4 will show that the genital region is immediately adjacent to the foot region.

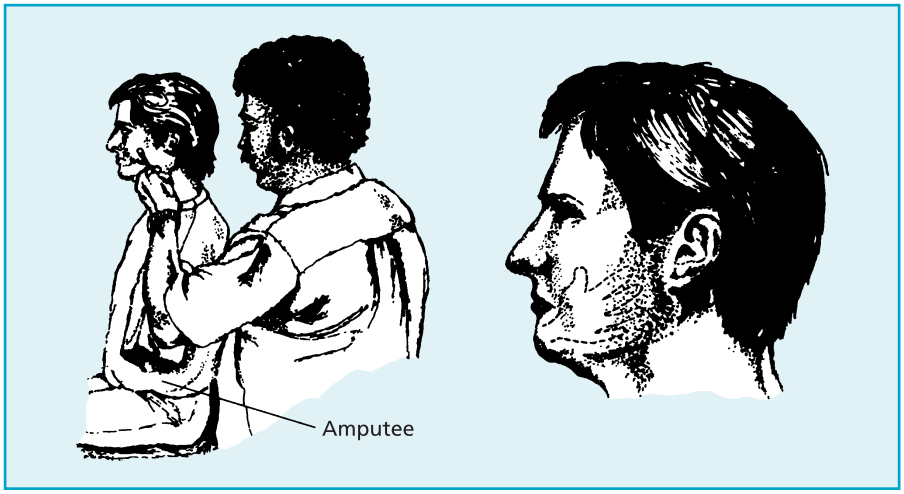


FIG. 4.7 Referred phantom experiences from facial stimulation. The amputee experienced phantom limb sensations when his cheek was gently touched. Ramachandran (1994) observed that different regions of the face evoked sensations in different parts of the amputated limb in a quite precisely mapped way: brushing the lower jaw evoked feelings in his little finger and brushing his cheek evoked feelings in his thumb. Source: Gazzaniga et al. (2002). *Cognitive neuroscience: The biology of the mind* (Figure 12.23). Copyright © 2002 by W. W. Norton & Company, Inc. Reproduced with permission of W. W. Norton & Company, Inc. Reproduced with permission.

KEY TERMS
Silent synapses: Synapses that are not currently transmitting neuronal signals.
Lateral inhibition: A relatively common feature of nervous system "wiring" in which active neurons tend to suppress activity of adjacent neurons.

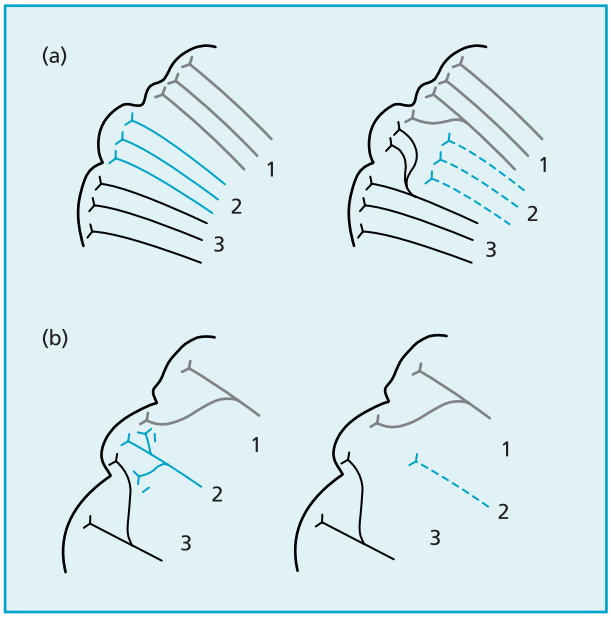


FIG. 4.8 Ramachandran's explanation of phantom limb experiences. Sensory input from the face region now begins to stimulate adjacent hand regions of S1. (a) This could be due to the growth of new axon branches—offshoots from the inputs to the face region (1 and 3) as input 2 is lost—but the speed of the effect is too quick to be accounted for by the relatively slow growth of new axons. (b) A more likely explanation is that previously inhibited (silent) inputs to the hand region become active because they are no longer inhibited by the missing input (2) from the hand itself.

To explain how inputs to one area of cortex can begin to exert an influence at adjacent regions, the growth of new axons (from adjacent inputs) has been suggested. Axons can sprout new branches, but this can be discounted in this case because of the speed with which the effect is observed: axons just do not grow this quickly. Ramachandran's explanation invoked the activation of previously **silent synapses**. He argued that although sensory input travels preferentially to target cortical regions, some also travels to adjacent (non-target) regions, but that this is normally inhibited by the direct inputs to that region. However, loss of this input (after amputation) means loss of **lateral inhibition**, so that neighbouring regions' inputs now get through, and this is what evokes the phantom experience (see Figure 4.8).

Ramachandran also argued that at least some phantom limb discomfort stemmed from a mismatch between the patient's "perceived" and actual sensory experience. To remedy this, he invented the "mirror box", an example of which is shown in Figure 4.9. Essentially the idea is that the amputee places his/her intact arm/hand in the box in such a way that s/he cannot directly see it but the position of the mirror gives the appearance of both limbs being present. Once positioned, s/he is encouraged

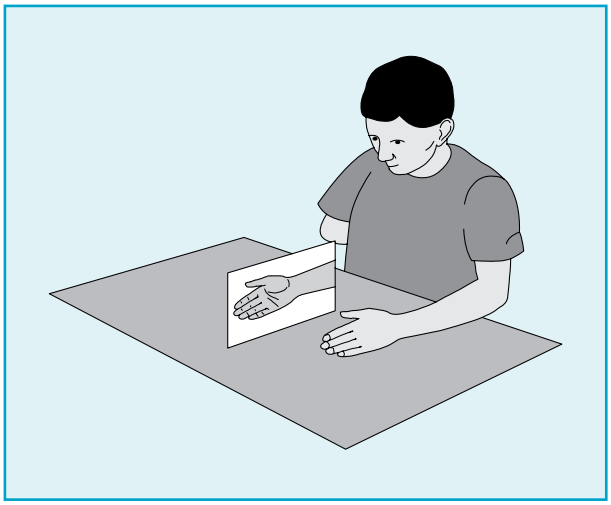


FIG. 4.9 Ramachandran's mirror. A mirror is positioned in relation to the seated patient, so that the reflection of the remaining intact arm appears in the position that the now amputated arm would have appeared. When asked to imagine making movements with both arms, some amputees find this arrangement provides relief from phantom pain, and a sense of well-being. Ramachandran has suggested that this is because the patient now experiences movement in the phantom limb from the "illusory" visual feedback. Source: Adapted from Ward, J. (2006). *The student's guide to cognitive neuroscience*. Hove, UK: Psychology Press. Reproduced with permission.

to make synchronous movements with "both" limbs! This means that the individual "intends" actions that are consistent with the visual feedback from both the real and the mirror-image limb. Astonishing though it may seem, this simple procedure seems to be beneficial for some phantom limb sufferers. In Box 4.2 we invite you to play a game closely related to Ramachandran's mirror box which demonstrates the power of illusory feedback suggested by the famous neuroscientist himself.

Box 4.2 Illusory feedback and fake limbs

Purchase a realistic but fake arm/hand.

- Sit at a table with one hand resting on the table, the other beneath the table.
- Position the fake arm/hand on the table in the corresponding position as though both hands/arms are resting on the table.
- Have an associate tap both the real hand that is beneath the table and the fake hand in synchrony, as you watch the fake hand.
- Notice how sensations appear to originate from the fake hand/arm.

Carry out the same procedure on a naïve associate.

- Once the effect has been achieved for a while, pull out previously hidden hammer and hit the fake arm/hand.
- Run!

INTERIM COMMENT

As is so often the case, further research, including in-vivo imaging of phantom limb patients, has painted a somewhat more complex picture than the one proposed by Ramachandran (see Flor, Nikolajsen, & Jensen, 2006, for a concise review of some of these developments). For example, contrary to Ramachandran's observations, phantom experiences can sometimes be evoked by stimulating body regions somatotopically distant from the amputated limb. Additionally, although MEG studies indicate both somatosensory and primary

motor strip remapping after amputation, this is apparent in *all* cases, not just in those who experience the phantom phenomenon. Actually, phantom *pain* rather than phantom *experience* best correlates with the extent of remapping, and vivid memories of chronic pain from the now-amputated body part are actually the best predictor of post-amputation phantom pain (Flor et al., 2002).

Additionally, touching the stump itself usually evokes some feelings, suggesting that peripheral input is still involved. Moreover, phantom limb sensations are also often evoked when an amputee tries to move his/her amputated limb, suggesting that re-afference or feed-forward* of motor output directly into somatosensory cortex is also involved. This idea would fit well with the findings from the mirror box, which, in effect, tries to re-establish connections between "the wish/intention to make movements" and the observation of those same movements. Lotze et al. (1999) have reported that amputees fitted with a myoelectric prosthesis (a fake limb that moves in relation to residual nerve impulses in the stump) not only experience less phantom pain but also evince less somatosensory reorganisation.

These are important findings because they may lead to the development of new strategies to help people to overcome a range of phantom experiences—not, incidentally, restricted to limb amputation but also seen following breast removal, ear surgery, and even removal of genitals. This work may additionally aid recovery of lost function after nerve damage.

* In this context feed-forward refers to nerve impulses from the motor strip that travel directly to somatosensory regions (S1 and S2) where they appear to be used to compare intended with actual movements in order, if necessary, to make fine anticipatory adjustments to subsequent movements.

NEUROPLASTICITY BEYOND S1

PLASTICITY IN THE MOTOR CORTEX

It is now time to broaden our brief review of neuroplasticity beyond the focus of our attention thus far, namely S1. For example, in their study of "phantom-limb-experiencing" amputees, Lotze et al. (2001) reported plastic changes in primary motor strip (M1) as well as S1, confirming earlier reports by Karni and colleagues. In this study (Karni et al., 1998), healthy volunteers were asked to practise a simple sequence of digit movements (touching fingers to thumb in a particular order) for a few minutes every day over a period of weeks. Unsurprisingly, both the speed and accuracy of participants at this task improved markedly over time. However, when subsequently required to perform both the practised task and a different unpractised sequence in an fMRI scanner, there was significantly more activation in M1 for the former than the latter, and this difference was still apparent 8 weeks later although no further practice had been undertaken in the interim. These important findings bear on our understanding of both functional brain changes that underpin skill acquisition, and recovery of motor function through physiotherapy: an issue to which we return briefly later.

PLASTICITY IN AUDITORY AND VISUAL CORTEX

Several studies have reported evidence of plastic changes in auditory and visual cortices in relation to both damage and training/change in use (although we should note that for obvious reasons, most of this work has been undertaken with animals). In the auditory modality, Recanzone, Schreiner, and Merzenich (1993) found evidence of remapping in the primary auditory cortex of monkeys trained over a period of weeks on an auditory discrimination task. Behavioural performance was, in fact, directly related to the extent of cortical reorganisation. Robertson and Irvine (1989) reported that discrete monaural lesions in the cochlea (of guinea pigs) brought about a functional reallocation of auditory cortex resource within 1 month.

In the visual modality, Kaas et al. (1990) lesioned discrete regions of a monkey's retina and subsequently showed that the region of V1 (primary visual cortex) previously responsive to the lesioned area had become responsive to adjacent retinal inputs. Hubel and Weisel (1977) showed that both V1 functionality and the integrity of the "ocular dominance column" arrangement usually seen here could be permanently compromised by occluding visual input from one eye during a critical period of post-natal development: roughly the first 6 months in macaques.

CROSS-MODAL PLASTICITY?

In the film "SNEAKERS", a team of investigators finally track down the criminal gang thanks to the extra-sensitive hearing of a blind agent. There are, in fact, many anecdotal reports of individuals with various sensory impairments who seem to overcome adversity by developing increased "acuity" in their intact sensory systems, although scientific investigations of this phenomenon have produced mixed findings. For example, a range of measures of absolute sensory threshold (for an intact sensory modality) usually fail to distinguish healthy from sensory-impaired individuals, suggesting absence of compensation at least at this level (Finney & Dobkins, 2001). However, ERP studies of congenitally blind or deaf people have provided convincing evidence of enhanced functionality in more integrative tasks involving remaining intact sensory systems. For example, congenitally blind people can process sounds faster than sighted people, and localise them more precisely (Roder et al., 1999), and congenitally deaf people show enhanced visual acuity and visual attention (Bavelier et al., 2000). Functional imaging studies of such individuals usually show evidence of enhanced activity in both the primary sensory region and in adjacent multimodal (i.e., non-specific/association) cortical regions such as posterior temporal and inferior parietal lobes (responsive to both visual and auditory input) (Buchel et al., 1998). These effects are either absent or markedly less pronounced in individuals who develop sensory impairments later in life (Bavelier & Neville, 2002).

These are, in themselves, impressive examples of neuroplasticity, but not specifically of cross-modal plasticity, for which we should additionally expect evidence of activations in regions of sensory cortex linked to the congenitally damaged sensory system. Early evidence of this came from a PET study of Braille readers (Sadato et al., 1996). The researchers reported enhanced activation in both primary and secondary *visual cortex* in congenitally blind Braille readers, though

not in sighted but blindfolded Braille readers. Moreover, simple non-Braille tactile stimuli failed to recruit these regions in any respondents. The functional significance of these findings was later tested by the same group (Cohen et al., 1997). They showed that the application of TMS (see Chapter 2) to occipital cortex interfered with efficient Braille reading for the blind respondents, strongly hinting that they were recruiting visual cortex to facilitate the tactile skill of reading Braille. Incidentally, equivalent findings of enhanced activation in auditory cortex to visual stimuli in profoundly deaf individuals were reported by Finney, Fine, and Dobkins (2001). These studies *do* provide evidence consistent with cross-modal plasticity.

More recently, both Fine et al. (2005) and Lambertz et al. (2005) have provided further evidence consistent with cross-modal plasticity in deaf people. In the former study, activations in right *auditory* cortex were apparent in congenitally deaf adults viewing a moving peripheral *visual* stimulus, although it should be noted that the areas in question (BA 41, 42, and 22) are known to be involved in the perception of *auditory* motion in intact individuals. In the latter study, deaf participants familiar with German sign language showed increased fMRI activations in their auditory cortex (BA 42 and 22) when viewing videos of people signing. In other words, visual input activated auditory cortex. Bringing the debate up to date, Ptito et al. (2005) used PET to show that a tactile stimulus applied to the tongue (the so-called Snellen task) could, after a short period of training, lead to activations in occipital cortex in a group of blind people, but not in a matched group of sighted controls.

INTERIM COMMENT

To the evidence cited above in support of cross-modal plasticity in humans with particular long-standing sensory deficits, we might add a wealth of experimental data from well-controlled animal studies, which are also consistent with it (e.g., Kahn & Krubitzer, 2002; Lee, Lo, & Erzurumlu, 2005). However, the existence of this type of neuroplasticity remains a matter of debate for the following reasons:

- First, there is a possibility that the recorded activity in the "wrong" cortex is an ephiphenomenon brought about by disinhibition, rather than a genuine functional effect. In other words, it is irrelevant activity that would normally be inhibited in non-sensory-impaired individuals. However, Cohen et al.'s study would tend to count against this.
- Second, the activations may be functionally relevant, but only in so far as they reflect the use of mental imagery: i.e., the blind person uses visual imagery to perceive the configuration of dots and lines that make up the Braille figures. This is hard to discount but runs counter to subjective reports of some blind people who claim never to use/experience visual imagery.
- A third problem is that we presently have no hard evidence of the formation of new connections or pathways into "wrong" cortical regions: Supporters of cross-modal plasticity simply assume either that existing minor pathways are strengthened or silent pathways are activated—the speed of change observed in the Ptito study (over 1 week) favours the latter explanation over the former. However, the reality is that cross-modal

plasticity will stand or fall only when DTI (tractography; see Chapter 2) has been used to look for the presence of new functional connections between sensory inputs and the "wrong" regions of sensory cortex.

NEUROPLASTICITY AND PHYSIOTHERAPY

Physiotherapy aims to restore body function that has been lost through disease, injury, disability, or ageing. The therapist will probably employ a raft of techniques to achieve this: exercise, massage, manipulation, and increasingly, technological procedures such as ultrasound. Often, the problem may be muscular or skeletal (and thus of little interest to the neuropsychologist): for example, the need to build up muscle strength or develop greater joint flexibility following a period of enforced inactivity. Increasingly, however, physiotherapists will be called on to help people rehabilitate after brain damage or disease that might, at one time, have been fatal. (Up-to-date figures in this area are hard to come by, but even 14 years ago in the US alone, Dobkin (1993) estimated there were 300,000 survivors of stroke and 100,000 survivors of traumatic brain injury each year.)

Physiotherapy research has, for the most part, tended to be about optimising practical outcomes rather than developing neuropsychological models to explain its efficacy. However, Randolph Nudo is a pioneer of a more experimental approach to physiotherapy for brain injury, and his work merits attention in the present context. One of his enduring interests has been recovery of function following circumscribed (small, localised) strokes. These typically lead to a permanent loss of tissue in the vicinity of the stroke itself, and a ring (sometimes called a penumbra) of adjacent tissue whose functioning, while initially compromised, may recover over time (the phenomenon of depressed but redeemable functioning is referred to as **diaschisis**). To examine this issue experimentally, Nudo et al. (1996) dealt not with human stroke victims, but with animals in which localised strokes were deliberately induced by manipulating blood supply to the "hand" area of the motor cortex. Five days later the researchers initiated a regime of "physiotherapy" in which the stroke-induced monkeys had to pluck hundreds of tiny food pellets from different-sized containers for several hours each day. Exercise was associated with both a greater recovery of function in the affected hand and with a reduction in the amount of long-term damage (tissue loss) in the penumbra region adjacent to the stroke site. These experimental findings are represented schematically in Figure 4.10.

A second example of research linking physiotherapy and neuroplasticity is the study by Weiller and Rijntjes (1999) (see Taub, Uswatte, & Elbert, 2002) employing "constraint-induced" therapy. The rationale for this study was that during development neurons seem to be in a form of competition, with active ones surviving at the expense of inactive ones. The researchers reasoned that if the same situation prevailed after brain damage, some inactive neurons may die simply through lack of use. They therefore sought to promote recovery of function in a limb in which movement was compromised following unilateral stroke, by "forcing" the recovering patient to use it (the unaffected limb would be tied up or otherwise immobilised in a sling). Even after just 2 weeks of constraint, functioning in the affected limb improved significantly, and there was a noticeable functional increase in the area of motor cortex controlling it. That is, enforced practice led to improved behavioural functioning which corresponded to increased

KEY TERM
Diaschisis: Sudden loss of function in a region of the brain connected to, but at a distance from, a damaged area.

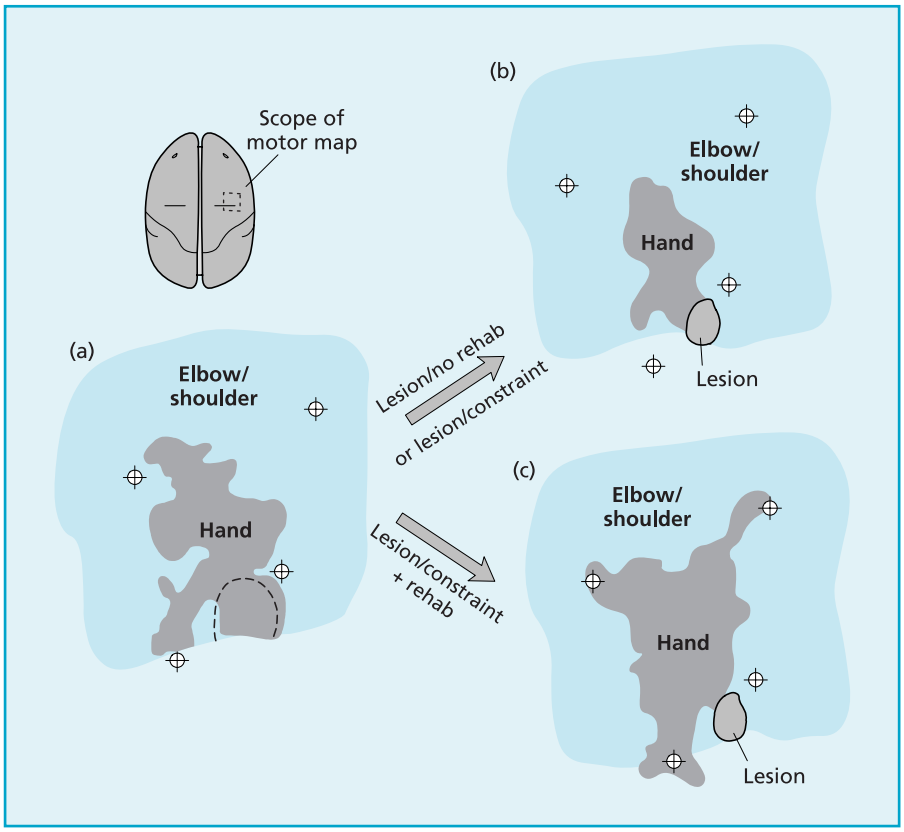


FIG. 4.10 The effects of physiotherapy on cortical remapping in monkeys with experimentally induced strokes (Nudo et al., 1996). Functional mapping of the spared motor cortex adjacent to the location of induced stroke reveals expansions of motor representations of the hand area related to the rehabilitative task + constraint of the unaffected hand (lower right figure), compared to "control" animals (upper right figure). Source: Nudo, R. J., Milliken, G. W., Jenkins, W. M., and Merzenich, M. M. (1996). Use dependent alterations of movement representations in primary motor cortex of adult squirrel monkeys. *Journal of Neuroscience, 16*, 785–807. © 1996 by the Society of Neuroscience, reproduced with permission.

functional activation in motor cortex. Landers (2004) has provided a succinct review of this line of research. A variant of constraint-induced therapy in which patients are strongly discouraged from using partial or para-linguistic utterances rather than "proper" verbal communications has also been shown to be effective in speeding up recovery of function in stroke-induced aphasic individuals (Pulvermuller et al., 2001; Wittenberg et al., 2003).

OTHER EXAMPLES OF NEUROPLASTICITY

Browsing through this book, readers will come across several other examples of observed (or inferred) neuroplasticity. To avoid duplication, we simply list some of these here, identifying the relevant chapter(s) for reference.

- The relocation of language function in individuals with localised or generalised left hemisphere damage in childhood (Chapter 3).

- The development of rudimentary language skills in the right hemisphere of split-brain adults post-surgery (Chapter 3).
- The functional and structural enhancement of remaining commissures in individuals with callosal agenesis (Chapter 3).
- The compensatory actions of surviving nigro-striatal dopamine cells in the pre-symptomatic stages of Parkinson's disease (Chapter 5)
- The control of prosthetic limbs using the BrainGate set-up (Chapter 5).
- Behrmann et al.'s (2005) fMRI study of remedial training of an agnosic individual, indicating that behavioural improvement was accompanied by functional reorganisation in the fusiform gyrus (Chapter 8).

THE PLASTIC BRAIN: A DEVELOPING PICTURE

As we have already mentioned, a long-standing view in neuropsychology held that the brain was, essentially, a "hard-wired" organ: its structure and connectivity genetically pre-determined and, once mature, immutable (except, of course, for age- or disease-related loss of tissue). Rare observations running counter to this viewpoint were, for the most part, accounted for by the idea of **critical periods** early in development where some flexibility may, under extreme circumstances, be possible. How things have changed: The genetic blueprint certainly exists, but what it lays out is not a fixed wiring diagram, but a plan for a highly flexible dynamic system whose components (neurons) are capable of sustaining enduring functional changes and probably enduring structural changes too. Certainly, scope for flexibility may be greatest during development, but more limited neuroplasticity seems possible at some sites well into adulthood, and even old age (Buonomano & Merzenich, 1998).

Even the long-held view that the brain cannot generate new neurons once it is fully developed now requires revision following recent discoveries of **neurogenesis** in adult hippocampus and olfactory bulb, albeit in rodents. A detailed review of this research is beyond the scope of our text but interested readers might wish to browse papers by Cameron and McKay (2001), Brown et al. (2003), and Ziv et al. (2006) for more information. When Merzenich, Kaas, and colleagues first described S1 neuroplasticity, two mechanisms were mooted to explain it: axon sprouting and disinhibition (freeing of silent synapses). As with neurogenesis, evidence of these processes is now well documented in animals (O'Leary, Ruff, & Dyck, 1994; Sengelaub et al., 1997) although not explicitly yet in humans, where they remain putative rather than established mechanisms. Mogilner et al. proposed the freeing of "silent synapses" as the most likely explanation of the rapid remapping observed in his syndactyly cases, and Ramachandran evoked the same mechanism to explain the rapid development of "phantom" experiences in amputees.

To this list of possible mechanisms of neuroplasticity we can now add a fourth, related to changes in dendritic structure of cortical neurons. Working with rodents, Hickmott and Steen (2005) have shown that peripheral denervation (severing sensory inputs) in rats leads to rapid changes (within 4 weeks) in the **arborial structure** of dendrites of neurons in S1, presumably reflecting loss of some synaptic inputs and the gaining of others during remapping.

Finally, our list would not be complete without mention of **long-term potentiation** (LTP) which refers to enduring changes in the functional connectivity

KEY TERMS

Critical periods: The early stages of an organism's life during which it displays a heightened sensitivity to certain environmental stimuli, and develops in particular ways.

Neurogenesis: The process by which neurons are generated.

Arborial structure: The branching pattern of neuronal dendrites.

Long-term potentiation: The enduring increase in functional activity (at synapses) that may be related to memory storage in the brain.

between neurons (strengthening of synaptic connections) mediated by changes at glutamate synapses (Bliss & Lomo 1973; Sheng & Kim, 2002; and see Appendix). This mechanism is thought to underpin some aspects of both long-term memory (see Chapter 7) and long-term changes in pain sensitivity (allodynia) in which, for example, innocuous stimuli can invoke extreme discomfort following nerve damage (Svendsen, Tjolsen, & Hole, 1998). In sum, we now have several possible neurobiological mechanisms to explain the functional changes seen in studies of neuroplasticity A key task for researchers in coming years will be to establish which of these mechanisms underpins the various examples of functional plasticity that we have reviewed.

However, to complete the picture, alongside these (and other) examples of neuroplasticity, we must consider instances of behavioural plasticity: deliberate adaptive changes to achieve the same (or similar) outcome by alternative means, either in the face of adversity or simply in response to change. Humans are, arguably, the most resourceful of all animals, and countless examples of behavioural adaptation attest to this. The ability of deaf people to communicate effectively with one another using sign language is one obvious example.

CHAPTER SUMMARY

Somatosensation depends on a polymodal sensory system handling exteroceptive information about touch, pressure, and vibration, and interoceptive information from muscles and joints. It also deals with temperature and pain. The sensory input is garnered from at least 20 different types of receptor located predominantly in the skin or muscles, and each relays sensory information in the form of frequency-coded volleys of action potentials via one of two major afferent pathways—the dorsal columns and the spinothalamic tracts—towards the brain. Much of this sensory input is received by S1, which is a topographically organised gyrus at the front of the parietal lobe, along which the entire body is, in effect, mapped contralaterally and upside-down. Further bilateral and higher-order perceptual processing is undertaken in S2 and posterior regions of parietal cortex.

Despite its highly consistent topography S1 can, under certain circumstances, undergo quite marked functional changes. Initially it was thought that this capacity was only present in the immature nervous system, but further investigation has confirmed that plasticity can also be observed in "adult" mammalian nervous systems under certain circumstances, even after relatively short periods of "changed" input. One particular example of functional plasticity is thought to be responsible for some of the features of the phantom limb phenomenon. After injury, it appears that input from body regions mapped cortically adjacent to the missing limb can invade and "innervate" the cortex attendant to the missing limb and evoke phantom limb experiences. However, other mechanisms contribute to the overall experience too.

Neuroplasticity is by no means restricted to primary somatosensory cortex and, under appropriate circumstances, can also be observed in primary motor, auditory, and visual cortices, and subcortical structures too. There is additional evidence to support the idea of cross-modal plasticity although it is difficult to completely rule out alternative explanations at present. Recent research has strongly hinted that the success of physiotherapy following brain injury/damage is underpinned by neuroplastic changes.

Five neurobiological mechanisms have been proposed to explain neuroplasticity: neurogenesis, axonal growth and sprouting, the freeing of silent synapses, changes in dendritic structure (and by implication, changes to the pattern of synaptic inputs), and synaptic plasticity itself, as exemplified by LTP.

CHAPTER 5

CONTENTS

5

Motor control and movement disorders

INTRODUCTION

The psychological study of overt behaviour is, substantially, the study of movement. But even if you were just imagining movements, you would be activating many of the same brain regions that become active during *actual* movement (Roland, 1993). For all of your waking lives, "behaviour" is fundamentally and inextricably linked to action, whether of discrete muscles in our mouth and throat to bring about spoken language, or of massive muscle systems in our trunk and limbs giving rise to the movements required to approach and then hit a tennis ball.

There is no escaping the fact that the nervous system's control of movement is complex: it has to be in order for individuals to engage successfully in behaviours requiring precise muscle coordination. Think, for example, of the skill of a trained acrobat or the dexterity of a concert pianist. Yet skilled movement is something that most of us can develop with a little practice. When considered objectively, riding a bicycle is quite clever, so too is touch-typing, and even tying a shoelace requires bimanual coordination of a series of accurately timed precise movements.

Movement is possible only through the control of "skeletal" muscles (muscles attached to bones). These are under voluntary control and can obviously stretch, but this is a passive process: movement only occurs when muscles are made to contract. In all mammals, the contraction results from the release of the neurotransmitter acetylcholine from the terminals of motor neurons, although there will, of course, be passive expansion of any "opposor" muscles. The cell bodies of motor neurons are to be found in the spinal cord. They are controlled by a variety of descending neurons from the brain and some ascending neurons in the cord itself, and whether or not they fire will depend on the summed influence of inputs (both excitatory and inhibitory) on them. But to understand the control of movement we need to work backwards: to examine the origin of the inputs that can influence motor neurons.

For many years it was thought that intentional (voluntary) movement was under the direct control of the motor cortex via the so-called pyramidal system, and that all other movement was controlled by a separate so-called extrapyramidal system and/or the spinal cord itself. But, as usual, the true picture turns out to be rather more complicated. First, there are not one but several pathways

from different parts of the cortex to the spinal cord, and thus to the cell bodies of motor neurons. Second, in the brain itself there are several regions that are involved in the control of movement: the frontal lobes of the cortex, the subcortical structures of the basal ganglia, and the cerebellum, to name but three. Finally, there is good evidence that the parietal lobes, traditionally associated with various sensory and perceptual functions, may also be important in certain kinds of motor function. Our review of the nervous system's control of movement must give due consideration to all these components, and should also take into account certain characteristic movement disorders linked to nervous system damage or disease.

BRAIN–SPINAL CORD PATHWAYS

Although neurons in the cortex do not make direct contact with muscles, it has been known since the pioneering work of Fritsch and Hitzig (1870) that electrical stimulation of the brain can rapidly induce movement. In fact, there are at least four major tracts from the brain that can convey nerve impulses about movement (see Figure 5.1), and we need to consider briefly the specialised roles of each in turn.

THE CORTICOSPINAL TRACT

As the name suggests, this pathway comprises neurons whose cell bodies are found in the cortex (mainly the primary motor strip, also known as M1). This strip is the most posterior gyrus of the frontal lobes, and is located immediately forward of the primary somatosensory cortex (S1) on the other side of the central sulcus. Like S1, the motor strip is highly topographically organised. The axons of pyramidal neurons in this region descend within the brain to the medulla, where most cross (decussate) to the opposite side, before continuing into the spinal cord to synapse with motor neurons. These then relay the impulses to the muscles themselves. Actually, this pathway comprises two functionally distinct tracts: the "lateral" tract helps to control distal muscles (in the forearm, lower limb, hand, and fingers) mainly on the opposite side of the body, while the "ventral" tract controls more medial muscles (in the trunk, upper limbs, and so on) on both sides. Damage to the former will compromise skilled movement involving hands or fingers; damage to the latter will affect posture and ambulation.

THE CORTICOBULBAR PATHWAY

This pathway also has its origins in the primary motor strip, although the axons descend no further than the pons where they innervate some of the cranial nerves to control facial, mouth, and tongue muscles. Projections to the upper part of the face tend to be bilateral, whereas those to the lower face and mouth regions tend to be contralateral: you can, for example, easily raise one side of your mouth, but it is harder to raise one side of your forehead.

THE VENTROMEDIAL PATHWAY

Once again, this pathway actually comprises several interlinked tracts, but unlike the corticospinal tract and corticobulbar pathways, the point of origin of each

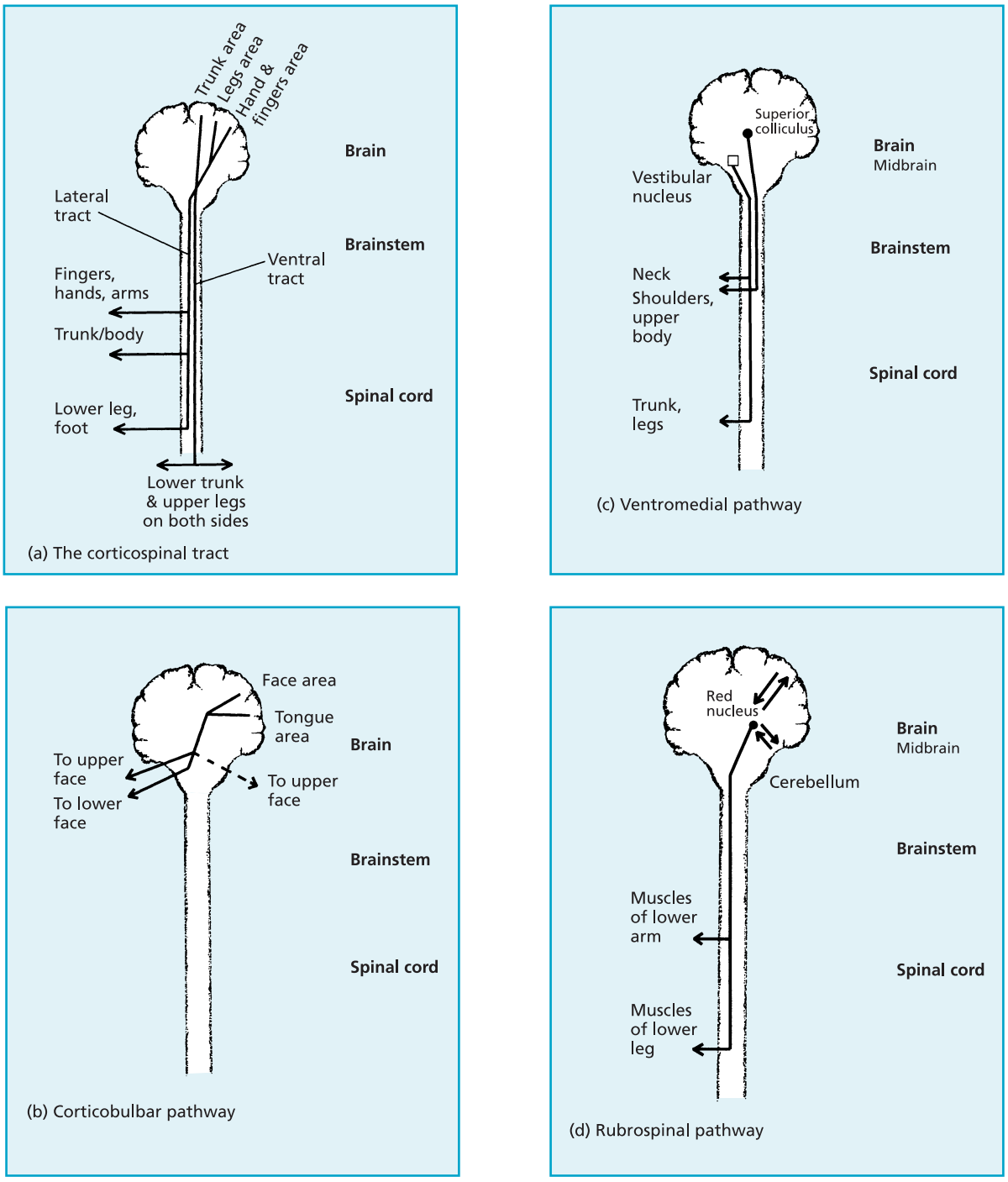


FIG. 5.1 Descending "movement" control pathways. (a) The corticospinal tract originates in the primary motor strip and comprises a "lateral" component to control distal muscles on the opposite side of the body, and a "ventral" component that controls medial muscles in the trunk and upper limbs on both sides. (b) The corticobulbar pathway also originates in the primary motor strip, sending axons to innervate some of the cranial nerves in the pons to control facial, mouth, and tongue muscles. (c) The ventromedial pathway comprises several interlinked tracts that originate in the brainstem or midbrain and project to trunk, shoulders, and neck. This pathway is concerned with body posture and balance, and the coordination of various automatic processes such as sneezing, breathing, and so on. (d) The rubrospinal pathway. In non-humans this pathway runs from the red nucleus of the midbrain to distal limb muscles (excluding fingers) to coordinate movement of limbs independent of movements of trunk. The functional significance of this pathway has been questioned in humans.

component is in the brainstem or midbrain rather than the cortex, and projections terminate in proximal (i.e., close to midline) muscles in the trunk, shoulders, and neck. One component whose cells originate in the superior colliculus is important for coordinating eye movements in relation to body posture. A second component whose cell bodies reside in the vestibular nuclei of the brainstem helps to coordinate balance. Other brainstem components coordinate relatively automatic processes such as sneezing, breathing, and so on.

THE RUBROSPINAL PATHWAY

The point of origin of this pathway is the red nucleus of the midbrain, which receives inputs from both the motor cortex and the cerebellum (with which it has reciprocal connections). The main projections, however, are to distal limb parts (excluding fingers), and the primary function of the tract is thought to be the movement of limbs independent of movements of trunk. The importance of this pathway in humans has come into question because, in comparison with other primates, and especially other mammals, the size of the red nucleus is small, and the axons of the pathway are unmyelinated.

INTERIM COMMENT

Earlier we introduced the terms "pyramidal" and "extra-pyramidal" to delineate two separate systems of motor control. Although these terms have, to some extent, fallen into disuse (because they oversimplify the organisation of motor control both in the brain and the spinal cord) it is easy to see how the distinction came about in the first place. Two major descending pathways link the motor cortex to muscles in different body regions in a fairly direct way, and two other pathways (which in the case of the ventromedial system may be further subdivided) act on muscles in an indirect or more automatic way. Incidentally, the pyramidal tract got its name from the wedge-shaped structures that are visible in the brainstem at the point where the axons decussate to the contralateral side. Fibres that did not form part of this pathway were "extra-pyramidal". Today, a more useful distinction (supported by lesion studies) is that between lateral and medial pathways. Animals with lesions to lateral pathways lose the ability to engage in skilled digit coordination (such as reaching for food), whereas animals with ventromedial lesions manifest enduring postural and whole body movement abnormalities (Kuypers, 1981).

THE CEREBELLUM

This structure accounts for at least 10% of the brain's complement of neurons yet, perhaps because it lies outside the cortex, it has received relatively little attention until recently. Two vital observations should be noted at the outset. First, although this structure is now known to be involved in a range of psychological phenomena (such as learning, and self-monitoring) in addition to movement, its pivotal role in movement coordination is unquestioned. In the higher mammals at least,

the cerebellum is fundamentally involved both in the modulation of motor coordination and the acquisition of motor skills. This is made possible by the large number of reciprocal connections between the cortex and parts of the cerebellum. Second, we should note that a quirk in the nervous system's wiring diagram (the right side of the cerebellum connects to the left cortical hemisphere, and the left side to the right cortex) means that the cerebellum influences motor control on the **ipsilateral** side, so right-sided damage affects movement on the right side of the body. We consider some of the deficits associated with cerebellar damage in due course. First, we need to summarise the key anatomical regions and functional components of the structure.

CEREBELLAR STRUCTURE

The cerebellum vaguely resembles (and is about the same size as) two walnuts connected to each other and, via two short stalks, to the brainstem in the pons region. The structure is bilaterally symmetrical, and each hemisphere comprises a highly regular neuronal structure. In fact, the cerebellum contains just four different neuron types. The innermost (medial) regions of each hemisphere comprise the vermis. This region receives somatosensory and kinaesthetic information from the spinal cord. The next region (moving outwards) is the intermediate zone. This region receives information from the red nucleus, and returns output to it. Finally, the lateral zones (the left and right outer sections of the cerebellum) receive information from motor and association cortex. Embedded deep within the cerebellum on each side are three nuclei. The vermis projects to the fastigial nuclei, which in turn influence medial descending motor systems. The intermediate zones project to the interpositus nuclei, which influence lateral descending motor systems. The lateral zones project to the dentate nuclei, which in turn project to motor and premotor cortex, and these regions are thought to be involved in motor planning (see Figure 5.2).

CEREBELLAR FUNCTIONS IN HUMANS

In view of its somatosensory inputs and its descending medial outputs, we should not be surprised to learn that damage to the vermis is likely to affect balance and posture, and may lead to a person staggering or even falling over as they try to carry out some simple movement such as bending to pick up an object. Damage to the intermediate zone gives rise to a phenomenon known as "intentional tremor": an action can still occur, but the execution of it is jerky or staggered. This observation reinforces the view that a normal function of the intermediate zone is to "smooth out" otherwise poorly coordinated actions, especially of the distal regions of limbs.

Damage to the lateral zones also affects movement of limbs, especially for tasks that require complex muscle coordination (sometimes called "ballistic" movements) over a short period of time. This type of skilled movement requires the concerted and temporally organised action of many muscles, but in a particular sequence that is too quick for the action to be modified by feedback. An excellent example would be a well-practised tennis serve, or playing a scale on the piano. After lateral damage the movement may still be attempted, and even completed, but instead of being smooth and well rehearsed, it is tentative and often inaccurate. The more joints involved in the action, the worse the deficit seems

KEY TERM
Ipsilateral: Same-sided. An unusual anatomical "wiring" arrangement in which brain function is linked to behaviour function on the same side (the norm being contralateral or opposite side control).

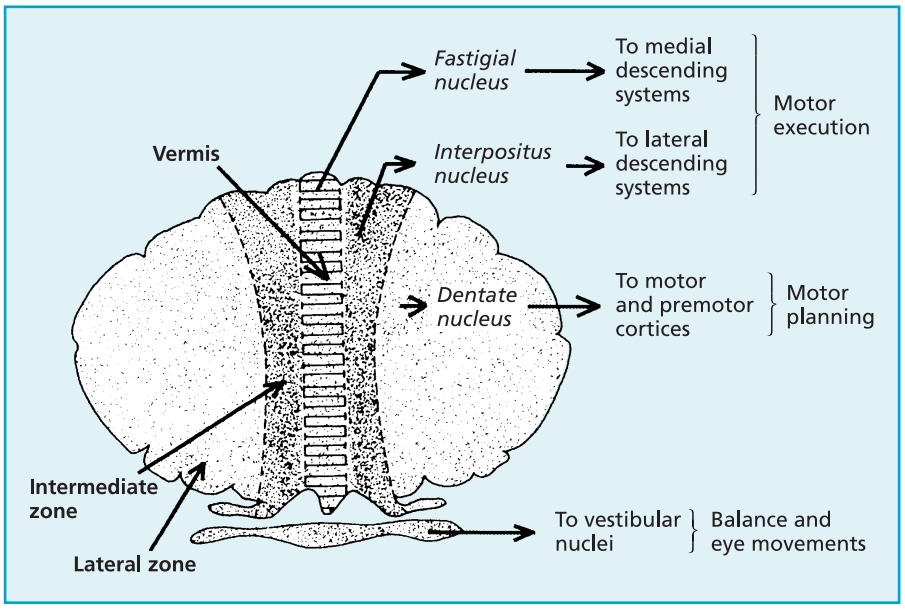


FIG. 5.2 The cerebellum and its connections. Output from the vermis influences medial descending systems to affect motor execution. In similar vein, output from the intermediate zone affects more lateral descending systems. Output from the lateral zone is primarily to the frontal lobes. The lateral zone is thought to be involved in motor planning, particularly in relation to responding to external stimuli. (Adapted from Kandel et al., 1991.)

to be. Moreover, it will probably not improve much with practice because people with this type of brain damage are not only clumsy, they also find it difficult to learn new motor skills.

INTERIM COMMENT

The cerebellum (translation, "little brain") can be subdivided into three anatomically separate regions. These can also be distinguished in terms of inputs and outputs: the medial regions modulate and "smooth out" movements initiated elsewhere, whereas the lateral regions coordinate skilled movements enacted "in time". The cerebellum is involved in a wide range of motor skills including balance, posture, multi-limb movement and, of course, the acquisition and enacting of ballistic movements. It is important to realise that damage to the cerebellum does not eliminate movement per se: rather it seems that tasks that were once effortless become a struggle after cerebellar damage. A modern-day take on the functions and modus operandi of the cerebellum is provided by Ohyama et al. (2003)

KEY TERM
Subcortical: The portion of the brain immediately below the cerebral cortex.

THE BASAL GANGLIA

These are a group of **subcortical** structures that connect with each other and the cortex in a series of at least five parallel "closed loops" first characterised by

Alexander, Delong, and Strick (1986). They also have important reciprocal connections with various brainstem and midbrain structures (McHaffie et al., 2005). Because of the likely involvement of the basal ganglia in a raft of conditions and disorders of interest to the neuropsychologist, in the following sections we pay particular attention to their circuitry and functionality.

BASAL GANGLIA COMPONENTS AND CIRCUITRY

Earlier we described the brain's control of movement as complex; this is the moment where our case is proved! Each of Alexander et al.'s circuits originates from, and ultimately returns output to, a particular region of cortex. The routing of these circuits through the basal ganglia is substantially parallel but segregated, hence the authors' reference to "closed loops". Actually, the segregation is relative rather than absolute as there is evidence of (some) "cross-talk" between them, but it is easier to understand their functions if we think of them as working independently. Readers wanting to know more might refer to a concise review of this circuitry by Tekin and Cummings (2002). A simplified description of the anatomy and possible functions of the cortical → basal ganglia → cortical circuits is provided in Box 5.1.

Box 5.1 Alexander, DeLong, and Strick's taxonomy of closed cortical → basal ganglia → cortical loops

Motor loop

- originates in the supplementary motor area (SMA);
- inputs (mainly) to the putamen;
- then the internal segment of the globus pallidus;
- then the thalamus and back to the SMA.

Main function: The initiation, maintenance, and switching of actions.

Oculomotor loop

- originates in the frontal eye fields (FEFs) region of the frontal lobes;
- inputs mainly to the caudate nucleus;
- then the internal segment of the globus pallidus;
- then the thalamus and back to the FEFs;
- an output also travels from the substantia nigra pars reticulata (SN-pr) directly to the superior colliculus.

Main function: The direction of voluntary (and probably involuntary) eye movements.

Dorsolateral prefrontal loop

- originates in the dorsolateral prefrontal cortex (DLPFC);
- inputs to the caudate nucleus;
- output travels to the internal segment of the globus pallidus;
- then to the thalamus and back to the DLPFC.

Main function: Probably related to the maintenance of spatial working memory and other executive functions, shifting sets, and temporal ordering of recent events.

Orbitolateral loop

- originates in the lateral orbitofrontal cortex;
- and inputs to the caudate nucleus;
- output travels to the internal segment of the globus pallidus;
- then to the thalamus and back to the orbitofrontal region.

Main functions: Switching/inhibiting behaviours, perhaps including the inhibition of inappropriate behaviours in relation to social setting. Possibly also involved in empathy and imitation.

Limbic loop

- originates in the anterior cingulate area (plus additional inputs from the hippocampus, entorhinal cortex, and amygdala);
- inputs to the ventral striatum (especially the nucleus accumbens);
- output travels to the internal segment of the globus pallidus;
- via the thalamus and back to the limbic cortical regions.

Functions remain vague but likely to involve selection of emotional expression(s) or tone, and motivated behaviour.

Before delving any deeper, we suggest that a working understanding of what follows may more easily be achieved if you think of an excitatory effect as one that encourages activation in the "innervated" tissue, whereas an inhibitory effect tends to reduce activation in "innervated" tissue (sometimes likened to an accelerator and brake effect respectively). Incidentally, and critical for the following discussion, inhibition of an inhibitory neuron or pathway will probably give rise to a "net" excitation because, in our simple terms, the "brake" itself would be inhibited (i.e., be less effective).

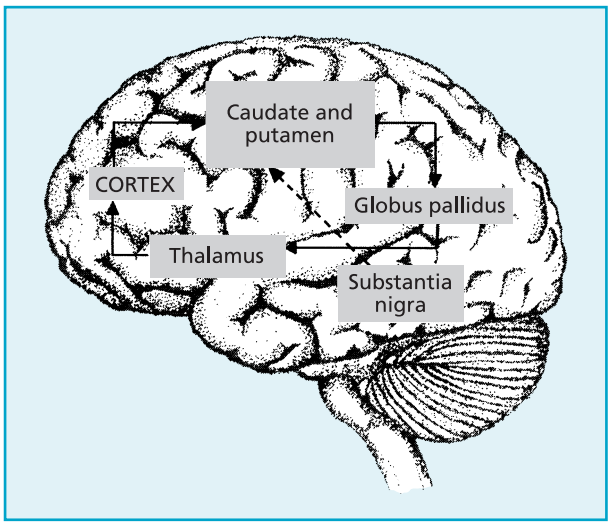


FIG. 5.3 Components and connections of the basal ganglia. The structures form a series of loops with the frontal cortex (particularly the supplementary motor area). A current idea is that plans and intentions for movement are channelled through the basal ganglia prior to being put into effect. The overall excitability of the basal ganglia can be influenced by release of dopamine from neurons originating in the substantia nigra (dotted line in figure). (Adapted from Wichmann & Delong, 1996.)

Returning to the main theme of this section, the principal components of the basal ganglia include the caudate, putamen, and ventral striatum (referred to collectively as the striatum), the internal and external segments of the globus pallidus, the subthalamic nucleus, and the substantia nigra, which actually divides into a pars compacta (SN-pc) and a pars reticulata (SN-pr). The former has reciprocal connections with the caudate and putamen whereas the latter projects outside the basal ganglia to contribute to the control of head and eye movements. (see Figure 5.3). The main inputs to the striatum are excitatory, chiefly via the closed loops from the frontal lobes identified in Box 5.1. Generally (and simplistically), it is possible to distinguish between the cognitive-limbic inputs which tend to project preferentially to the caudate and ventral striatum, and motor inputs which project more to the putamen. As

mentioned above the striatum also receives both excitatory and inhibitory inputs from the SN-pc, and a further excitatory input from the thalamus. For good measure, both excitatory and inhibitory interneurons are found in the striatum itself.

The caudate and putamen send outputs to inhibit the globus pallidus, whose principal output to the thalamus is also inhibitory (remember that inhibition of an inhibitory relay usually leads to net excitation). One path additionally diverts to innervate the subthalamic nucleus (of which more below). The final part of each pathway is an excitatory output from one of the thalamic nuclei back to the frontal lobes, and a smaller output direct to the spinal cord. However, at rest, we might fairly characterise the activity level of the striatum as quiescent (low). This will of course change depending on the balance of inputs mentioned above. In this respect the SN-pc is particularly important because it has the ability to modulate the overall activity of the striatum.

KEY TERMS
D_1 receptors: A class of dopamine receptor found particularly in the frontal lobes and striatum.
D_2 receptors: Another class of dopamine receptor found particularly in the striatum and pituitary.

Direct and indirect routes

If this is not already sufficiently complicated, a further twist is that for each of the major parallel loops, two competing paths through the basal ganglia, known as the direct and indirect routes, have also been proposed (Albin, Young, & Penny, 1989, 1995; and see Figure 5.4). The direct route is in fact well established, comprising a path from the striatum to the internal region of the globus pallidus, then on to the thalamus and back to the cortex. There are two serial inhibitory synapses (into the globus pallidus from the striatum, and from the globus pallidus into the thalamus), and then an excitatory output from the thalamus back to the cortex (the double inhibition effectively gives rise to an excitatory influence). Thus, activity in the direct route could be thought of as excitatory, enabling or facilitatory. In essence, in respect of motor function for example, *actions are more likely*.

Now consider the indirect route. There is an inhibitory output from the striatum into the globus pallidus (the external part this time), which in turn sends inhibitory outputs to the subthalamic nucleus (double inhibition again). But this structure exerts an excitatory effect on the internal region of the globus pallidus, which we know (from the direct route circuitry) tends to inhibit the thalamus, so if the indirect route is active, the overall effect will be inhibitory and, in terms of the motor loop, *actions will be less likely*. The precise functional role of this route has recently been questioned (Redgrave, Prescott, & Gurney, 1999) and redefined as a "control" route rather than an

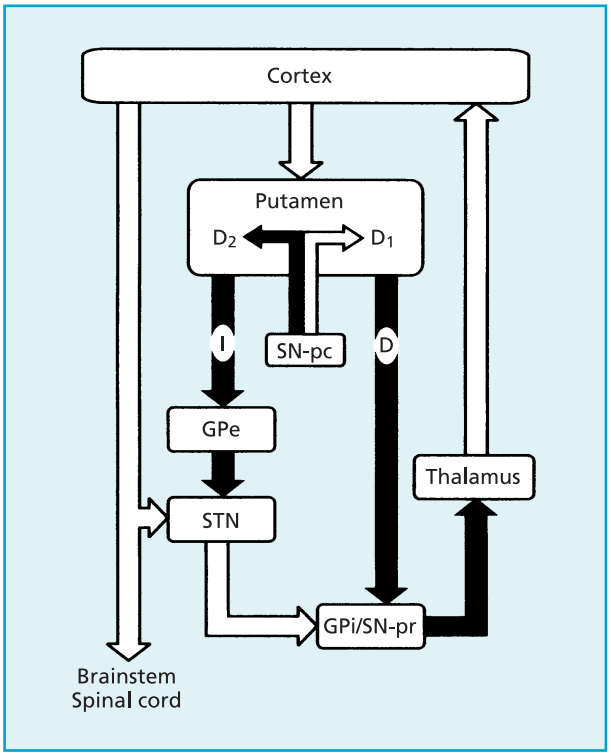


FIG. 5.4 Direct and indirect basal ganglia pathways. Activation of the direct (D) pathway permits selection of a desired action. The exact function(s) of the indirect (I) pathway are currently under review. However, activation of this route, either via the striatum to STN path or directly via cortical control of the STN, appears to put "on hold" possible alternative actions, and put a "brake" on current actions, respectively. (Key: GP = globus pallidus; STN = subthalamic nucleus; SN = substantia nigra; white arrows indicate excitatory influences and black arrows indicate inhibitory influences.)

"inhibitory" alternative to the direct route by Wood, Gurney, and Redgrave (2001). Whatever functions are eventually attributed to it, activation in this indirect route will tend to put a rapid "brake" on ongoing actions.

The final piece of this complicated jigsaw is that dopamine release into the striatum from neurons originating in the SN-pc has opposite effects on the direct and indirect routes: it stimulates the direct route by exciting **D_1 dopamine receptors**, while inhibiting the indirect route by stimulating **D_2 receptors** (Wichmann & DeLong, 1996). In other words, in the motor loop, the net effect of dopamine release into the striatum is to promote actions by simultaneously activating the direct route and inhibiting the indirect route.

BASAL GANGLIA FUNCTIONS

That the basal ganglia are important in movement now seems self-evident although there is still no firm agreement on the extent of basal ganglia influence. An early model held that they were concerned primarily with slow medial postural adjustments, because people with basal ganglia damage sometimes have "writhing"-like movements or other postural disturbances. Another idea was that the basal ganglia were important for initiating movements: damaged individuals sometimes struggle to start movements but are OK once they get going. However, recent research has indicated far more extensive roles for the basal ganglia, for they are ideally placed to selectively enable certain actions/behaviours (via the direct route) while holding others in check. Moreover, a direct excitatory influence from the cortex into the subthalamic nucleus provides a means for rapid termination of an action or actions that were being "enabled" by the direct route. As Grillner et al. (2005) comment, being able to terminate an action with precision is probably as important as being able to initiate one. The basal ganglia are thus able to select and promote particular actions/behaviours, but rapidly terminate these, if necessary, to enable alternative actions to be implemented. We have provided a (simplistic) example of the selective and switching capacity of the basal ganglia in Box 5.2. A modern view of basal ganglia function, based on more extensive neurological investigation in human disease (which we review below) and experimental studies with animals, is that they operate rather like a "gatekeeper" for behavioural action plans locked away in the frontal lobes (Bradshaw & Mattingley, 1995). The upshot of the arrangements described above (and illustrated in Figure 5.5) is that the direct loop effectively works as an "enabling" mechanism that, if active, facilitates ongoing or preferred activity. This regulatory function is supported by the observation that electrical activity in the basal ganglia increases in anticipation of, rather than initiation of, intended movements, and again as movements are about to be terminated (Steg & Johnels, 1993).

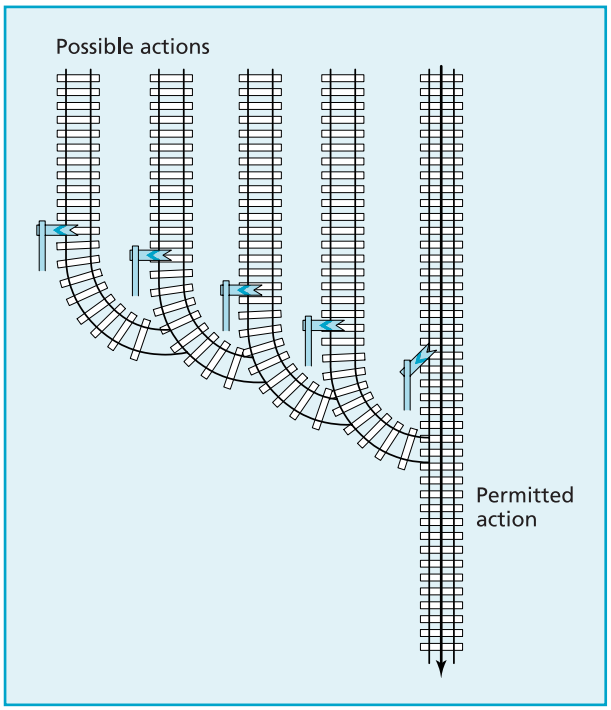


FIG. 5.5 The basal ganglia as facilitators/inhibitors of action plans. Conceptually, we might think of the basal ganglia as facilitating selection of the appropriate movement by holding in check all but the most desired response.

According to Bolam and Magill (2004), an unresolved question concerns the funnelling of competing action plans from the cortex into the striatum, and the selection process that is presumed to occur there. This issue currently represents a major challenge for researchers.

Box 5.2 Approach–avoidance behaviour and the basal ganglia

A hungry animal is contemplating moving towards some food (perhaps another animal). It wants to approach the prey, but is anxious that other predators may be in the area. In the end, hunger dictates that it should approach the food; a movement plan for this is fed though the direct route, and the animal approaches. But, ever wary, it has an alternative escape plan at the ready should a predator show up. As the animal closes in on its prey, it notices a predator in its field of vision. Simultaneous cessation of dopamine release into the striatum and cortical influences on the subthalamic nucleus would enable rapid cessation of the approach behaviour, and the chance to switch to the avoidance plan which would now gain access to the direct route.

THE CORTEX

At one time, motor function (in the brain) was thought to involve all cortical tissue forward of the central sulcus—"the motor unit" in Luria's terms (1973). With more research, this view has required revision. First, it ignores the fact that the frontal lobes have various non-motor functions in addition to responsibilities for the control of movement (see Chapters 10 and 11). Second, it ignores the apparently critical role of parts of the parietal lobe, especially on the left side, in controlling movement in particular circumstances. Today, attention has turned to unravelling the relative responsibilities of different cortical regions in organising and controlling movement, and to trying to understand how these regions interact with each other and with the subcortical structures already mentioned. The emerging model remains essentially hierarchical; region A is controlled by region B which, in turn, is controlled by region C. But the further away from A one looks, the more abstract and widely distributed are the mental operations linked to movements. Researchers have, additionally, found it necessary to make the important distinction between internally generated movement and stimulus-driven or externally prompted movement.

THE MOTOR STRIP

As we have already mentioned, the primary motor cortex or motor strip (BA 4), like the somatosensory cortex, is highly topographically organised (also referred to as somatotopic organisation). In our analogy, this would be region A. All regions of the body that have voluntary muscles are represented, and there is predominantly contralateral control: the right motor cortex coordinates muscles in the left

side of the body, and vice versa. As with the somatosensory cortex, the relationship between cortical "space" in the motor strip and body region is not proportionate: there is over-representation of regions capable of fine motor control, such as the hands and fingers, and the mouth area of the face, and under-representation of less "movement-critical" regions such as the back and top of the head, the trunk, and the upper limbs. The axons of pyramidal neurons, whose cell bodies are found here, make up much of the corticospinal and corticobulbar pathways identified earlier.

With more precise instrumentation (basically amounting to finer electrodes), researchers have discovered that the primary motor strip comprises not one but several parallel bands of topographically mapped pyramidal neurons (as many as nine have been proposed). Moreover, Georgopoulos, Taira, and Lukashin (1993) have shown that muscles actually require a pattern of activity in several adjacent cortical cells in order to bring about movement. (Such patterns of activity are referred to as "population vectors", and understanding these has been critical in the development of prosthetic aids that can be controlled by brain activity. We briefly consider this exciting field or research in Box 5.3.) Georgopoulus et al.'s finding also explains why damage to one or a few pyramidal cells weakens, but rarely eliminates entirely, movement in the corresponding body region. However, it is also clear that more extensive damage to this region can bring about a widespread loss of muscle function and paralysis. In cases where accident or stroke has damaged the entire left or right primary motor cortex, the result is contralateral **hemiplegia**, which usually involves lasting impairments. In addition to his aphasia, Broca's "Tan" was hemiplegic on his right side.

KEY TERM
Hemiplegia: Loss of sensory awareness from, and muscle control of, one side of the body.

Box 5.3 Neural prosthetics and the "bionic man"

In recent years, the goal of achieving recovery of motor function in individuals with extensive damage to their nervous systems resulting from disease or injury has been pursued with renewed vigour. Recall that the outlook for someone with a broken neck is (currently) a life of quadriplegic paralysis (and loss of sensory input) that will probably include inability to breathe independently. The actor Christopher Reeve suffered such an injury when he was thrown from his horse, and lived the remainder of his life as a quadriplegic, although he did appear to regain very modest motor function some years after his accident. He campaigned tirelessly for more research into the nature of spinal injury and for the development of procedures to aid subsequent recovery.

Reeve became interested in neural repair—the promotion of growth of new connections in the nervous system to circumvent the loss of function caused by the traumatic event itself. He believed that this process was somehow activated in him by the intense physiotherapy he underwent, and that this perhaps unpinned his own modest degree of recovery. Although this approach is intriguing, progress has been slow, and Reeve's explanation remains an open question at present. The field of neural prosthetics represents an alternative but equally promising line of inquiry, which takes advantage of the rapid developments in computing, to bypass the area of injury altogether and connect brain to muscle via a microprocessor interface.

Recall that earlier we described muscle contraction (and hence movement) as depending on the collaborative actions of many primary motor strip neurons, to generate a so-called "population vector". This composite neural activity, rather than one or a few neurons acting in isolation, is what determines the force and direction of a particular movement. Obviously the motor strip contains millions of neurons and it is not currently possible to record individually all the neuronal activity here. However, researchers have found that a reasonable proxy for this activity can be gleaned from a sensor with about 100 microelectrodes in it.

An American company, "Cyberkinetics", has developed a system called BrainGate for this purpose (see Figure 5.6). It comprises a microelectrode array that has to be implanted so the electrode tips are in direct contact with the brain (usually a particular part of the motor strip), and a computer that "interprets" the recorded activity with a complex software algorithm (which generates quasi-population vectors). These can be used to drive either a cursor on a computer screen or a prosthetic limb.

Initially, researchers tested the system with primates, reporting on a series of monkeys with motor strip implants who could reach with a prosthetic limb to grasp food (their own limbs were restrained) (Schwartz, 2004). Most intriguingly, the monkeys were able to demonstrate "learning" through biofeedback on how to refine the limb's movements by modifying the firing patterns of the recorded neurons.

Then, early in 2006, a group led by Hochberg reported on two humans with the same implants. One was forced to drop out of the study for technical reasons but the other, known as MN, quadriplegic following a knife attack in 2001, has so far been able to use the cursor interface to open emails, do simple drawings, play video games, and adjust the volume and channel of his TV. When the system was linked up to a robotic limb, MN was able to open and close the hand, and grasp an object and move it from one location to another . . . all by imagining (or willing) the desired action that he had been unable to perform since his injury (Hochberg et al., 2006).

Obviously, these are very preliminary research findings and considerable work needs to be done to refine both the hardware and software of the BrainGate system. For example, there is currently intense research underway to identify other brain locations that may be better sources of motor control output than the motor strip; the posterior parietal lobe and the premotor cortex are two such candidate regions (Anderson et al., 2004). Progress will be slow but the concept of a bionic man or woman can no longer be written off as sci-fi nonsense!

The main inputs to the primary motor strip are bilaterally from BA 6 (see below). It also receives rather precise inputs from primary somatosensory cortex, which appear to be intimately involved in providing rapid feedback to motor neurons from, for example, sensory input during manual manipulation of objects (Evarts, 1974).

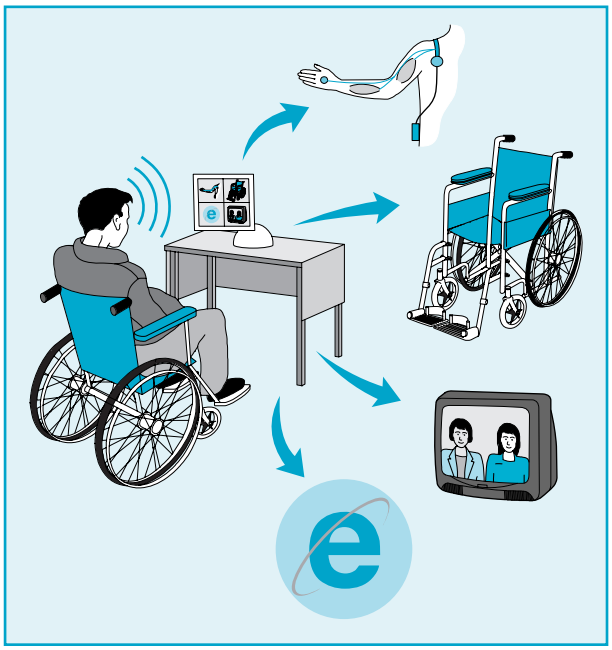


FIG. 5.6 BrainGate technology. This experimental technology involves implanting microelectrodes in the brain to detect neuronal activity about *intended* movements. This information is fed into a computer that, in turn, generates signals to drive limbs or interact with another computer or TV. The hope is that in due course the technology may permit individuals with profoundly damaged nervous systems to move about and interact with their environment through the power of thought. Source: Adapted from illustration by Leigh Hochberg, Massachusetts General Hospital, with permission from Cyberkinetics Neurotechnology Systems, Inc.

THE SUPPLEMENTARY MOTOR AREA AND PREMOTOR CORTEX

Having established the link between the primary motor cortex and muscles, we now need to consider how a person "initiates" a movement. As we hinted earlier, cortical control of movement is organised "hierarchically" by different regions of the frontal lobes. As we have already seen, pyramidal cells in the primary motor cortex (region A) control muscle contractions via their connections with motor neurons in the spinal cord. These pyramidal cells are, in turn, partly controlled by neurons in the region of frontal lobe just forward of the primary motor cortex; in our analogy, this would be region B. This area actually divides into two functionally distinct regions (both occupying BA 6 as mentioned above): the more medial supplementary motor area or SMA (towards the top of the brain) and the more lateral premotor cortex or PMC (towards the sides). Cells in each region influence neurons in the motor strip when a particular movement is carried out. In other words, SMA and PMC neurons control hierarchically the activity of individual pyramidal cells (see Figure 5.7). People with damage to these regions retain fine motor control of fingers but are impaired on tasks that require the coordination of two hands (such as tying a knot).

The main outputs from the SMA are to the primary motor cortex bilaterally. The main inputs are from the prefrontal cortex and the basal ganglia. This arrangement places the SMA in a strategic position (in the hierarchy) to coordinate motor plans (which, as we saw earlier, have been "approved" by the basal ganglia for execution) via the pyramidal neurons of the primary motor strip. It provides a buffer store for such plans prior to their execution. Several important observations reinforce this view. First, it is possible to record a negative ERP (see Chapter 2) from the SMA that builds over a period of 1 or 2 seconds prior to executing the movement. This is known as the readiness potential (also called the *bereitschaftspotential*), and is observable even when movements are only imagined (Roland, 1993; Tyszka et al., 1994). Second, stimulation of the SMA is reported to produce an urge to perform movements (Bradshaw & Mattingley, 1995). Third, bilateral damage of the SMA can bring about complete loss of voluntary movement including speech (Freund, 1984). Fourth, Gerloff et al. (1997) have reported that the subjective experience of temporary SMA "lesions" induced by TMS is one of apparent loss/forgetting of the goal that the ongoing actions were intended to achieve.

In many respects, the PMC works in analogous fashion to the SMA, except that it is more concerned with coordinating motor plans related to external cues. Like the SMA, the main outputs from the PMC are to the primary motor strip. The main inputs are from the parietal lobe, the cerebellum, and, to a lesser extent,

the prefrontal cortex. Activity is greater in the PMC in response to external cues (than internally generated plans). For example, Roland et al. (1980) showed that blood flow increased markedly in this region as the subject was required to keep a spring in a state of compression between the fingers. The PMC, along with the prefrontal cortex, also appears to be more active during the acquisition of skilled movements, whereas the SMA becomes more active when well-practised movements are required (Jenkins et al., 1994).

OTHER FRONTAL REGIONS INVOLVED IN MOVEMENT

As we mentioned earlier, both the SMA and, to a lesser extent, the PMC receive inputs from the area of frontal lobe in front of them (area C, to return to our analogy). This "association" area is known as the prefrontal region, and it becomes active when an individual begins to plan behaviours in a relatively abstract way, or when new motor skills are being acquired. Prefrontal damage actually impairs an individual's ability to plan, whether or not movement is involved. For example, frontal patients often perform badly on strategy tests such as the "Tower of Hanoi", which we discuss in more detail in Chapter 11. And in the Jenkins et al. study mentioned above, increased metabolic activity was observed in the lateral prefrontal cortex *only* during the motor learning stage, not once the skill had been acquired.

These findings support the idea of a three-stage hierarchy in the frontal lobes to control movement, which we illustrate, in very simple terms, in Box 5.4. However, it would be grossly misleading of us to suggest that area C was localised in the way that area A is. In fact, our understanding of where "ideas" (that may become actions) originate from is distinctly hazy and based, as often as not, on case studies of brain-damaged individuals with deficits in this realm. Frontal damage can affect idea generation, but so too can damage to other cortical and subcortical regions. The initial representation, perhaps a goal that the individual wishes to achieve, may be highly abstract, and shaped by any number of influences: prior experience, current predicament, motivational state, desirability of outcome, feasibility of the action plan, and so on. And there will usually be a raft of alternative ways of achieving the goal, necessitating a competitive process to select the most appropriate actions (Rosenbaum et al., 1991). It seems likely that this initial stage of action planning must be underpinned by distributed and parallel processing rather than

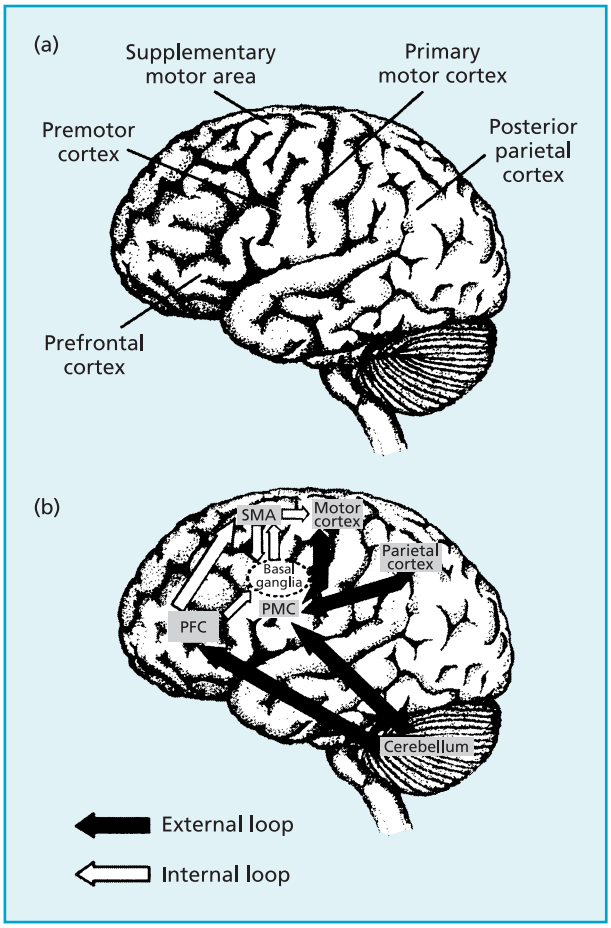


FIG. 5.7 (a) The four hierarchically organised areas of the frontal lobe (the prefrontal cortex, the SMA and PMC, and the motor strip.). (b) "Motor" areas outside the frontal lobes. In general terms, internal (self-generated) actions involve the prefrontal cortex, SMA, and primary motor strip mediated by the subcortical basal ganglia (internal loop). Actions prompted by external events engage the cerebellum and probably the parietal lobe, both of which send outputs to the PMC that, in turn, outputs to the primary motor strip (external loop).

hierarchical serial processing. Teasing apart the constituent mental operations involved will be a major challenge for researchers in coming years.

Scientists have, however, begun to identify some of the other brain regions, in addition to the prefrontal cortex, involved in this early stage of motor control. The anterior cingulate is active when attention must be directed towards novel stimuli that require effortful responses, particularly where there is conflict between response options (Rushworth et al., 2004). A region of medial frontal cortex, tagged the pre-SMA by Matsuzaka and Tanji (1996), appears to be important in organising sequential actions together (Kennerley, Sakai, & Rushworth, 2004). The "frontal eye fields" are of critical importance in controlling **voluntary gaze**. And, as we shall see below, the parietal lobe may be important in storing memories of actions and perhaps their semantic connotations too.

Box 5.4 A motor hierarchy for quenching your thirst

- Dehydration leads to activation of "osmoreceptors" in the anterior hypothalamus. This is translated into consciously feeling thirsty, leading to a motivational state represented in the prefrontal areas (area C) as a *plan* or *intention* to drink.
- The act of raising a glass, tipping, and swallowing (the appropriate *motor pattern*) is coordinated by the SMA and/or the premotor cortex (area B). Remember that these areas exert bilateral control: after all, you could pick up the glass with either hand.
- The SMA and PMC control the pyramidal cells in the primary motor strip (area A) in the coordination of individual muscles as the glass is raised and the drink consumed.
- Moment by moment sensory feedback from touch receptors in the fingers and hand holding the glass ensures that it is gripped tightly enough to prevent it falling, and not too tightly to cause it to break.

INTERIM COMMENT

Motor control is organised hierarchically. Plans or intentions to act are "hatched" in a distributed network including, but extending well beyond, the prefrontal cortex. Motor plans are coordinated in the SMA and PMC, and control of muscles is mediated by the primary motor strip. Although this organisational hierarchy has been speculated about for many years, the use of in-vivo imaging procedures such as SPECT and rCBF (see Chapter 2) has confirmed it. Roland (1993) reported that when an individual was asked to complete a simple repetitive movement such as wiggling a finger, only the contralateral primary motor cortex showed increased activity. However, if a more complex sequence such as touching the ends of each finger with the thumb was required, both the SMA and the prefrontal cortex showed increased activity, as well as the primary motor cortex. Even asking the subject to imagine the complex sequence caused increased activation in the SMA and prefrontal regions.

The distinction between internally and externally cued movement is also important. The basal ganglia interact with the SMA to enable (or inhibit)

KEY TERM
Voluntary gaze: Intentional adjustments of eyes in the deliberate process of attending to a feature in the visual field.

internally generated movement plans. The cerebellum interacts with the PMC to regulate actions related to *external* stimuli or events. Thus the novice tennis player will rely mainly on the second set of connections to return serve, hoping to make contact with the ball (the external stimulus) and hit it anywhere in their opponent's court. The experienced player, on the other hand, will use both systems: the cerebellar–cortical connections will control contact with the ball, and the basal ganglia–cortical connections will allow them (via internally generated intentions) to place their shot deliberately, to maximum advantage. The same distinction probably underpins the different areas of brain activity seen during skill acquisition (learning) and performance of a well-learned skill (Jenkins et al., 1994). This is because there is a high degree of dependence on external cues during skill acquisition, whereas skilled individuals may (not unrealistically) boast of being able to do "such-and-such" with their eyes shut!

PARIETAL INVOLVEMENT IN MOVEMENT

The parietal lobes make at least two independent contributions towards motor control (in addition to their primary role in somatosensation). Proprioceptive information from muscles and joints arrives in the primary somatosensory strip, relaying details about the position of body parts in relation to one another. This information is, in turn, fed to superior-posterior parietal regions BA 5 and BA 7, which also receive "feedback" from more anterior motor regions. This region is therefore in the position to both guide and correct movements, especially when actual movements do not correspond to those intended. A significant minority of pyramidal neuron cell bodies are located in these parietal areas and, as we have seen, the region also has reciprocal links with motor regions in the frontal lobes. More lateral regions of the left parietal lobe (the rostral inferior parietal lobule) seem to have a different motor role involving the storage of complex gesture and action representations. Damage here is associated with a condition known as apraxia in which the patient appears to lose the sense of what a particular movement is for (the concept of it, so to speak), so may be unable to either recognise a gesture made by others or implement a movement to order. We consider this, and other forms of apraxia, below.

THE FRONTAL-PARIETAL "MIRROR NEURON" CIRCUIT

In the early 1990s, a group of Italian researchers discovered a region of premotor cortex in the macaque containing neurons that became "active" *both* when the animal engaged in a particular meaningful action in relation to an object (such as grasping an item of food: a so-called transitive gesture) *and* when it observed another animal engaging in the same (or similar) action. These cells quickly came to be known as "mirror neurons" (Gallese et al., 1996). Further investigation revealed that the rostral (front) part of the inferior parietal lobule also contained mirror neurons that respond to a range of specific biological movements or actions. Subsequently, the superior temporal sulcus, which feeds into the inferior parietal lobule, has also been implicated in this "mirror neuron circuit" although neurons here do not possess motor properties (they only respond to observed actions/gestures).

Interest in this system has intensified following the realisation that the human brain too has a "mirror neuron circuit". Far from being an evolutionary "quirk", researchers have realised that the mirror neuron system might have played a critical evolutionary role in the development of several cognitive faculties that are either unique to or more highly developed in humans than any other species. These include imitation (as a form of learning) and the emergence of a spoken language from hand gestures (as discussed in Chapter 3). Some researchers have argued that humans routinely use this system to understand other people's actions (and emotions) in order to "mind-read" (Baron-Cohen, 2003) and empathise (Dapretto, 2006). Interest in the human mirror neuron circuit is currently intense, and one recent line of inquiry related to movement is the possible overlap between it and apraxia, a condition that we examine below (see, for example, Lewis, 2006). We have provided an outline of ongoing research developments in this exciting area in Box 5.5, and we briefly revisit some of the links between it and other cognitive processes and emotion in Chapter 10.

Box 5.5 The mirror neuron system

Mirror neurons are a particular class of sensory-motor neuron, first discovered in area F5 of the monkey premotor cortex (DiPellegrino et al., 1992). Their unique feature is that they become "active" *both* when the animal engages in a particular meaningful (transitive) action in relation to, for example, an item of food, *and* when it observes another animal engaging in a similar action. It is important to realise that neither the sight of the object alone nor a "meaningless action" unrelated to a specific object (a so-called intransitive gesture) will activate mirror neurons in monkeys. On the other hand, mirror neurons seem to show considerable generalisation in the sense that quite different representations of the same object–action interaction will all activate them to varying degrees. To give just one example, monkey mirror neurons that respond to seeing another monkey grasp a food pellet will also respond if a human hand grasps a food pellet (Rizzolatti et al., 1996). (See Figure 5.8 for an illustration of Rizzolatti et al.'s study.)

In the "early" primate studies, researchers initially sought to establish the proportion of neurons in F5 with "mirror" properties. In the upper sector of this region, at least 20% of neurons showed such properties in relation to hand movements and gestures, and in the lower sector, at least 15% of neurons showed "mirror" properties related to mouth movements, which in turn subdivided into ingestive (eating-related) and communicative functions. (In the macaque, lip smacking was one such example.) Further investigation revealed that the rostral (front) part of the inferior parietal lobule also contained neurons with "mirror" properties, responding to a range of species-specific movements, gestures, or actions. Subsequently, the superior temporal sulcus, which feeds into the inferior parietal lobule, has also been implicated in this "mirror circuit". However, although it contains movement-sensitive neurons, relatively few of these also possess true "mirror" properties, so its role is thought to be somewhat peripheral. Incidentally, these functions are essentially bilaterally distributed in monkeys.

Researchers have been able to measure the functional activity of individual neurons in primates using electrode implantation and unit recording, techniques

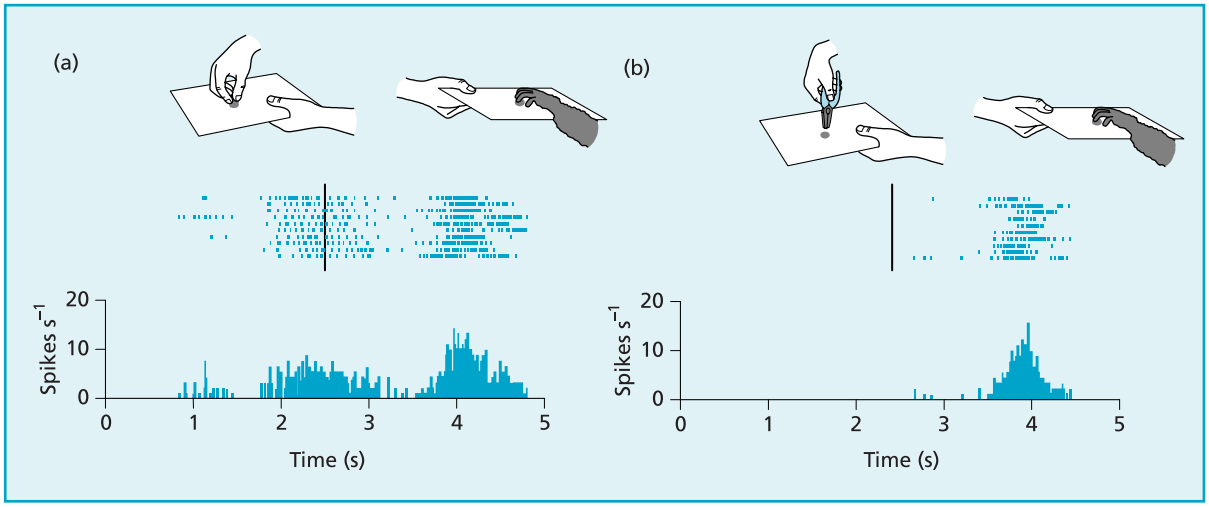


FIG. 5.8 Unit recording of mirror neurons in a macaque's area F5. (a) A piece of food is placed on a tray in front of the macaque. The experimenter grasps it, then replaces it and moves the tray (with the food) towards the macaque. Neuronal firing over a period of 5 seconds is indicated in the lower panels. Note the strong firing both when the experimenter grasps the food and when the macaque grasps it. (b) As (a) except the experimenter initially grasps the food with a pair of pliers, before moving the tray (with food) towards the macaque. Note the absence of neuronal firing when the observed action is performed with a tool rather than a hand. Source: Rizzolatti, G., Fadiga, L., Gallese, V., and Fogassi, L. (1996). Premotor cortex and the recognition of motor actions. *Cognitive Brain Research*, *3*, 131–141. Reproduced with permission, © Elsevier, 1996.

not ordinarily possible with humans. But using a range of procedures such as EEG, fMRI, and TMS it has become clear that humans too possess a mirror neuron system. Anatomically, this includes the human homologue of macaque area F5 which is Broca's area (specifically BA 44). However, the circuit also appears to extend into superior temporal and inferior parietal regions. Although both left and right cortical regions are implicated, bilateral symmetry of the system may not be as complete in humans as in other primates (Aziz-Zadeh et al., 2006). For example, Iacoboni et al. (1999) used fMRI to identify activations when human volunteers made imitative finger movements compared with when they made the same movements in response to a cue. Activation in the imitative condition was greater than in the cue condition in the left inferior frontal lobe, and right inferior parietal and superior temporal regions. In a very similar study to Iacoboni's, Heiser et al. (2003) used TMS to disrupt imitative but not cue-initiated finger movements. This effect could most reliably be induced with TMS to BA 44 on either the left or right side.

Despite these anatomical similarities, comparison of the mirror neuron systems of macaques and humans has revealed at least two functional differences (Rizzolatti & Buccino, 2004). First, the human system appears responsive to mimed actions without an object (macaques require both a transitive action and an object to activate). Second, even meaningless intransitive gestures can activate the system in humans (Maeda, Kleiner-Fisman, & Pascual-Leone, 2002). These differences are important because they raise the possibility that the systems as a whole may have slightly different functions in humans than in other primates. Animal studies have generated two main hypotheses: imitation (Jeannerod, 1994) and action understanding (Rizzolatti, Fogassi, & Gallese, 2001). The first,

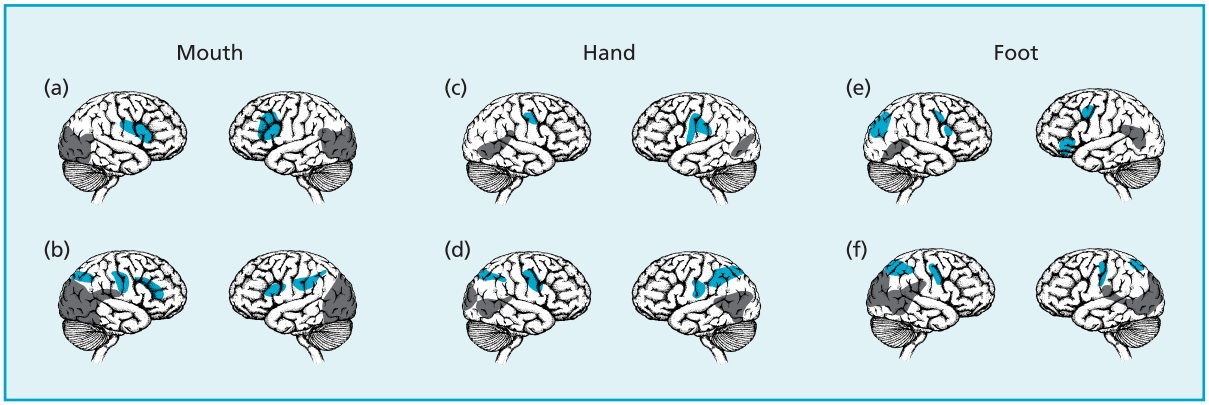


FIG. 5.9 Brain activations during observed mouth, hand, and foot actions (adapted, with permission from Blackwell Publishing, from Buccino et al., 2001). The upper images indicate (bilaterally) areas of activation during observation of movements not involving objects: (a) chewing; (c) mimed hand grasping; and (e) mimed kicking. The lower images indicate (bilaterally) activity to observed actions when objects are involved: (b) biting food; (d) grasping an object; and (f) kicking an object.

imitation, is an obvious candidate because, as we have seen, the system activates when there is correspondence between observed and actioned behaviour. However, there is considerable debate among animal behaviourists as to whether non-human primates actually do much "imitating", although, of course, humans certainly do. Thus the fMRI study of imitation by Buccino et al. (2001) is of interest. Respondents observed a series of transitive or mimed actions involving hand, mouth, or foot, and the main findings are summarised in Figure 5.9. In each case, action observation activated a network of inferior frontal and parietal regions bilaterally (but more pronounced on the right). And parietal activation seemed to be particularly associated with object-directed (as opposed to mimed) actions.

There is, however, more support for involvement of the mirror neuron system in action understanding in both humans and other primates. Consider the findings from Umilta et al.'s (2001) study. Macaques observed either complete transitive actions (a hand moving to grasp some food), or a partially obscured action sequence in which a food pellet was first clearly placed behind a screen and the approaching hand also disappeared behind the screen as it neared the food. (In a control condition the same actions were mimed without a food pellet.) Researchers found that at least 50% of the neurons that activated in the fully visible condition also activated just as vigorously in the obscured condition (though not in the mimed condition). These findings strongly suggest that activations related to the animal's understanding of the "purpose" of the action rather than simply to its mimicry. In essence, each time an animal observes a transitive action, the action activates neurons in its premotor cortex corresponding to when it makes the same action itself, the outcome of which it knows. So, the mirror system rather neatly transforms visual input directly into knowledge for the observer.

As we hinted earlier, the human and non-human mirror systems are similar but not identical. This has led to considerable speculation about other possible roles for it in humans. In particular, its established role in facilitating imitation has led to suggestions about its importance for skill and language acquisition

(Ramachandran, 2006). Its role in action understanding has led to speculation about its importance for human communication in general, and in predicting the actions of others in particular (Ramnani & Miall, 2004). In this context, damage to the system might be relevant in disorders of human communication such as autism and Asperger's syndrome, and some psychotic disorders (Blakemore et al., 2005). We revisit this line of inquiry in Chapter 10 when we review the neuropsychology of emotion and motivation.

PERIPHERAL AND SPINAL MOVEMENT DISORDERS

By now, it should be apparent that movement disorders can result from damage or loss of function to many different regions of the nervous system. Literally dozens of disorders, often thankfully very rare, are described in the neurology literature, but for present purposes we will restrict our list to specific examples that either illustrate the importance of particular components of the motor system or are of special interest to neuropsychologists. We begin the review in distal regions of the nervous system with a brief mention of some disorders related to peripheral or spinal cord abnormalities, before moving into the brain. Here we will consider a small number of disorders related to cortical damage, but spend more time reviewing motor disorders associated with basal ganglia or other subcortical structures.

MYASTHENIA GRAVIS

The main symptoms of myasthenia gravis (which are highly variable and range from mildly disabling to life threatening) are those of muscle weakness or fatigue, especially in the head–neck region. (A tell-tale early symptom is drooping eyelids.) The weakness results not from damage to, or loss of tissue from, the muscles themselves, but from impaired neuromuscular synaptic transmission. In most cases, normal amounts of the neurotransmitter acetylcholine (ACh) are released from motor neurons but this fails to have the expected effect on the target muscles. In the 1970s it became apparent that myasthenic individuals have a reduced number of ACh receptors (Albuquerque et al., 1976), which is thought to occur as a result of an inappropriate immune response in which (for reasons that are not currently known) the body's immune system inadvertently attacks the receptors as if they were "foreign". Myasthenia gravis therefore joins a growing list of auto-immune diseases (Engel, 1984; Shah & Lisak, 1993).

If the symptoms are mild they can be treated quite effectively with drugs that have the effect of boosting activity in the synapses between motor neurons and muscles. It is not presently possible to promote the growth of new ACh receptors, but certain drugs can partially override the problem by ensuring that released neurotransmitter remains in the synapse for longer before it is inactivated. The drugs in question achieve this by inhibiting the enzyme that normally breaks down ACh soon after it is released. The enzyme is acetylcholinesterase (AChE) and the drugs are therefore known as acetylcholinesterase inhibitors (AChEIs). Examples include physostigmine and neostigmine. However, these medications are far from ideal, because they influence all ACh synapses including many in the brain, where they may induce unwanted side effects including sleep disturbances, cognitive impairments, and even **hallucinations**.

KEY TERM
Hallucinations: Perceptual experiences unrelated to physical sensation. They may occur in any sensory modality, and are often associated with mental illness.

DISEASES ASSOCIATED WITH NEURONAL DAMAGE/LOSS

Multiple sclerosis (MS) is one of a group of demyelinating diseases, meaning that the principal pathological process involves the progressive loss of myelin. In MS this can occur throughout the nervous system and may affect all myelinated neurons. There are broadly two patterns of progression in MS: the more common relapsing-remitting form (four out of five cases) involves periods of hiatus (relapse), coinciding with inflammation of regions of CNS white matter, followed by recovery, although an underlying trend of disease progression is still apparent, particularly in later stages. The progressively disabling form (about one in five cases) involves a slow but steady deterioration of function. In either case, progression is often slow, although eventually white matter in the brain, especially that surrounding the ventricles, will be lost. More recent evidence indicates that in addition to demyelination, the axons themselves may be damaged by the disease process (Waxman, 2005). Early signs include loss of (or disturbed) sensation in hands or lower limbs, and loss of, or impaired, muscle control. Blurred vision is also a common early feature. As the disease progresses, more widespread paralysis (and loss of sensation) will be seen, and there may be cognitive changes as well.

Although MS is described as an auto-immune disease, the trigger for the self-harming immune response is, as yet, unknown. The drug beta-interferon is thought to work by modifying the responsiveness of the immune system (Arnason, 1999). Recently a second medicine, glatiramer acetate, has been developed to reduce relapse rate and intensity in the more common form of the disease. The mode of action is unclear but, like beta-interferon, it affects the immune response, promoting the release of anti-inflammatory substances such as interleukin 4.

As the name implies, **motor neuron disease** (MND) is more restricted in terms of its pathology, but also usually more aggressive, with death generally occurring within a few years of onset as the motor neurons that normally control respiration and swallowing become affected (death usually occurs as a result of respiratory failure). MND actually comprises a group of related disorders with variable course. One of the most common forms, amyotrophic lateral sclerosis (ALS), is also known as Lou Gehrig disease after the New York Yankees baseball player who developed this disorder. As motor neurons in the spinal cord and cranial nerves die, there is progressive and unremitting loss of muscle function. Intellectual abilities may remain intact until later stages of disease (Bruijn, Miller, & Cleveland, 2004), although cognitive impairments correlate with pyramidal cell loss in the premotor and prefrontal cortex in a proportion of cases (Maekawa et al., 2004), suggesting that MND is not in fact restricted to loss of motor neurons (see also Al Chalabi, 2006).

The cause(s) of MND remain a mystery, although a small proportion (< 5% of cases) are thought to be genetic (Boillee & Cleveland, 2004). Other possible causal factors include as yet unknown viruses, possible exposure to toxins, and even head injury. Nevertheless, the pathology of MND *is* known and appears to involve the over-expression of genes coding for a particular glutamate receptor (glutamate is a widespread neurotransmitter in the CNS). This leads to **excito-toxicity** in the glutamate system and resultant loss of tissue (Kawahara et al., 2004).

It might be noted that **poliomyelitis**, an infectious disease caused by a virus

KEY TERMS

Multiple sclerosis: A disease in which progressive loss of myelin leads to loss of function.

Motor neuron disease: One of a group of disorders characterised by progressive destruction of the motor neurons that control voluntary action.

Excito-toxicity: The process by which nerve cells are killed by excitatory substances.

Poliomyelitis (polio): A viral disease where motor neurons are damaged resulting in muscle weakness and/or paralysis.

and otherwise unrelated to MND, also targets motor neurons. Although rarely fatal, polio may leave lasting muscle wastage as a result of peripheral nerve damage and the resultant loss of innervation to muscles.

SPINAL DAMAGE

There are a number of rare diseases of the spinal cord but the most common damage to it results from accidental injury. Although the nerve tissue is normally well protected by the backbone that encases it, spinal injury often involves a displacement of vertebrae resulting in a "shearing effect" in which axons are literally torn apart. Transection of the spinal cord brings about a permanent paraplegia (lower body paralysis) in which there is loss of sensation and motor control of the body regions below the point of damage. Ironically, spinal reflexes below that point may still be intact, and even more pronounced as a result of loss of inhibitory influence from the brain. Transection in the neck region resulting from injury (usually breaking of the neck) is likely to bring about quadriplegia: paralysis of all four limbs and trunk.

CORTICAL MOVEMENT DISORDERS

HEMIPLEGIA

This condition has already been described as a loss of contralateral voluntary control. This means that an affected individual is no longer able to intentionally move parts of their body on the side opposite to that of the brain damage. The most common cause of hemiplegia is interruption of blood supply via the mid-cerebral artery, due to **aneurysm**, **haemorrhage**, or **clot** to the primary motor strip. Other causes include accidental head injury, epilepsy, and tumour. Hemiplegia can also occur after damage to subcortical structures, including the basal ganglia, which are also served by the mid-cerebral artery.

Usually with hemiplegia there will be a modest but discernible degree of recovery of function over time. This is because initial symptoms result not just from cell death due to loss of blood supply, but additionally from temporary loss of function in surrounding neurons. Diaschisis, as it is known, is in effect a short-term reduction in activity levels because of reduced inputs from the now-dead cells. These adjacent neurons may also be affected by a temporary change in blood supply. (However, exposure to excess blood in the event of haemorrhage can cause cell death.) Many neurons later appear to return to a normal or near normal level of functioning, leading to (partial) behavioural recovery of function. Functional improvement may also occur as recovering patients develop entirely new ways of achieving movement, making use of quite different brain regions. A primary aim of physiotherapy is to promote recovery of function in this way, by teaching the use of alternative muscle systems to achieve the same goal.

KEY TERMS

Aneurysm: A form of stroke caused by a blood vessel in the brain suddenly expanding then bursting.

Haemorrhage: A general term for bleeding. In the brain, this may occur following an aneurysm, or other damage to a blood vessel.

Clot: A solid deposit in the blood that may block a narrow blood vessel leading to a form of stroke.

Signs: The indications of some abnormality or disturbance that are apparent to the trained clinician/observer (as opposed to symptoms, which are things an individual describes/complains of).

Symptoms: (See signs above.) Symptoms are the features of a disorder or disease that the individual reports/complains of.

CEREBRAL PALSY

Cerebral palsy is not a unitary disorder, and may take a variety of forms encompassing many **signs** and **symptoms** depending on extent of damage. It

usually results from trauma during late foetal development or birth. Because of its heterogeneous nature, it is difficult to talk in general terms about the condition. However, a hallmark is motor disturbance, which may include difficulties in making voluntary movements (ataxia), unwanted involuntary movements (athetoidy), and excessively tensed muscles (spasticity). These problems are probably also responsible for the speech difficulties that are often seen in cerebral palsy, although language difficulties may also be linked to more general intellectual impairment which is a frequent but by no means ubiquitous feature of the condition.

APRAXIA

The term refers to a collection of movement disorders in which the ability to perform certain purposeful actions on command is compromised. A diagnosis is made mainly on exclusionary grounds: for example, that the disturbance cannot be attributed to a deficit in the control of muscles. Thus, an apraxic individual may be unable to make a particular gesture when asked, but may make the same gesture spontaneously. To add to the confusion there are several ways of categorising apraxia, and some forms are also known by more than one name. A final concern is that apraxia often co-occurs with aphasia, and in such patients it is important to establish that an apparent apraxic deficit is not secondary to a primary language deficit, for example a failure to understand basic instructions.

Given these complications, some neuropsychologists (e.g., Heilman & Rothi, 1993) have found it instructive to revisit the original ideas of Liepmann, who first characterised different forms of apraxia over 100 years ago (Liepmann, 1905). In what he called ideo-motor apraxia, the patient makes errors when asked to "pantomime" particular actions such as hammering a nail or brushing teeth (Leiguarda & Marsden, 2000). The patient seems to have some basic knowledge of the required action, but not of the use of the relevant tool, a hammer or toothbrush in this example, and may thus use their fist (as a hammer) or their finger (as a toothbrush). Conversely, in ideational apraxia (sometimes called conceptual apraxia) patients may be able to make well-formed movements, which are nevertheless inappropriate and/or disorganised. Such individuals may also misuse tools, but additionally behave as if they have effectively lost the "idea" (memory representation?) of the requisite action sequence: they can neither correctly implement a movement to order nor recognise the same movements made by others (Heilman, Rothi, & Valenstein, 1982). Thus, in this conceptualisation, ideational apraxia would be regarded as the more serious (and rarer) condition (see Figure 5.10).

Problems with this taxonomy arise, however, when specific testing arrangements are taken into account. Although inability to imitate so-called "transitive" actions (actions in relation to specific objects) is regarded as a hallmark feature of apraxia (Buxbaum, Johnson-Frey, & Bartlett-Williams, 2005), some apraxic individuals who cannot initiate "pretend" actions (i.e., cannot "pantomime") can in fact imitate someone else carrying out the same action. Others may appear apraxic until they are given the actual objects with which to carry out the required action (Ietswaart, Carey, & Della Sala, 2006). Still others may struggle with transitive actions (such as stirring a drink with a spoon) but perform intransitive ones (such as waving or signalling *STOP!*) normally (Haaland & Flaherty, 1984). According to DeRenzi, Pieczuro, and Vignolo (1968), over half of all

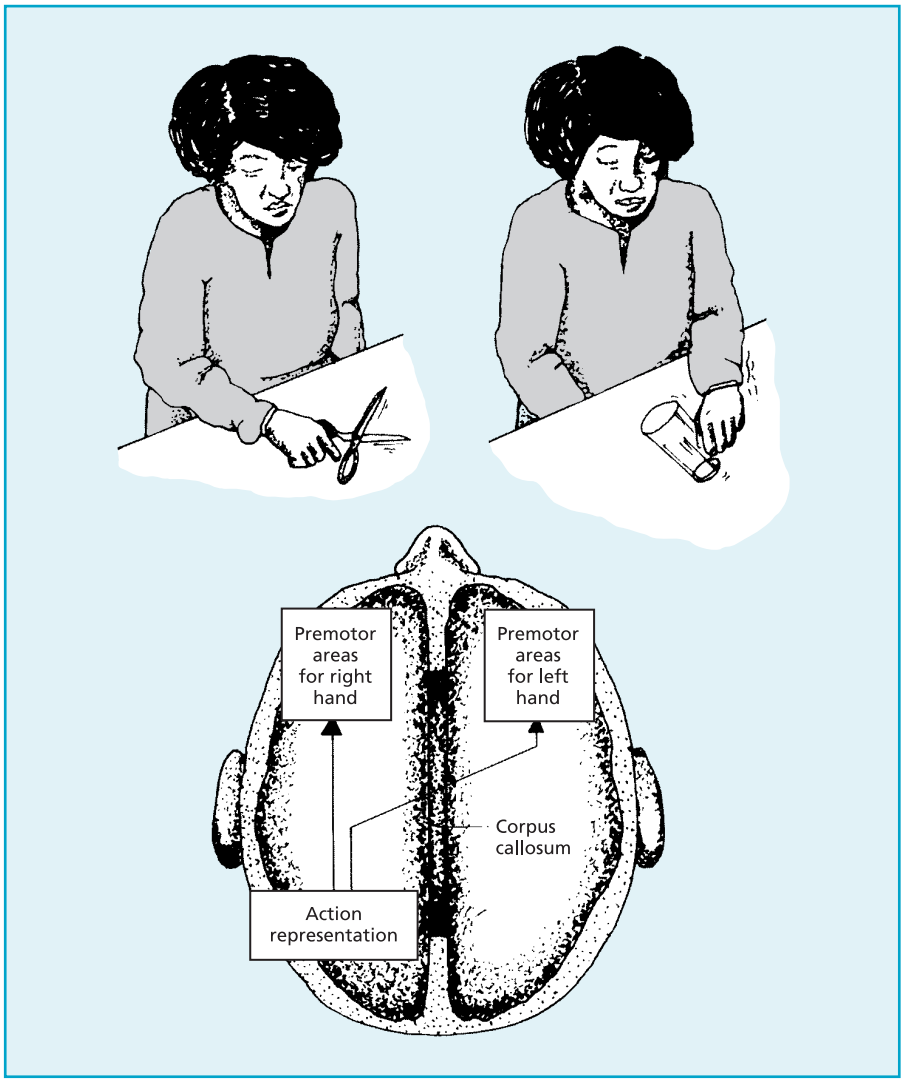


FIG. 5.10 Ideational apraxia. Movement of the left and right hands is coordinated by the right and left motor cortex. Patients with apraxia may be unable to engage in purposeful movement with one (or both) hand(s), being clumsy or otherwise responding inappropriately. However, damage restricted to the left parietal lobe is sufficient to induce bilateral ideational (limb) apraxia. In this condition, the patient seems to have lost their internal representations for movements, so can neither recognise actions by others, nor implement movements on instruction. Source: Gazzaniga et al. (1998). *Cognitive neuroscience: The biology of the mind* (Figure 10.32). Copyright © 1998 by W. W. Norton & Company, Inc. Used by permission of W. W. Norton & Company, Inc.

apraxic individuals show features of both ideo-motor and ideational apraxia (as traditionally conceptualised) and this has prompted some neuropsychologists to emphasise the similarities rather than the differences between Liepmann's two forms. To further complicate matters, re-examination of Liepmann's original work by Goldenberg (2003) indicates ambiguous use of the terms for the two forms of apraxia by both Liepmann and his colleague Pick (Pick, 1905). Today, the term "limb apraxia" is frequently used to encompass both conditions, although

there is clearly a graduated scale of impairment. Damasio and Geschwind (1985) characterised this hierarchy as follows:

1 A failure to produce a correct movement in response to a verbal command.
2 A failure to correctly imitate a movement.
3 A failure to correctly perform a movement (or sequence of movements) in response to an observed object.
4 A failure to even correctly handle an object.

An advantage of grouping together Liepmann's two forms of apraxia under the single heading of "limb apraxia" is that it creates a clearer distinction with a third form also described by Liepmann—motor apraxia, now (confusingly) called limb-kinetic apraxia. Although this can co-occur with limb apraxia, in its isolated form there can be a bilateral loss of hand/finger dexterity which affects all types of movement (symbolic and non-symbolic; transitive and intransitive, etc.) without any marked "conceptual" impairment (Goldenberg, 2003).

Whatever the eventual resolution regarding a definitive taxonomy of apraxic disorders, the most severe presentations of bilateral limb apraxia are consistently associated with left parietal damage (Rizzolatti & Matelli, 2003). According to Heilman and Rothi, representations of movement plans are stored here (specifically in BA 40 on the left side, also known as the supra-marginal gyrus/inferior parietal lobule), and damage may either degrade or completely obliterate the representation, making both generation and recognition of gestures/actions either problematic or impossible. However, a small number of cases of limb apraxia have also been associated with damage to more anterior regions (still in the left hemisphere), such as the SMA or the PMC, or to the pathways connecting parietal and frontal regions. This suggests that normal praxis is mediated by a distributed network encompassing parietal, frontal, and possibly subcortical structures on the left side.

Other forms of apraxia have also been described: Unilateral callosal apraxia is associated with damage to the anterior part of the corpus callosum. This prevents motor commands from the left hemisphere travelling to the right side which, of course, controls the left hand. So callosal apraxia almost always affects the left hand in right-handed individuals. Constructional apraxia may follow right parietal damage. Limb movements are normal but individuals cannot generate representations of objects by building models or copying 3D geometric patterns. This is seen as a disorder of the organisation of complex spatial actions. Buccofacial (oral) apraxia is actually the most common apraxic condition and is characterised by an inability to produce particular oro-facial movements, such as sticking out one's tongue or blowing a kiss, on demand. It is invariably associated with specific localised damage to BA 44 of the left frontal lobe (part of Broca's area).

Finally, as we mentioned above, there are some intriguing points of overlap between some forms of apraxia and the mirror neuron system. Anatomically, for example, areas of damage seen in limb and buccofacial apraxia partially overlap with the mirror circuit in the left (but not right) hemisphere (Rizzolatti & Matelli, 2003). Both are, essentially, disorders of transitive gesture/actions, and hand and mouth transitive gestures are also likely to activate the mirror system (Buxbaum et al., 2005). Finally, many apraxic patients are unable to imitate gestures despite having normal (or near normal) capacity to plan and execute goal-directed

movements with visual feedback (Ietswaart et al., 2006). These points of convergence are currently being explored by researchers.

SUBCORTICAL MOVEMENT DISORDERS

Within a period of a few months in the early 1980s, a group of young patients came to the attention of a hospital in California. All presented with profound Parkinson's disease-like symptoms including marked and unremitting akinesia (immobility). Research indicated that each individual was a drug addict and had recently used synthetic heroin contaminated with an impurity known as MPTP. This substance is converted in the brain to the closely related and highly toxic substance MPP, which has an affinity for cells that contain the dark pigment neuromelanin. The substantia nigra (as its name, from the Latin for "black substance", suggests) is rich in such cells, and these had been obliterated by the MPP. The individuals came to be known as "the frozen addicts". They had an unusually "pure" and enduring drug-induced form of **Parkinsonism** (Martin & Hayden, 1987).

Most neurological disorders that affect the basal ganglia are less clear-cut than the damage seen in the frozen addicts: in these disorders, damage tends to be localised, and/or progress slowly. Because of this selectivity, there is rarely complete loss of function. Rather, we find a raft of intriguing disorders in which movement is compromised rather than abolished. Actions may still be possible but they now occur in unregulated or poorly coordinated ways.

PARKINSON'S DISEASE (PD)

Of all the subcortical movement disorders this is perhaps the best understood. It affects relatively few people under 50, but the incidence steadily increases to about 1% in 60-year-olds and at least 2% in 85-year-olds. It is a progressive and relentless disorder and, although the symptoms may develop quite slowly, it is in principle a terminal illness. (Its progress is so slow that most people die of unrelated illnesses before PD has run its full course, thought to be at least 15 years.) The features of the disorder were recorded by the ancient Greeks, and the constellation of symptoms was known by its common name of "shaking palsy" for many years, before its full characterisation by the English physician James Parkinson. Incidentally he did not name it after himself. This honour was suggested by the famous French neurologist Charcot.

Through careful observation of affected individuals, Parkinson realised that the disorder that came to bear his name comprised a cluster of movement-related symptoms. These need not all be present for the diagnosis to be appropriate, and the severity of symptoms will become more pronounced over time. The symptoms in question comprised resting tremor, rigidity, bradykinesia–akinesia, and postural disturbance. This list has now been expanded, and the full range of Parkinson's features are clustered into what are often referred to as positive and negative symptoms (see Box 5.5).

Resting tremor is so called because it disappears or at least becomes less marked when the person engages in some deliberate act. It can usually be seen in the hands or lower limbs. The rigidity (sometimes called cog-wheel rigidity because an external force can induce "give", only for rigidity to reappear after a brief movement) is thought to be related to dysregulation of usually antagonistic

KEY TERM
Parkinsonism: Signs and symptoms that resemble Parkinson's disease. Certain drugs (such as neuroleptics) can induce these as a side effect.

Box 5.5 The positive and negative symptoms of PD

Positive symptoms

Tremor at rest: alternating movements that usually disappear during deliberate actions. The "pill-rolling" action of fingers and thumb is common.

Muscular rigidity: caused by antagonistic muscles being tensed at the same time. This is apparent when limbs are manipulated passively (by someone else). A resistance, followed by loosening, then further resistance is often found, giving rise to the term "cog-wheel rigidity".

Involuntary movements: changes in posture, known as akathesia, may be almost continual, especially during inactivity. Involuntary turns to the side (of the head and eyes) are sometimes apparent.

Negative symptoms

Disordered posture: for example, the inability to maintain a body part (such as the head) in the appropriate position, or failure to correct minor imbalances that may cause the patient to fall.

Loss of spontaneous movement: akinesia is the inability to generate spontaneous intentional movement. A blank facial expression is another manifestation.

Slowness in movement: bradykinesia is a marked slowing of repetitive movements such as tapping or clapping.

Disordered locomotion: walking may be slow and poorly coordinated—more a shuffle than a stride.

Disturbed speech: bradykinesia also affects the production of speech, which may slow markedly, sound atonal, and be difficult to understand.

actions of flexor and extensor muscles. Under normal circumstances, as one muscle is tensed, the opposor muscle passively extends. Rigidity occurs because both muscles are tensed at the same time.

Akinesia and bradykinesia are two prominent negative symptoms that also merit close consideration. These terms describe absence or severe slowing of movement. They both become most apparent when the patient is required to act by his or her own volition. A classic illustration of akinesia is to play a game of "catch" with a Parkinson's patient. Gently toss a ball to him/her and they might catch it without difficulty; this would, of course, be a stimulus-driven action. Now ask the patient to throw the ball back. Although they will certainly understand the instruction, they may find this (internally driven action) impossible.

Bradykinesia might be observed by asking a PD patient to clap their hands together. Although, once again, the instruction will have been understood, they may find this simple task extremely effortful (starting somewhat hesitantly, and rapidly tailing off altogether). Curiously, some background music with a strong beat may do the trick—another case of an external cue driving the action. The mask-like visage of the Parkinson patient is a further tell-tale sign of either bradykinesia or akinesia affecting facial expression.

That this set of diverse symptoms all depend (in some way) on dysfunction in the basal ganglia circuitry has been known for over 30 years. Indeed, post-mortem studies had shown clear evidence of loss of tissue in the caudate/putamen region (particularly the putamen) even before this. The discovery by Hornykiewicz in 1966 that these changes may be secondary to loss of dopamine innervation from neurons originating in the substantia nigra-pc (and making up the nigro-striatal pathway) eventually led to the development of drug treatments aimed at replacing missing dopamine or restoring the balance between dopamine and the principal intrinsic striatal neurotransmitter ACh.

You might think that dopamine itself would be a suitable drug to treat PD. However, when taken orally most is quickly broken down in the gut. But a related substance, L-dopa, can be taken orally, does not get metabolised in the gut to the same extent, and is converted to dopamine by cells in the brain. This drug has therefore assumed a central role in the treatment of PD. It does not "cure" the disease, but it does provide some symptomatic relief, although its effects lessen as the disease progresses.

Two other developments in treatment for PD merit attention. Deep brain stimulation involves the surgical implantation of very fine electrodes into the basal ganglia (usually either the globus pallidus or the subthalamic nucleus; see Freund, 2005, for a concise review). Battery-powered tonic high-frequency electrical stimulation of these nuclei aims to reduce their outputs, thus lifting the inhibitory effect of the globus pallidus on the thalamus. Although still in its experimental stages, results so far suggest that this treatment may be especially effective in reducing bradykinesia (Anderson et al., 2005). A radically different treatment for PD involves the implantation of tissue from foetal brains. The idea (no matter how distasteful to some) is to implant cells that are dopaminergic (i.e., that manufacture and release dopamine). However, it is too early to judge the true effectiveness of this procedure: An initial review of more than 20 cases by Olanow, Kordower, and Freeman (1996) gave early cause for optimism, but more recent studies by Freed et al. (2001) and Olanow et al. (2003) suggest that the beneficial effects of grafts may be limited to young patients. More worryingly, Freed's group found that about 15% of treated patients may develop side effects that are as debilitating as the disease itself. A synopsis of foetal transplant research for PD is provided in Box 5.6.

Box 5.6 The viability of foetal transplants for Parkinson's disease

From 1987 to 2003, five reports were published detailing procedures to transplant tissue from (aborted) foetuses into the brains of individuals with advanced Parkinson's disease. The pooled sample included just 23 patients. The tissue itself comprised cells capable of producing and releasing dopamine, usually drawn from neuroblasts (cells able to divide into either neurons or glia) taken from several embryos, which were transplanted into multiple sites in, and adjacent to, the striatum. After a period of recovery it was possible to assess these patients both in terms of Parkinson's symptomatology, and functionally in terms of renewed dopamine activity and concomitant reduction in requisite L-dopa medication.

The results of these trials were very encouraging. Overall, grafted patients showed a significant improvement in motor function, a reduced need for medication, and an increase in the uptake of precursors for dopamine, strongly suggestive of increased dopamine turnover (use). These changes were maintained for more than 10 years in some patients.

However, each of these studies was "open-label", meaning that both patients and clinicians were aware of the treatment and its anticipated consequences. Moreover there were no control patients despite the fact that placebo effects can be prominent in PD. To overcome this problem, two placebo controlled trials were initiated and have now reported their findings (Freed et al., 2001; Olanow et al., 2003). To try to control for placebo effects, some patients in each trial even underwent "sham" surgery in which they were anaesthetised and operated on, but no tissue was implanted. Although the clinical procedures used in each of these studies differed in terms of amount and type of tissue implanted, and whether or not immunosuppressant drugs were given, the findings failed to replicate those of the earlier open-label trials. The Freed study reported some evidence for symptom reduction in younger patients although the average change across all patients did not reach statistical significance. This study used tissue from only two donors (somewhat less than the open-label trials) and no immunosuppressant medication. Moreover, two patients died after grafting. The Olanow study did employ immunosuppression, but the group used solid tissue rather than tissue in liquid suspension. There was no significant improvement in symptomatology at 24 months, although patients grafted with tissue from multiple ($n = 4$) donors fared better in the first 6 months post-surgery.

Winkler, Kirik, and Bjorklund (2005) have provided a concise summary of and commentary on tissue transplantation for PD, which to date (early 2007) has been conducted in about 400 patients worldwide. They conclude that while transplantation remains both a viable and promising approach, there are many parameters that require further research before a safe and effective standardised procedure can be developed. These include patient variables such as age, duration of illness, medication levels, and symptomatology; and methodological variables such as tissue source and type, and the duration of use of immunosuppression (see also Piccini et al., 2005).

Very recently, the prospect of using stem cells as an alternative tissue source has arisen, although as yet data concerning the effectiveness of this type of grafting have been restricted to work with animals.

HUNTINGTON'S DISEASE

Huntington's disease is a rare genetically determined disorder (which used to be known as Huntington's chorea). It leads to death within about 12–15 years of onset of symptoms. These usually take a characteristic course, although the exact transition point between "choreic" and "end-stage" is difficult to identify or predict. The "choreic" stage of Huntington's is marked by the presence of unusual and intrusive movements (so-called "choreform" movements) which may initially appear benign, taking the form of fidgeting or restlessness. But soon they become apparent in limbs, trunk, head, and neck, to the extent that they interfere with "normal" actions including walking, talking, and even swallowing. Psychological

KEY TERM
Huntington's disease: A rare, genetically determined, neurological disorder causing dementia and death due to progressive loss of neurons in the striatum.

and cognitive changes, which can sometimes lead to a misdiagnosis of mental illness, may also be apparent.

In the later stages of the disease involuntary movements may disappear, but so too do voluntary movements. The upshot is that "end-stage" Huntington's disease resembles, in certain respects, the negative symptoms of Parkinson's disease. The individual may be immobile, mute, bed-ridden, and even have difficulty breathing and swallowing. Memory and attentional impairments, **perseveration** and aphasia are also seen. Death is often due to **aspiration pneumonia**.

Although the disease remains rare, its pathology is now becoming better understood. In later stages there are widespread changes involving loss of tissue to several regions of cortex. These probably account for the psychological and cognitive changes that become progressively more prominent. However, these are thought to be secondary to more subtle and earlier changes in the striatum, or at least relatively independent of the main symptoms of movement disorder. Indeed, in early-stage Huntington's the only changes are found in the caudate, where a progressive loss of so-called "spiny" **interneurons**, initially in the medial region and later in more lateral regions, is observed. Because these neurons normally help to regulate the inhibitory output to the external part of the globus pallidus and substantia nigra, their demise brings about a dysregulation of the indirect (inhibitory) route through the basal ganglia, and the appearance of unwanted (disinhibited) involuntary movements (see Figure 5.4). However, as the disease progresses to affect neurons throughout the striatum, with up to 90% of spiny interneurons lost, the entire regulatory function of the basal ganglia is compromised, including the "enabling" facility of the direct route. At this point negative symptoms prevail, as intentional actions (including basic vegetative processes such as breathing and swallowing) no longer gain the "assent" of the basal ganglia.

Huntington's disease is caused by the presence of a single dominant gene on chromosome four which has mutated to become extra long by dint of the unwanted presence of multiple **trinucleotide repeats**. If one of your parents has Huntington's you have a 50% chance of developing it. You may therefore wonder why this disorder has persisted, as far as medical records tell us, for at least 300 years. The answer is that the symptoms do not appear until middle age (typically about 40) and most people have had children by that time. However, it is now possible to test for the presence of this mutant gene (Gusella & MacDonald, 1994), and many people with a family history opt to have the test, to help them decide in advance whether or not to start a family.

Key Terms

Perseveration: The tendency to repeat the same (or similar) response despite it no longer being appropriate.

Aspiration pneumonia: Bronchial infection and congestion that affects ability to breathe and can lead to death.

Interneurons: The name for neurons that receive input from neurons and send their output to other neurons, found throughout the CNS.

Trinucleotide repeats: Stretches of DNA in a gene that contain many repeats of the same three-nucleotide sequence. A genetic cause of neurological disorders.

TICS, TOURETTE'S SYNDROME, AND OBSESSIVE-COMPULSIVE DISORDER

Tics are brief, involuntary, unpredictable, and purposeless repetitive gestures or movements that often seem to focus on the face and head. They may involve unusual facial grimacing, twitching, or other stereotyped actions. Sometimes vocal tics occur, wherein the individual makes clicks or grunts, or even barks. These are most common in children, and often disappear in adolescence. Evidence suggests that the appearance of tics is definitely associated with stress. If tics persist into adulthood the condition merges with Tourette's syndrome (TS).

TS is therefore a severe form of tic disorder. As well as the sort of tic already described, someone with Tourette's may display multiple involuntary mannerisms,

echolalia (parrot-like mimicry) and, in the most severe cases, coprolalia (expletive use of foul language often of a sexual nature). Although this constellation of symptoms sounds bizarre, people with TS are not considered mentally ill, and usually have insight into their condition. Rather, they cannot "control" action plans (including lewd thoughts) which therefore intrude on their other activities. Their manifestation is made worse by anxiety or stress, and ameliorated to some extent by relaxation and the use of dopamine-blocking drugs.

Earlier, we described the features of tics and TS as involuntary. Strictly speaking this is not the case. Most "Touretters" can muster sufficient will-power to inhibit a tic or mannerism for a short while, but the longer they hold off, the worse the compulsion to engage in the action becomes. Although this seems a world away from "normal experience", Bradshaw and Mattingley (1995) have likened this "compulsion" to the infectious nature of yawning and the developing struggle to suppress it.

Our inclusion of obsessive-compulsive disorder (OCD) alongside tics and TS may, on the face of it, seem a little fanciful. After all, OCD is a psychiatric disorder appearing in DSM IV (the current classification system) in the same section as other anxiety-related conditions, and the symptoms of OCD seem to support this. As the name suggests, people with this disorder display a range of symptoms including obsessive repetitive thoughts or feelings, and/or the compulsion to engage in ritualistic behaviours such as repeatedly checking locks or endless hand washing. The obsessions or compulsions are so intense that they interfere with other more routine behaviours, so that day-to-day living becomes completely disrupted by them. If the individual is, for any reason, unable to engage in the behaviour, they are likely to experience spiraling levels of anxiety.

Yet there are, increasingly, doubts about the purely psychological origin of OCD. For one thing, psychological treatments tend to be relatively ineffective against it, whereas selective serotonin re-uptake inhibitor medications (SSRIs) can have dramatic effects in reducing or even eliminating the obsessional and compulsive behaviours (Goodman, 1999; Leonard, 1997). This has led to speculation that OCD may be related either to low levels of serotonin, or underactivity at serotonin synapses in the striatum. Serotonin is known to interact with dopamine in this region and is generally thought to have an inhibitory action. So an SSRI drug, which has the effect of boosting serotonin neurotransmission, will in effect replenish the inhibitory influence whose absence leads to obsessive and compulsive behaviours in the first place (Rapoport, 1990). Intriguingly, McDougle et al. (1994) have reported that the addition of a dopamine antagonist drug such as haloperidol alongside an SSRI is more effective than an SSRI alone in the pharmacological treatment for OCD. Second, there is considerable overlap between OCD, tics, and TS: Tics are, in effect, compulsive actions, and at least 25% of people with TS also meet the diagnostic criteria for OCD. Grados et al. (2001) have reported a family association between tic disorders (including TS) and OCD consistent with a common underlying genetic predisposition.

If all other treatments for OCD fail, a surgical procedure known as cingulotomy can lead to a reduction of symptoms in a proportion of those operated on (Martuza et al., 1990). The surgery involves lesioning the pathway that funnels cortical output from the cingulate gyrus and/or the orbitofrontal regions into the basal ganglia. Finally, deep brain stimulation of the subthalamic nucleus may (as with Parkinson's disease) alleviate some OCD symptoms (Abelson et al., 2005).

OTHER DISORDERS LINKED TO BASAL GANGLIA DYSFUNCTION

Two other disorders merit brief attention. Ballism (or the more common unilateral hemi-ballism) is a rare movement disorder linked directly to damage to the subthalamic nucleus, usually from a stroke. The main features of this condition are wild flinging-like movements of the limbs and sometimes the neck and head, which are so pronounced that they can cause severe injuries. Treatment involves dopamine-blocking drugs, and symptoms sometimes resolve after a period of recovery.

Sydenham's chorea is a complication that may develop following rheumatic fever in about one in five affected children. Hallmark features of this disorder are tics, twitches and other motoric signs such as sudden aimless movements in the head, trunk, and limbs (Black & Mink, 1999). Although the condition usually resolves within a few weeks, there are reports of children who have had recurrent episodes over a period of several years. An MRI study by Geidd et al. (1995) reported enlargement of the caudate, putamen, and globus pallidus which resolved as symptoms abated.

INTERIM COMMENT

At the beginning of this section we suggested that damage to the basal ganglia (or the loops between the basal ganglia and the rest of the brain) would not bring about the abolition of movement, but rather its dysregulation. This is exactly what we see in both Parkinson's and Huntington's diseases. In the former, loss of dopamine input to the striatum from the substantia nigra leads to a change in the balance between the direct and indirect routes. Remember that ordinarily, dopamine promotes activity in the direct route and inhibits the indirect route. So reduced dopamine innervation will tend to bias basal ganglia output in favour of the indirect route which works as a "brake" on actions (Gerfen, 2006), and we see the negative symptoms of bradykinesia and akinesia. The positive symptoms are thought to be related either to changes in output from the basal ganglia and thalamus to the spinal cord secondary to the changes in the striatum itself, or to functional changes to reciprocal connections (between the subthalamic nucleus and globus pallidus) within the basal ganglia itself (Hamani et al., 2003). In either case, disturbance in the normal dynamic balance within the basal ganglia leads to impairments in the control of movement.

In Huntington's disease there is intrinsic progressive cell loss within the striatum, particularly in the caudate. Initially the indirect pathway is more affected so the "brake" effect is reduced, leading to the intrusion of unwanted (disinhibited) choreic movements. However, in the final stages of Huntington's the loss of cells in the striatum is so extensive that most output is compromised, and the symptoms now resemble the negative features of Parkinson's disease. A similar disruption to the normal functioning of the indirect route is seen in ballism and hemi-ballism, in which the subthalamic nucleus is damaged and we see, as a consequence, dramatic unwanted movements superimposed on an otherwise normal behavioural repertoire.

In the case of tics, TS, and OCD, the basal ganglia and its inputs from the

cortex again appear pivotal. Three structural imaging studies have reported reduced size of the caudate and/or putamen in TS (see Saxena et al., 1998, for a review). There are relatively few functional imaging studies in tics and TS, and their results are difficult to interpret (Albin & Mink, 2006). However, the available evidence points to underactivity in prefrontal and cingulate regions coupled with underactivity in the caudate (Moriarty et al., 1995), and increased dopamine innervation throughout the striatum (Singer et al., 2002). Dopamine-blocking drugs acting in the striatum will thus modify TS symptoms (Wolf et al., 1996). In the case of OCD, there is compelling evidence of overactivity in the orbitofrontal and cingulate regions and the caudate, especially if the individual is challenged or provoked by the object/situation that induces their symptoms (Breiter et al., 1996). Symptomatic relief may be achieved by severing the pathway connecting these regions, or by SSRI drugs, which potentiate serotonergic inhibition in the striatum and/or the orbitofrontal lobes. In this context, Sydenham's chorea could be conceptualised as a sort of temporary form of TS. It has also been linked to structural changes (swelling) in the basal ganglia, and symptoms can be lessened with the use of dopamine-blocking medications.

CHAPTER SUMMARY

At the start of this chapter, we warned that the nervous system's control of movement is complex, yet we are probably all guilty of taking for granted the skills that this control mechanism permits. These skills are not solely the domain of Olympic gymnasts or concert pianists: with very little practice we can all master skills currently quite beyond the scope of the most talented robots.

There are at least four major motor pathways carrying different types of motor information to various regions of the body. These in turn are innervated by different brain regions. At one time it was thought that there were two basic motor systems in the brain: the pyramidal and extra-pyramidal systems, controlling deliberate and automatic actions respectively. This distinction is not now thought especially helpful, because components of the two systems interact in the brain itself, and in the spinal cord and periphery.

In the brain, attention has focused on the various roles in movement of the cerebellum, the basal ganglia, and the cortex. The cerebellum is important for posture, balance, and skill acquisition, and it interacts with the spinal cord and the frontal lobes. The basal ganglia also interact with the frontal lobes with which they form a series of feedback loops. A current theory about basal ganglia function is that they play a vital role both in the selection of preferred actions and in terminating ongoing actions in anticipation of switching to a different action. The actions in question are ones that are internally generated, rather than those that are driven by external stimuli.

Cortical control of movement is essentially hierarchical. The primary motor strip is innervated by the SMA and PMC. These regions are, in turn, influenced by more anterior regions including, but extending beyond, the prefrontal cortex. There is increasingly strong evidence that the parietal lobes also have at least two important roles in movement control. Areas 5 and 7 seem to be important in adapting movements in light of sensory feedback, and the more lateral regions, especially on

the left, may be involved in the storage of representations of movement plans. Damage to this region leads to limb apraxia, which is viewed as a problem of recognising or conceptualising movement plans in time/space.

In the frontal lobes, damage in the primary motor strip may cause weakness or loss of movement in very discrete contralateral muscles. Damage in the SMA and PMC disrupts internally or externally driven motor plans bilaterally. Prefrontal damage will be associated with absence of motor plans and other features of the dysexecutive syndrome (which we review in Chapter 11). A mirror neuron circuit encompassing frontal, parietal, and possibly other cortical regions has recently been discovered. In humans, the circuit becomes active both during observation of actions and when similar actions are undertaken by the observer.

Damage to components of the basal ganglia is usually associated with dysregulation of internally generated movements. Several well-characterised neurological disorders including Parkinson's and Huntington's diseases, and probably tics, Tourette's syndrome, and even OCD, are associated with damage, disease, or disorder to components of the basal ganglia and/or its connections with the thalamus and cortex.

CHAPTER 6

CONTENTS

6

Language and the brain

INTRODUCTION

Think for a moment of the complex range of computational skills that are involved in understanding and generating language. Yet by the age of 4 or 5 most children can understand language (in their "mother" tongue at least) spoken at a rate of several words per second. This stream of sounds is continuous—not conveniently broken up like words on a page—and the listener has to know the boundaries between words in order to make sense from them. By late adolescence most humans will have a working understanding of many thousands of words (up to 50,000 for English speakers). Humans start to produce language as soon as they begin to acquire their vocabulary. In fact, some psychologists argue that using language precedes knowledge of words, and they cite the verbal-babble interactions of mother and child as examples of pre-vocabulary "speech".

By about 2 to 3 years old, children can effortlessly generate completely novel utterances according to implicit grammatical rules, and conduct meaningful conversations both with other children and with adults. Language development also seems to occur in the most adverse circumstances: consider, for example, the acquisition of complex language in deaf children. Indeed, of all psychological attributes, language is surely the one that sets humans apart. Other animals may use gestures and sounds to communicate, but the complexity and sophistication of human language suggests that extensive regions of the brain must be dedicated to dealing with it.

Scientific interest in language dates back to the earliest attempts by researchers to study the brain in a systematic way, with the work of Dax, Broca, and Wernicke in the 19th century. Since then, interest in all aspects of language has intensified to the point where its psychological study (psycholinguistics) is now recognised as a discipline in its own right. The development of research tools such as the Wada test and, more recently, structural and functional imaging procedures has enabled researchers to examine language function in the brains of normal individuals (see Chapter 2). Perhaps predictably, this research has necessitated extensive revision of earlier ideas about how the brain deals with language; as usual, the more closely one looks, the more complicated things appear. However, despite the complexities, it is reassuring to note that research findings from several different perspectives are now producing converging results, and we review some of this work towards the end of this chapter.

Meanwhile, we start with a review of the classic neurological studies of aphasia. This is a "catch-all" term meaning disruption to, or loss of, language function(s). Aphasia of some sort is commonly seen following brain damage or disease (for example, 40% of stroke victims develop some form of temporary or enduring aphasia). It is also seen in Alzheimer's and Pick's diseases (two forms of age-related dementia), and it can occur following head injury (for example, after a road traffic accident).

The classic approach to aphasia provided a framework for differentiating between different forms of language impairment, both anatomically and functionally. However, it was developed on the basis of a small number of case studies, and long before the advent of the modern structural and functional imaging techniques. Their arrival confirmed suspicions that were already felt in some quarters, namely that the classic approach grossly oversimplified both the brain processes in language, and its neuroanatomical substrates (e.g., Caplan, 1987). To set the record straight, subsequent research approaches have tried to address each of these areas of concern (albeit without much collaborative "cross-talk" until recently). There has, for example, been a move by some researchers away from the strictly neurological approach that has focused on the organisation of the brain (for language), to an examination of the organisation of language itself. We summarise the main areas of interest in psycholinguistics later in the chapter, and pick up this theme again when introducing the cognitive neuropsychological approach.

In-vivo imaging research into language is also reviewed. This work has tended to support the view that language is predominantly served by a series of interconnected cortical regions in the left hemisphere, as the 19th-century neurologists first proposed. However, it has also shown that additional brain areas in both the left and right hemispheres are involved. The use of structural imaging techniques to study aphasia, as typified by the work of Dronkers and her colleagues, is also introduced. Like the functional imaging research, it has prompted revision and significant elaboration of earlier ideas about brain language systems.

THE CLASSIC NEUROLOGICAL APPROACH AND APHASIA

Franz Joseph Gall, working almost 200 years ago, noticed that some of his more articulate friends (an early example being a school chum) had protruding eyeballs! This, he subsequently reasoned, must be due to the brain behind the eyes having grown to accommodate a superior language faculty—and thus was born the idea that language "resided" in the frontal lobes. Gall's ideas about localisation of language gained support when Broca was introduced to a patient with a serious leg infection, right **hemiparesis** and loss of speech. As we mentioned in Chapter 1, the patient was known as "Tan" because this was the only "sound" he could utter (which he tended to do repeatedly). Broca realised that this patient could serve as a test of Gall's theory, and when he died, a rudimentary post-mortem of Tan's brain revealed evidence of marked damage to the left posterior frontal gyrus (see Figure 6.1 later). Actually, Broca noted that there was damage to other cortical regions too, but the brain was never dissected, so the true extent of Tan's lesion was not known. The area of *marked* damage quickly became known as Broca's

KEY TERM
Hemiparesis: Partial or complete loss of movement in one side of the body.

area, corresponding to BA 44, extending into BA 45, and Tan's disorder was coined "Broca's aphasia" by fellow neurologists. Broca himself referred to Tan's language disorder as "aphemia" (disruption of voluntary speech production), signifying his belief that Tan's was essentially a speech programming disorder similar to what might today be called **speech apraxia**.

In 1874 Karl Wernicke described two patients who had a quite different type of language disorder. Their speech was fluent but incomprehensible and they also had profound difficulties understanding spoken language. Wernicke later examined the brain of one of these patients and found damage in the posterior part of the superior temporal gyrus on the left (see Figures 1.2 and 6.1). He argued that this patient's comprehension difficulties arose because the damaged region in question would ordinarily be involved in the auditory memory of words. His incomprehensible output was attributed to ineffective monitoring of self-generated speech.

At the same time as characterising this second form of language disorder, which came to be known as Wernicke's aphasia, Wernicke himself developed a theory of how the various brain regions with responsibility for receptive and expressive language function interact. His ideas were taken up and developed by Lichtheim, and later by Geschwind, and we will consider their work later in the chapter. For consistency, we will adhere to the nomenclature of these early pioneers. However, it is important to note that the following descriptions differ somewhat from those of the original authors, having broadened over the years to accommodate a wider range of aphasic features as more cases have come to light. It should also be realised that many modern-day researchers avoid altogether the use of these names to identify aphasic conditions. This is because "connectionist models" of language, which initially brought about renewed interest in the classic forms of aphasia, have themselves been found wanting, chiefly for failing to capture the true complexities of language systems in the brain. We review some of these concerns later, but we start the following section with descriptions and illustrations of the classic aphasic conditions.

BROCA'S APHASIA

In Broca's aphasia, as with most neurological conditions, impairment is a matter of degree, but the core feature is a marked difficulty in producing coherent speech (hence the alternative names of "expressive" or "non-fluent" aphasia). Although Tan's speech was limited to the one "sound", most Broca's aphasic patients can speak a little, but they seem to have problems in finding the words they want to use, and prepositions, conjunctions, and other relational words (words like "in", "and", "but", "about", "above", and so on) are often omitted. As a result, speech is slow, effortful, non-fluent, and deliberate, and may have only a very simple grammatical structure. The term "**telegraphic speech**" has often been used as a short-hand description for Broca's aphasia speech (". . . *in car* . . . *off to the* . . . *the match* . . . *City play* . . . *good watch* . . . *like City* . . ."). Despite these problems, some aspects of language function are well preserved. Patients with Broca's aphasia may be able to use well-practised expressions without obvious difficulty ("*It never rains but it pours!*") and they may also be able to sing a well-known song faultlessly. Reading aloud may be relatively unaffected. These abilities demonstrate that the problem is not related to the "mechanics" of moving the muscles that are concerned with speech, and to underline this point,

Key Terms
Speech apraxia: A characteristic sign of Broca's aphasia in which articulatory problems are apparent and speech is peppered with neologisms or paraphasias.
Telegraphic speech: A name to describe the non-fluent "stop–start" agrammatic speech associated with Broca's aphasia.

some Broca's aphasic patients have similar "agrammatical" problems when trying to write. (See Box 6.1 for an illustration of some Broca's aphasia features.) The alternative name of "expressive" aphasia is a reminder that the most obvious features of this condition relate to difficulties in language production, especially of novel (as opposed to well-learned) utterances. The lack of fluency is attributed to a speech programming deficit (aphemia in Broca's terms): a loss of the ability to execute speech movements despite an absence of facial or vocal muscle paralysis.

Notwithstanding the previous discussion, some patients with Broca's aphasia also have comprehension difficulties. For example, while the sentence "*the boy watched the girl talk with friends*" would probably not cause problems, a sentence such as: "*the girl, whom the boy was watching, was talking with friends*" might be difficult. (The test is to see if the respondent knows who was watching whom.) At present, however, it is unclear whether such comprehension deficits are related to problems with grammatical processing of the more complex sentence, or to problems with working memory or even attention. Moreover, it is generally accepted that comprehension problems in Broca's aphasia are both qualitatively and quantitatively distinct from those seen in Wernicke's aphasia (Dronkers, Redfern, & Knight, 2000). Finally, most Broca's patients are aware of their own language difficulties and have "insight" into their condition.

Box 6.1 Broca's aphasia (adapted from Stirling, 1999)

Therapist: "Tell me about your recent holiday."
Patient: ". . . Well . . . Well now . . . (long pause). We . . . err . . . I . . . holiday . . . you know . . ."
Therapist: "What happened?"
Patient: ". . . Oh, we . . . err . . . holiday . . . you know . . . seaside . . ."
Therapist: "Tell me some more."
Patient: "Beautiful weather . . ." (shows off suntan on arm)
Therapist: "Where did you get that?"
Patient: (bursts into song) "Oh, I do like to be beside the seaside . . . Oh I do like to be beside the sea . . ." (broad grin)
Therapist: "Did you go with your sister?"
Patient: "Sister . . . yes . . . sister. To . . . On holi . . . holiday . . . In a cara . . . cara . . . cara- thingy . . . caravan! That's it! A cara . . . caravan."
Therapist: "Did you take her, or did she take you?"
Patient: "Hey! You're . . . you're . . . trying to catch . . . catch me out . . .!" (grins broadly again)
Therapist: "I just wondered who made the arrangements?"
Patient: "We . . . we . . . you know, we go there . . . every . . . each . . . you know . . . year. Same place, same time, same girl." (laughs at own joke)

Comment: This vignette includes instances of telegraphic and agrammatical speech, effortful word finding, faultless expression of familiar material, and insight. Can you identify an example of each?

Earlier, we referred to the location of "Broca's area" as being in the left frontal lobe just forward from the primary motor cortex on the posterior surface of the third frontal gyrus (BA area 44 and part of area 45: see Figure 6.1a), roughly in front of and slightly above the left ear. However, recent research indicates that Broca's aphasia probably depends on more extensive damage than Broca originally thought. Indeed, lesions to Broca's area alone do not necessarily produce lasting aphasia (Dronkers et al., 1992). Adjacent cortical regions and/or areas of cortex normally hidden from view in the sulci (folds) under the surface have also been implicated. The insula is one candidate region. We will return to Dronkers' research later in this chapter.

WERNICKE'S APHASIA

Wernicke's first patient had difficulty in understanding speech, yet could speak fluently although what he said usually did not make much sense. This form of aphasia clearly differed in several respects from that described by Broca. The problems for Wernicke's patient were related to comprehension and meaningful output rather than the agrammatical and telegraphic output seen in Broca's patients. The fluent but nonsensical speech of someone with Wernicke's aphasia is all the harder to understand because of two further characteristic features. One is the patient's use of non-words or made-up words (known as "neologisms"). A second is the use of "paraphasias"—words that are semantically related to the desired word, but nevertheless inappropriate (binoculars instead of glasses for example). Most Wernicke's aphasic patients also have little or no "insight" into their condition. They talk nonsense without realising it, being unaware that other people cannot understand them (see Box 6.2).

Box 6.2 Wernicke's aphasia (adapted from Stirling, 1999)

Therapist:	"What's this for?" (shows patient a hammer)
Patient:	"Oh Boy! That's a . . . that's a thingy for . . . thing for . . . for knocking things."
Therapist:	"Yes, but what is it?"
Patient:	"It? I dunno . . . Umm . . . It's a nisby thing though!" (chuckles to himself)
Therapist:	"How about this?" (shows patient a nail)
Patient:	"That? Well, see you have those all over the place . . . In the doors, on the floors . . . everywhere's got 'em . . ."
Therapist:	"What is it?"
Patient:	"Mmm . . . See, I don't really get there much see, so . . . you know, it's kind of hard for me to spray . . ."
Therapist:	(hands patient the nail) "Do you recognise it now?"
Patient:	"Let's see now . . . it's sort of sharp, and long . . . could be a screw . . ."
Therapist:	"Do you use this (points to the hammer again) with that?" (points to the nail)

Patient: "Mmm. That's a good one! (laughs again) Let's see now, a screw and a nail eh? Maybe in a toolboss . . . Yes! That's it; they all go in the toolboss in the back of the shed you see. In the garden . . . the shed, in the toolboss."

Comment: This vignette includes illustrations of paraphasia, neologisms, incoherent speech, and lack of insight. Can you identify one example of each?

Wernicke thought that the underlying deficit in this condition was one of being unable to link sound images to stored representations (memories and conceptual meanings) of words. Although he only performed a post-mortem on one of his aphasic patients, damage was evident in the left posterior temporal region immediately behind Heschl's gyrus (the primary auditory cortex). Heschl's gyrus was known to receive massive inputs from the inner ear and is where speech sounds undergo initial analysis. Wernicke thought that the processed speech sounds would then be fed into the areas of cortex just behind Heschl's gyrus (the area commonly referred to as Wernicke's area) to be referenced to actual words (see Figure 6.1a and b). More recent evidence suggests, once again, that this analysis is somewhat simplistic, and that other areas of the cortex, in addition to Wernicke's area, may be important in understanding spoken language—a point that we return to later.

CONNECTIONIST MODELS OF LANGUAGE

THE WERNICKE-LICHTHEIM-GESCHWIND MODEL

Broca's and Wernicke's work generated considerable interest among fellow researchers. In 1885, Lichtheim proposed what has come to be known as a "connectionist" model (also called a "localisationist" model) of language to explain the various forms of aphasia (seven in all) that had by then been characterised. Incidentally, the term "connectionist" implies that different brain centres are interconnected, and that impaired language function may result from damage either to one of the centres or to the pathways between centres. The model is thus similar to the idea of a "distributed control network" that we introduced in Chapter 1, although, as originally conceptualised, it operated strictly serially (i.e., without parallel processing).

In Lichtheim's model, Broca's and Wernicke's areas formed two points of a triangle. The third point represented a "concept" centre (see below) where word meanings were stored and where auditory comprehension thus occurred. Each point was interconnected, so that damage, either to one of the centres (points), or to any of the pathways connecting them, would induce some form of aphasia. Lichtheim's model explained many of the peculiarities of different forms of aphasia, and became, for a time, the dominant model of how the brain manages language comprehension and production (see Figures 6.1 and 6.2). Although it fell out of favour in the early part of the 20th century, the model received renewed impetus in the 1960s following Geschwind's work (e.g., Geschwind, 1967).

Wernicke had actually been the first to suggest that the region of brain he had identified would be anatomically linked to Broca's area, and he reasoned that there

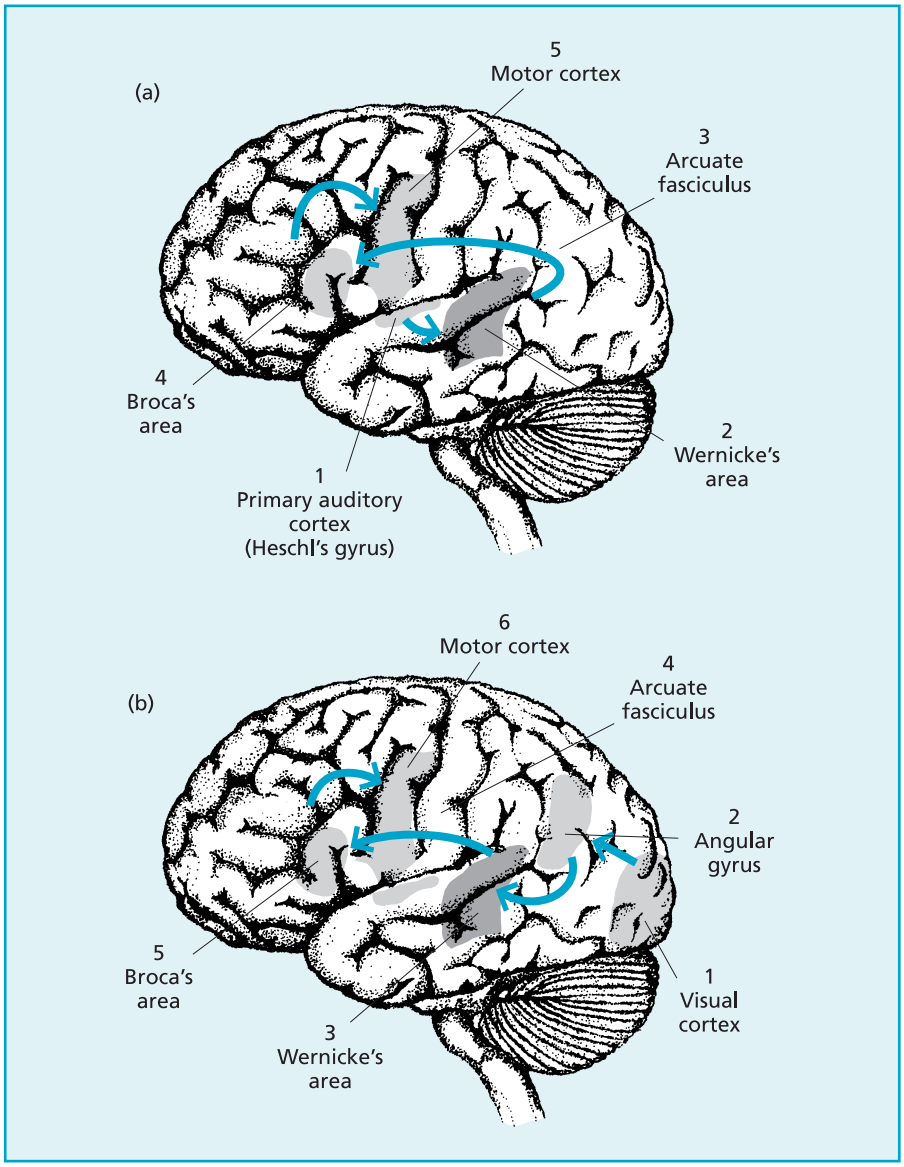


FIG. 6.1 Connectionist models of language. (a) A connectionist model for speaking a "heard" word. Sounds are initially coded in the primary auditory cortex (1) then fed to Wernicke's area (2) to be linked to meanings. The arcuate fasciculus (3) conveys information about the "heard" word forward to Broca's area (4) to evoke programmes for articulation. Output from Broca's area is supplied to the primary motor strip to produce the necessary muscle movements in the mouth and throat. (b) A connectionist model for speaking a "seen" word. As above except that following initial processing in the visual cortex (1), input is then relayed to the angular gyrus (2) where the visual image of the word is associated with the corresponding auditory pattern in the adjacent Wernicke's area.

could be a disconnection between the area for speech sounds (Wernicke's area) and the area for speech output (Broca's area), even if the two areas themselves were not damaged. The pathway in question is called the **arcuate fasciculus**, and Geschwind (1965) described a small number of aphasic individuals with *apparent*

KEY TERM
Arcuate fasciculus: Fibre bundle connecting Broca's and Wernicke's areas in the brain.

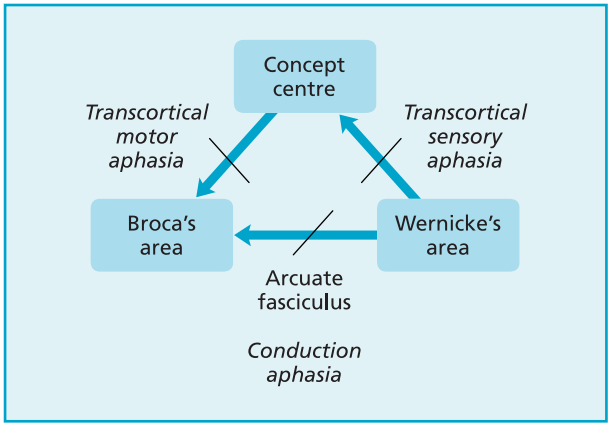


FIG. 6.2 Lichtheim's model in which Wernicke's area processed the sound image of words. This was fed forward via the arcuate fasciculus to Broca's area, which was responsible for the generation of speech output. Damage to this pathway led to conduction aphasia. A second route between Wernicke's and Broca's areas is via the concept centre, which Lichtheim envisaged as the part of the brain where meanings were stored. Damage to the pathway between Wernicke's area and the concept centre gave rise to transcortical sensory aphasia (marked by intact repetition skills but inability to understand auditory inputs). Damage to the pathway from the concept centre to Broca's area induced transcortical motor aphasia marked by a loss of spontaneous speech.

damage to it. Their disorder was known as "conduction aphasia" and, although comprehension and speech production were substantially preserved, the ability to repeat words, especially novel or unusual ones, was impaired (see Figure 6.1a and b, and Figure 6.2).

The exact location of the concept centre in Lichtheim's model was unclear, with Lichtheim himself arguing that concepts were actually distributed widely throughout the cortex. More recent interpretations (Geschwind, 1967) localised it to the left inferior parietal lobe encompassing the angular gyrus (see Figure 6.1a) and the region just anterior to this known as the supramarginal gyrus. This area is connected to (but separate from) Wernicke's area, and patients with damage to this region certainly have "receptive" language problems. However, this usually manifests as some form of "alexia" (loss of reading ability). On the other hand, damage to BA 37 (posterior medial temporal gyrus) in the left hemisphere *is* associated with lost access to semantic information about words that aphasic patients can nevertheless hear and repeat, making it a good candidate as the concept centre (Damasio & Damasio, 1989), or at least for word-level comprehension (Dronkers et al., 2004, and see below). (See Figure 6.1a and b, and Figure 2.1.)

Geschwind (1972) proposed that damage to the concept centre, or the connections between it and the other centres, readily explained the features of two further rare aphasic conditions: motor and sensory transcortical aphasia. The motor form, he argued, is similar to Broca's aphasia but, in addition, spontaneous speech is absent. Another feature is a marked tendency (which sometimes appears almost compulsive) to repeat things aloud (called "echolalia"). Damage to the pathway between the supplementary motor area (SMA) and Broca's area can bring about this disorder (Bradshaw & Mattingley, 1995). In the sensory form, difficulty with comprehension resembles that seen in Wernicke's aphasia but repetition is intact. Indeed, as with the motor form, echolalia may even be prominent. The loss of connections between Wernicke's area and BA 37 (which we mentioned earlier) may be responsible for transcortical sensory aphasia. To complete the picture, extensive damage to multiple parts of Lichtheim's system could account for global aphasia—a profound aphasic disorder affecting both comprehension and production of language. In sum, the Wernicke-Lichtheim-Geschwind connectionist model (circa 1972) provided an elaborated framework that could account for a range of both classic and more recently characterised forms of aphasia.

PROBLEMS WITH CONNECTIONIST MODELS

Despite its appeal, a number of observations soon emerged that could not easily be accommodated by the model. These coalesced under the headings of (a) lack of

symptom specificity in aphasia, (b) failure to appreciate the true complexities of requisite language processes in the brain, and (c) poor correspondence with recent neuroanatomical observations. A special issue of the journal *Cognition* (vol 92, 2004) addressed, in detail, most of these concerns and the interested reader should refer to this source. For present purposes, one illustration from each area of concern will suffice. Consider symptom specificity: Wernicke's aphasia was characterised as a receptive language disorder, yet some patients with Wernicke's aphasia produce agrammatical speech (an expressive deficit). Broca's aphasia, on the other hand, was characterised as an expressive aphasia yet, as we noted earlier, some patients with Broca's aphasia also make comprehension errors (a receptive deficit). In short, the classic aphasic syndromes actually comprise variable (perhaps overlapping) clusters of symptoms, suggesting a much more complex "neural architecture" than the connectionist model permitted.

Stemming from this point, now consider brain language processes. At one time, language processing was fractionated only into receptive and expressive functions. Later, linguists began to distinguish between syntax, semantics, phonology, and so on (see below) yet these linguistic domains are, themselves, divisible into multiple subsystems, as illustrated by the work of Levelt et al. that we review later. Third, consider recent concerns about the neuroanatomy of language. It is now apparent that damage to Broca's area does not necessarily lead to Broca's aphasia, and that Wernicke's aphasia does not usually result from specific damage to Wernicke's area (Dronkers et al., 2004). Finally, while speech production *does* appear to be the responsibility of the left hemisphere (in right-handers), effective speech perception appears to require the collaboration of both hemispheres. Thus, despite its heuristic appeal the connectionist model has, in the view of Poeppel and Hickok (2004) among others, outlived its usefulness and is no longer tenable.

INTERIM COMMENT

The study of language impairment in people with brain damage has provided a wealth of information about the role(s) of mainly left-sided cortical regions in language operations. Yet long-standing ideas about the nature of different aphasic conditions (and how they may map onto these cortical regions) cannot be reconciled either with recent observations about the true complexities of language processing, or with data from imaging studies of language, some of which we review below.

The types of aphasia identified over 100 years ago are still seen today, although careful case study has revealed additional forms of language disorder that may be related to subtle lesions/damage to other components of the brain's language system. As we shall see, recent research has led neuropsychologists to conclude that the forms of aphasia identified by Broca and Wernicke depend on more extensive damage to either frontal or posterior regions than was initially thought. It also seems that other "centres" (and interconnecting pathways) in addition to Broca's and Wernicke's areas and the arcuate fasciculus contribute to a distributed control network responsible for the full range of language functions, which is considerably more complex than the triangular connectionist model of Lichtheim. Finally, it is worth mentioning again that there is potential danger in relying on the study of damaged brains to form an understanding of normal brain function.

THE PSYCHOLINGUISTIC APPROACH

Psycholinguistics is, primarily, the study of the structure of language in normal individuals rather than the study of language dysfunction in neurological patients. (We could describe it as a "top-down" approach, whereas the neurological approach is "bottom-up".) Linguists such as de Saussure (1917) and Chomsky (1957, 1965) developed theories about the form and structure of language that were relatively independent of the neurological work described in the previous section; in fact, the two approaches initially represented quite distinct levels of inquiry into the study of language. Although it is beyond the scope of this book to provide a detailed account of contemporary psycholinguistic thinking, an understanding of some concepts and terminology is important, and will inform our discussion of the neuropsychology of language.

Psycholinguists generally divide language into four major domains:

1. *Phonology* is the investigation of basic speech sounds (*ba, pa*, and *ta* are all phonemes).
2. The study of meaning in language is known as *semantics*.
3. Words are strung together to form sentences according to particular implicit rules of grammar, known as *syntax* (*syntactic* is the adjective).
4. The study of using language in a natural social setting is known as *pragmatics*.

Phonemes are combined to form words, and our word store, which includes information about pronunciation, meaning, and relations with other words, is known as our lexicon. The structure of our mental lexicon has been a major research topic in psycholinguistics and evidence suggests that it is partly organised in terms of meaning.

From this summary you can see that psycholinguistics has a distinct approach and different level of inquiry. However, it is still of interest to ask whether there is any common ground between it and the classic neurological approach. Earlier, for example, we noted how Wernicke's and other "posterior" aphasias involve speech that, despite being correctly structured, is difficult to understand. There is also poor comprehension. A psycholinguistic interpretation would be that these aphasias are related to deficits in *semantic* processing rather than to problems with the brain's *syntactic* mechanisms. This may in turn imply that semantic processing was a function of these posterior regions.

Similarly, we earlier described individuals with damage to frontal regions (including Broca's area) as having non-fluent agrammatical aphasia. In psycholinguistic terms, this type of aphasia could be attributed to impaired *syntactic* processing. We know that some non-fluent aphasic patients have difficulties in understanding language, which would imply a problem with semantics too; however, these problems really become apparent when understanding depends on precise grammatical analysis in the absence of other semantic clues. Patients with Broca's aphasia would, for example, probably be able to distinguish between the meaningful sentence "*the boy ate the cake*" and the meaningless sentence "*the cake ate the boy*". Actually, Linebarger, Schwartz, and Saffran (1983) have shown that patients with Broca's aphasia can also distinguish accurately between grammatical and agrammatical sentences. So, it seems that the problem for individuals with this form of aphasia is not that grammatical processing mechanisms have been lost, but rather that they cannot be easily or quickly accessed.

INTERIM COMMENT

Psycholinguistics is a complex discipline and one that has been somewhat isolated. Progress has certainly been made in identifying the structure and form of language(s), its universal features, its acquisition, and so on, but until recently this work has tended to ignore pathologies of language. More recently, neuropsychologists have begun to draw parallels between aphasic disorders and disruption to specific linguistic processes. These data provide evidence of a double dissociation between semantic and syntactic processes, and illustrate clearly that no single brain "language centre" exists. This approach has been the springboard for cognitive neuropsychologists to study individual cases of language disorder in detail and, in the process, further tease apart specific components of the language system that may be selectively impaired. Functional imaging has also provided a tool for bringing psycholinguistics closer to the neuropsychology of language, as researchers attempt to map psycholinguistic concepts. See Grodzinsky and Friederici (2006) for an example where psycholinguistic concepts, classic neuropsychology, and functional imaging are brought together to propose a "map for syntax".

THE MODERN ERA OF LANGUAGE RESEARCH

The cognitive neuropsychological approach mentioned earlier is a relatively recent development (dating back no more than 25 to 35 years) and is considered in the following section. However, this is just one of three important contemporary lines of investigation that we need to review. In addition, we must consider recent explorations of language functions in the brain using neuroimaging and neurophysiological imaging techniques, and revisit some more carefully conducted neuroanatomical research.

THE COGNITIVE NEUROPSYCHOLOGY APPROACH

In this approach, which is exemplified in the work of Caplan (1992) and Ellis and Young (1996), researchers try to understand the true nature of language disturbances in relation to underlying cognitive dysfunctions. Although this approach has evolved from the psycholinguistic approach reviewed above, it differs in two important respects. First, it tries to relate language and cognitive processes, and second it focuses on pathologies of language rather than normal language. Cognitive neuropsychologists tend to focus on specific language impairments rather than **syndromal** (multi-faceted) conditions like Broca's and Wernicke's aphasia. One reason given for this approach (as we mentioned in Chapter 1) is that studying groups of people with Broca's or Wernicke's aphasia is pointless because the conditions are both broad and poorly defined (Ellis & Young, 1996). A second is that since brain damage is inherently variable, potentially informative individual differences are lost in "group"-based research (Caramazza, 1984). Thus on both counts, so the argument goes, it makes more sense to conduct detailed case study investigations on individuals with very specific language impairments.

KEY TERM
Syndromal: A feature of a syndrome, the latter being a term for a disorder or condition (such as split-brain syndrome) characterised by a cluster of interrelated signs and symptoms rather than one defining feature.

Although cognitive neuropsychologists have made progress in understanding many aspects of language impairment, we will illustrate their approach with reference to just one condition—**anomia**—defined here as a specific problem in naming objects. (Note that, confusingly, the term "anomia" is also sometimes used to identify a general word-finding problem.) If you followed the descriptions of the classic aphasias that we gave earlier you will be aware that some form of anomia is common to both Wernicke's and Broca's aphasias, which, on the face of it, is not a promising start. Yet detailed case study reveals several subtly different forms of anomia, and thorough neuropsychological testing indicates that they may have quite distinct origins in terms of cognitive dysfunction.

Consider first patient JBR, reported by Warrington and Shallice (1984). He had developed widespread temporal lobe damage following **herpes simplex** infection. He was impaired at naming living things (such as a daffodil or lion) but not inanimate objects (like torch or umbrella). However, his problem was not limited to naming because he also struggled to understand the spoken names of items that he himself couldn't name. Compare JBR with Hart et al.'s patient MD, who also had a deficit in naming animate objects, yet could sort pictures of animate and inanimate items well, and could also discriminate heard and read words from each category (Hart, Berndt, & Caramazza, 1985). This subtle distinction suggests that whereas JBR might have incurred loss (or degradation) of semantic knowledge of specific categories, MD had retained the semantic representations but his access to it from pictures or actual objects was impaired.

A third anomic patient, JCU, reported by Howard and Orchard-Lisle (1984), seemed at first glance to have a widespread generalised anomia for objects from various categories, yet could often be prompted to name items correctly if given the initial phoneme (sound) of the word. However, he was also prone to naming semantically related items if given the wrong phoneme! For example, when asked to name a tiger, and given the phoneme "L", he incorrectly said *lion*.

In contrast, patient EST, studied by Kay and Ellis (1987), had pronounced anomia with no apparent damage to semantic representations, a profile similar to classic Broca's aphasia. Although he clearly struggled to name objects from many categories, he nevertheless retained semantic information about items, voluntarily providing associated semantic information about an object even if the name eluded him. This suggests that EST's anomia was related to a problem in generating the actual words (perhaps through inaccessibility to his speech output lexicon) rather than any loss of semantic representation. To reinforce this view, patients like EST know when they have generated an approximation to the required word rather than the word itself, and will comment to this effect, saying, "*that's not quite it . . . it's like that but I forget what it actually is*".

Another word production disturbance, often encountered in Wernicke's aphasia, is known as "neologistic jargonaphasia". Patient RD studied by Ellis, Miller, and Sin (1983) was anomic, especially for rare or unusual items, yet evidence from other tests indicated that he retained semantic knowledge of the unnameable items. He could name items he had used before or was very familiar with, but for other items he generated phonological approximations—neologisms that sounded similar to the target word ("peharst" for "perhaps" for example). The major difference between EST and RD is that the former could understand speech well, but RD could not—in fact, his comprehension had to be assessed using written words. His neologisms are likely to be the result of a failure

Key Terms
Anomia: Inability to name objects or items.
Herpes simplex: Infection with this virus can affect brain function, leading to permanent damage.

TABLE 6.1 THE UNDERLYING DIFFICULTIES OF FIVE ANOMIC PATIENTS

Patient	Can understand speech	Can generate speech	Can name living things	Can name inanimate things	Has semantic knowledge about things	Likely understanding problem
JBR	Yes	Yes	Only poorly	Yes	Not about living things	Loss of semantic knowledge for specific categories
MD	Yes	Yes	Not fruit or vegetables	Yes	Yes	Loss of access (via pictures or objects) to preserved semantic knowledge
JCU	Yes	Yes	No (unless prompted with auditory cues)	No (unless prompted with auditory cues)	Partial at best	Object recognition and comprehension relatively intact but a general non-specific impairment to semantic representations
EST	Yes	Yes (but only high-frequency words)	No	No	Yes	Loss of access to speech output lexicon for low-frequency words
RD	No	No (produces neologisms)	No	No	Yes	Failure to understand speech or monitor own speech

to properly monitor his own speech, which would explain his lack of awareness of his own errors.

These types of observation have enabled researchers to develop detailed models of the cognitive processing stages involved (in this instance) in object naming. We can see, for example, that JBR's anomia appeared to be related to a problem with specific components of his semantic system, and represents a deficit in object recognition (see Chapter 8). Other operations were intact. EST, on the other hand, had problems accessing his speech output lexicon, especially for rare words, while the lexicon itself and his semantic system were probably intact. These examples also show us that, with appropriate testing, subtle differences can be identified in the form of anomia that a patient presents with. We have summarised the cases described above in Table 6.1.

In recent years, the insights provided by the cognitive neuropsychological approach have led to the development of possible treatments for anomia. Various approaches can be used. For example, patients can be taught compensatory strategies, whereby intact processes are used to support impaired ones. For individuals whose impairment is more extensive, targeted teaching tasks can lead to improvements in performance, at least for certain words. Just as cognitive neuropsychology theory can inform therapy, the success (or otherwise) of therapeutic approaches can inform cognitive neuropsychology theory. Nickels (2002) provides a good theoretical overview of the issues, while Laganaro, DiPietro, and Schnider (2006) present a more recent example focusing on three different patients with different patterns of deficit who responded to treatment in different ways.

INTERIM COMMENT

Earlier we said that the cognitive neuropsychological approach focused on language dysfunction in brain-damaged individuals. However, Ellis and Young (1996) have pointed out that the anomic disturbances seen in brain-damaged individuals are, in certain respects, simply more pronounced forms of disturbance that we all experience from time to time. Slips of the tongue, malapropisms, spoonerisms, and the "tip of the tongue" phenomenon are all features of "normal" language usage (see Freud, 1901), and may be related to brief disruptions of the same processes (or components) that are more severely affected in cases of clinical anomia. The cognitive neuropsychological approach has developed rapidly as researchers exploit in-vivo imaging techniques for exploring brain–language relations, as discussed in the following section.

NEUROPHYSIOLOGICAL APPROACHES

Structural and functional in-vivo imaging techniques such as CT, MRI, and PET (see Chapter 2) are gradually leading to important discoveries about many aspects of brain function, and language is no exception. CT and structural MRI scan data tend to reinforce the classic post-mortem findings of extensive damage and loss of tissue in frontal areas in people with Broca's aphasia, and posterior damage in individuals with Wernicke's aphasia (Damasio & Damasio, 1989; Naeser & Hayward, 1978). See the section on neuroanatomy later in this chapter for some more detailed studies. When PET is used to examine "resting" brain function, patients with non-fluent (Broca's type) aphasia show underactivation in left frontal regions, while patients with fluent aphasia show underactivation in more posterior regions. However, when anatomical and activation data are compared in the same individuals, underactivity is sometimes observed in areas that are not damaged. Moreover, the functional measures correlate more closely with language disturbance than do the anatomical measures. This is a reminder that visible anatomical lesions may only reveal part of the story.

PET and fMRI have also been used to examine functional activity in normal individuals while they undertake different types of linguistic task. Compared to other areas of neuropsychology, PET continued to be relatively widely used even as fMRI became more popular. There are two reasons for this. First some of the critical areas in language research are areas that are particularly prone to artefacts in MRI imaging. Second, fMRI is an extremely noisy procedure and in studies employing spoken language as stimulus material this presents a significant technical challenge—it is obviously essential that participants can hear the stimulus input clearly! However, over the last few years technological advances in MRI physics and stimulus presentation have overcome both of these problems at many imaging centres and therefore fMRI is now more widely used for language studies.

Since the initial pioneering PET studies of normal language (Petersen et al.'s 1988 study of word generation, for example, is widely regarded as a "classic"), hundreds of neuroimaging studies of language have been published. Taken together, these have significantly refined our understanding of the brain basis of normal language. For example, Vigneau et al. (2006) published a meta-analysis based on 260 articles published between 1992 and 2004. This led them to conclude

that language is represented in large-scale distributed control networks in the left hemisphere. For example, Figure 6.3 shows brain activations associated with semantic processing.

A detailed review by Demonet, Thierry, and Cardebet (2005) subdivided neuroimaging language research into certain core processes. They reviewed research on single word processing as well as research on sentence and discourse processing. We will return to the latter issue later in this chapter when we consider laterality. For single word processing, Demonet et al. identified five distinct research areas: spoken word perception, visual word perception (reading words), semantic processing (extracting meaning), spoken output, and written output. Figures 6.4a and b show the brain activations associated with processing spoken and visual words respectively. While an exploration of all these areas is beyond our scope, certain illustrative examples highlight the advances that neuroimaging methods have brought about. Neuroimaging of spoken word perception has shed new light on classical aphasia-based models of comprehension, suggesting that the left posterior superior temporal gyrus (Wernicke's area) is functionally heterogeneous. Wise et al. (1999, 2001) report two distinct subregions. One is activated during both perception and production of speech and appears to serve as a temporary buffer for the storage of speech sounds. Another is activated during articulatory speech movements and appears to act as an interface between speech sounds and the motor codes needed to generate them.

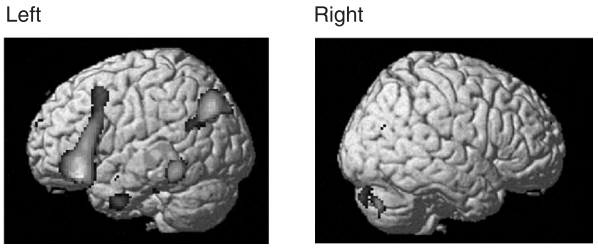


FIG. 6.3 Regional brain activations associated with semantic processing. This figure demonstrates a network of interacting cortical structures, predominantly on the left side. We are very grateful to Professor Cathy Price of the Wellcome Trust Centre for Neuroimaging, London, for providing these images.

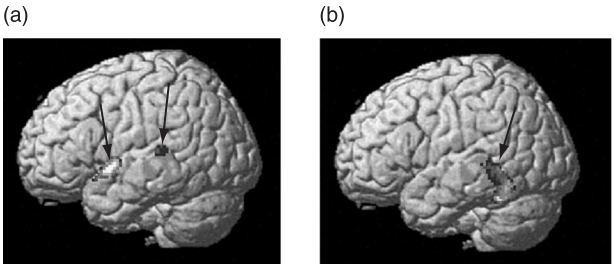


FIG. 6.4 Regional brain activations associated with lexical processing of (a) auditory words and (b) visual words. (a) Activations associated with listening to words compared to listening to reversed words; (b) activations associated with viewing words compared with viewing false fonts (strings of pseudo-letter symbols). We are very grateful to Professor Cathy Price of the Wellcome Trust Centre for Neuroimaging, London, for providing these images.

Studies of reading single words have also produced informative results. For example, Jobard, Crivello, and Tzourio-Mazoyer (2003) showed that distinct regions of the left posterior inferior frontal gyrus (Broca's area) are activated depending on whether participants are reading regular or irregular words. The reading of irregular words is thought to be dependent on a direct association between the visual form of the word and its meaning, since "sounding out" the word phoneme by phoneme does not produce a recognisable word (if you read the word "yacht" by making the component sounds, you generate something that makes no sense; to understand the word you have to recognise the visual form and translate that directly to meaning). Interestingly, this distinction is relevant to studies of reading different languages. For languages like English, where there are many irregularities, word reading activates subtly different regions than languages like Italian, where letter-to-sound conversion is much more reliable (Paulesu et al., 2000).

A number of the earlier neuroimaging studies selected tasks that were adjudged to be "simple". For example, Petersen et al.'s classic PET study of 1988 chose word generation. However, psycholinguists such as Levelt (1989) have long argued that word generation is, in fact, a task of considerable complexity involving

multi-tiered processing components. Although the precise details of Levelt's theory need not concern us (but see Levelt, Roelofs, & Meyer, 1999, for further information), a version of his model of word generation does merit consideration and is summarised in Box 6.3.

Box 6.3 A summary of Levelt's model of word generation

- First, the speaker needs to be aware of the social context in which word generation is occurring, to remember the rules of the experimental task, and to know what is expected of him/her.
- Next, there must be some conceptual preparation, which may depend on semantic processing of the stimulus material that is to be responded to: e.g., "*generate a verb which relates to the following noun*".
- Since there may be many alternatives (i.e., lots of potential verbs), the mental lexicon must be accessed, and some form of selection undertaken.
- Once selected, the mental representation of the word must be articulated. But word articulation is itself a compound task, involving the sequential processing of phonemes.
- These in turn permit the generation of syllables. (Although most spoken English is based on reassembling no more than 500 syllables, the language itself contains about 50,000 words.)
- Quite how these are translated into sounds is not known, but it is clear that the actual articulation process is flexible—people can make themselves understood with their mouth full, or when smoking a cigarette for example!
- Humans can produce about 12 speech sounds per second, and this involves the precise coordinated control of at least 100 different muscles.
- Generated speech is also monitored by the speaker and, if necessary, corrected for errors, sometimes before the errors are even articulated.
- Speech is also effortlessly adjusted for volume and speed of delivery to suit the particular environment.

This summary makes it abundantly clear that the task of selecting a single word (in response to a picture, word, or other stimulus) involves multiple processing stages, and is in fact an enormously complex undertaking. According to Indefrey and Levelt (2000), it is still possible to make sense of functional imaging data by taking advantage of the fact that most studies have used slightly different experimental procedures. For example, some, like Petersen et al.'s, have used verb/word generation. Others have employed word repetition, or picture naming. Sometimes, word generation has been overt, while in other studies silent, or delayed. The different procedures involve different core processing stages; so, for example, word repetition does not make demands on conceptual preparation. Similarly, the first core process implicated in reading pseudo-words (non-words that sound like words) is phonological encoding, and so on. Thus, it is possible to tease apart the individual components involved in different word generation studies, and Indefrey and Levelt (2000) have presented such a provisional meta-analysis. More recent

functional imaging studies have used more subtle experimental designs and more carefully chosen control tasks that acknowledge the complexity of even apparently "simple" language tasks.

fMRI and PET have also provided valuable tools for assessing language processing in individuals whose language abilities are in some way abnormal. Most obviously this involves the use of neuroimaging in aphasic patients, although this approach has been relatively little used. This may reflect the heterogeneity of patients preventing the usual neuroimaging group studies, however Price et al. (1999) made a convincing case for applying neuroimaging to single case studies. Another interesting angle has been to study individuals who are not aphasic but who have atypical language abilities. For example, there have been studies of multilingual people. Kim et al. (1997) showed that in bilingual people who learned their second language as adolescents or later, distinct regions of the left inferior frontal gyrus represent the two languages. However, in people who were exposed to both languages from early childhood, there is far less distinction. This finding has important implications for understanding language development. Another interesting study group are the congenitally deaf. These people have never been exposed to spoken language and use sign language to communicate. Sign language is effectively their native language. The striking finding of neuroimaging is that sign language recruits remarkably similar brain areas to oral language (Neville et al., 1998), suggesting that these brain regions are biased to represent language even in a non-auditory form.

NEUROANATOMICAL RESEARCH

The "neurological/neuroanatomical" approach was an obvious choice for the early researchers who relied on case studies of individuals with brain damage. Cases of Broca's and Wernicke's aphasia have been reported and described for over 100 years and are relatively commonplace today. Each is widely accepted as a legitimate clinical entity. But the real question is not how many cases of these syndromes conform to the description and anatomical model of Lichtheim, but how many do not. This matter has been carefully explored by Dronkers and her colleagues at the University of California (Dronkers et al., 2000; Dronkers, Redfern, & Ludy, 1995). Her starting point was the realisation that certain problems with the connectionist model have been routinely "forgotten" in the quest to find supportive evidence for it. For example, as we mentioned earlier, the grammar-based comprehension difficulty of many Broca's cases does not fit well with the idea of this aphasia as a disturbance of expressive language function. Moreover, the connectionist model has somewhat conveniently ignored the fact that many patients with Wernicke's aphasia make significant recoveries, ending up with few lasting comprehension problems despite obvious posterior damage. As we also mentioned earlier, the true neuroanatomical locations of Broca's and Wernicke's areas have even been questioned.

By 1992, Dronkers' group had detailed evidence on 12 right-handed Broca's aphasic patients, two of whom had lesions that spared Broca's area. Ten more cases were identified in whom damage to Broca's area was apparent, but who had no true Broca's aphasic features. In a similar vein, Dronkers et al. (1995) reported seven cases of Wernicke's aphasia, of whom two had no damage to Wernicke's area at all, and seven additional cases with damage to Wernicke's area but without the persistent features of Wernicke's aphasia.

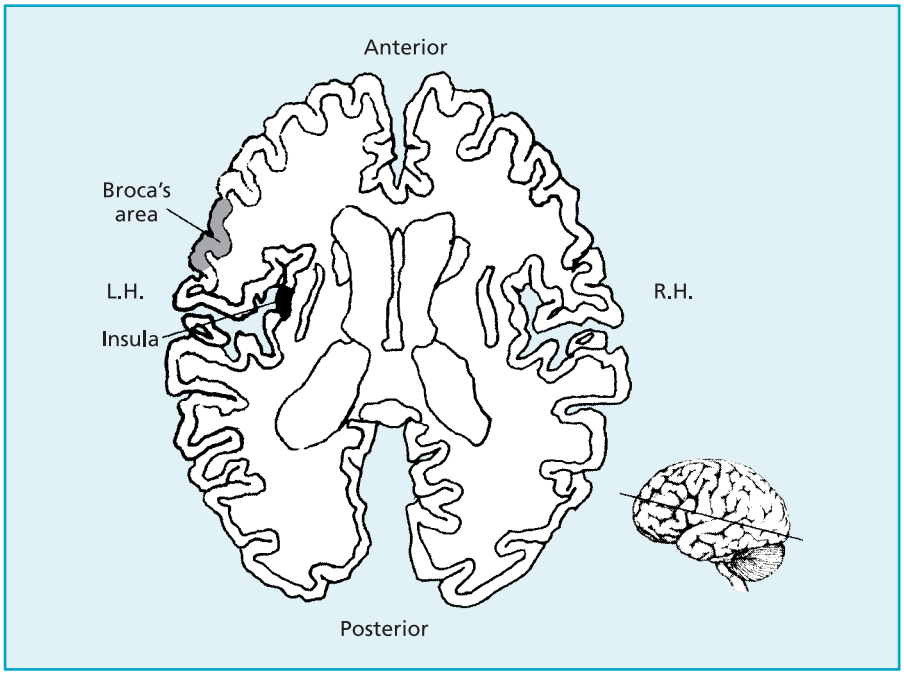


FIG. 6.5 The location of the superior tip of the left insula. This region, identified by Dronkers et al., is consistently damaged in aphasic patients with speech apraxia. Broca's area is indicated for reference.

Dronkers' patient pool has grown to over 100 very clearly defined and extensively imaged people with aphasia, and it has been possible to look for anatomical commonalities within aphasic groups. For example, every person who met the full diagnostic criteria for Broca's aphasia had damage to a specific part of a deep cortical region in the left frontal lobe known as the insula (the superior tip, see Figure 6.5), though posterior inferior frontal gyrus (IFG) damage was not ubiquitous (actually found in 85% of cases: Dronkers, 2000). The immediate conclusion from this observation might be that the insula (rather than the IFG) is the true location of Broca's area—but this would be incorrect because the research group also had a small number of patients with damage to the superior tip of the insula who did not have Broca's aphasia. However, they all had speech apraxia (an articulatory speech programming disorder encountered earlier, in which the individual may produce neologisms—i.e., approximations to the correct word, or distortions of it, rather than the word itself). This is, of course, a prominent though not defining feature of Broca's aphasia. The most parsimonious explanation for this finding is that if, as is often the case, frontal damage includes this region of the insula, the individual is likely to experience speech apraxia as one of the features of their aphasia.

Dronkers' work has stimulated renewed interest in the anatomical substrate(s) of Broca's aphasia, although her conclusions have not gone unchallenged. For example, Hillis et al. (2004) failed to find an association between left insular damage (assessed by MRI) and speech apraxia, but they did find a strong association between the disorder and underactivity in the left posterior inferior frontal gyrus (i.e., Broca's area). A strength of this study was the large sample ($n = 80$) of both acute and chronically speech-apraxic patients—an important consideration

because stroke-induced speech apraxia is often transient, showing substantial recovery over a period of months. Dronkers' cases were chronic, suggesting much larger areas of stroke damage, but also making it more likely that her findings were partly artifactual, because the insula is particularly susceptible to large mid-cerebral artery strokes.

Borovsky et al.'s (2007) study of anatomical correlates of conversational speech deficits perhaps moves us closer to a satisfactory conclusion to this debate: This group reported that both poor fluency and low complexity were associated with lesions in a cluster of left anterior locations including the insula, inferior frontal gyrus, primary motor cortex, and underlying white matter. They suggest that these form a network mediating the production of complex and fluent speech, and that further specificity (localisation) is not currently possible; Broca's area, for example, being anatomically large and functionally diverse, should be subdivided (which neither Hillis's or Borovsky's imaging procedures permitted) in order to truly map structure to function.

Dronkers' group has also explored the anatomical basis of the comprehension difficulties often reported in Broca's aphasia (see Bates et al., 2003). Almost all such cases have damage to anterior regions of the superior temporal gyrus (on the left). This area is frequently damaged in Broca's aphasia but is, of course, in the temporal rather than frontal lobe. At present it is difficult to ascertain whether this region is truly a grammar "node" in the language network, or part of a working memory network that is needed to process longer sentences. However, functional imaging studies by Mazoyer et al. (1993) and Bavelier et al. (1997) have also confirmed the importance of this region in sentence comprehension in normal individuals. As for Broca's area itself, it seems to serve a number of functions including, for example, a role in verbal working memory, in addition to its involvement in the programming of motor control of speech production, the function that Broca originally ascribed to it. However, concerns remain about the anatomical boundaries of this region: In a fascinating recent MRI re-analysis of the actual brains of Broca's first two patients (Leborgne and Lelong) by Dronkers et al. (2007), damage *was* apparent in the left inferior frontal gyrus (BA 44 and 45) but also in left medial structures and associated white matter tracts. Clearly, progress in establishing the exact role(s) of Broca's area will be contingent on a consensus about both its boundaries and if/how it should be subdivided.

In the case of Wernicke's aphasia, enduring symptoms are only found in individuals with extensive damage to the posterior regions of the mid-temporal gyrus and underlying white matter. Smaller lesions, either in Wernicke's area itself or to other posterior temporal sites, usually produce only transient aphasic features that resolve in a matter of months. According to Dronkers et al. (1998), damage to Wernicke's area alone is more likely to be associated with repetition deficits than comprehension problems. The authors have suggested that this deficit could primarily be an auditory short-term memory problem in which the individual cannot hold on to the **echoic trace** of an item long enough to repeat it.

In a more recent study (Dronkers et al., 2004), 64 patients with left hemisphere brain damage were studied using a combination of neuropsychological and structural imaging techniques. This revealed five brain regions involved in language comprehension and, notably, neither Broca's nor Wernicke's areas were among them. However the regions identified were adjacent to either Broca's or Wernicke's area and Dronkers therefore suggests that the classical findings were actually due to damage to these closely adjacent regions. A critical region identified in this

Key Term
Echoic trace: A form of very short-term auditory memory (a sort of acoustic after-image) thought to last no more than 1 or 2 seconds.

study was the middle temporal gyrus. Patients with damage to this region had the most pronounced comprehension deficits and the authors suggest that this region is involved in word-level comprehension. Damage to the other regions, including other regions of temporal cortex and inferior and mid-frontal cortex, is proposed to cause sentence-level comprehension problems. The patients in Dronkers' study showed different patterns of deficit depending on which region, or combination of regions, was damaged and this raises the obvious possibility that differences in presentation of "classic" Broca's and Wernicke's aphasias may reflect differences in the extent of damage within these closely connected regions. Dronkers believes that none of the five regions identified is dedicated to sentence comprehension per se, but that they work together as a network supporting language comprehension.

Dronkers' approach has shown that it is possible to draw conclusions about brain–language relations if one has access to aphasic individuals with carefully characterised symptoms/features and anatomically accurate information about brain lesions. The work of her group indicates that, in addition to Broca's and Wernicke's areas and the arcuate fasciculus, many other regions, mainly on the left in the temporal lobe, contribute to both receptive and expressive language functions. It also generates hypotheses about normal language function that can be tested by functional brain imaging. Like Levelt, Dronkers et al. (2000) acknowledge that the neuropsychology of language has, for too long, been guided by an oversimplified model of how the brain deals with language. The emerging model must integrate the new language areas with the traditional ones, but also factor in attentional, executive, and working memory processes in order to provide a more realistic framework of brain–language networks.

INTERIM COMMENT

Three recent lines of research have taken our understanding of the neuropsychology of language well beyond the revised connectionist model of the early 1970s. The cognitive neuropsychology approach has shown how, by careful observation and neuropsychological testing, it is possible (and informative) to distinguish between subtly different forms of language dysfunction. The neuroimaging approach has not only tended to reinforce, but also to extend classic models of how the brain processes language. In particular, this approach has led to the identification of brain regions not previously thought to be involved in language. The neuroanatomical approach of Dronkers et al., Hillis et al., and Borovsky et al. has shown how it is possible to relate loss of function to cortical damage, provided that patients are thoroughly tested and the damage is precisely mapped. A picture emerging from all three approaches is that language itself is far more complicated than the early researchers thought. Thus, the neural networks serving language comprise many more discrete regions, albeit mainly on the left side, than earlier models suggested. Additionally, functional imaging suggests that these regions function as extensively interconnected networks.

LANGUAGE AND LATERALITY

From our review of brain–language research, it would be reasonable to conclude that language is mediated by a series of interconnected regions in the left hemisphere. This pattern of "distributed control" is found in almost all right-handers, and the majority of left-handers (Rasmussen & Milner, 1977). Over 100 years ago Broca declared "*nous parlons avec l'hemisphere gauche*", and both the functional and structural imaging findings bear this out to a certain extent, as does much of the research on language function in the split-brain syndrome and data derived from the Wada test (see Chapters 2 and 3).

So is the left hemisphere *the* language hemisphere? Not exclusively. Although hundreds of neuroimaging studies have revealed strong left-sided activity in language tasks, many have also shown activity (usually to a lesser extent) in corresponding regions on the right. For example, Figure 6.6 shows a bilateral network of brain regions involved in speech production. Indeed, there is evidence to show that certain aspects of language are managed, perhaps predominantly, by the right hemisphere. One aspect that appears to be the preserve of the right hemisphere is the processing of emotional aspects of language. For example, individuals with right hemisphere damage, and with otherwise intact language skills, may speak in a monotone, despite *understanding* the emotional connotations of what they are saying (Behrens, 1988). The region of right cortex in question is in the equivalent location to Broca's on the left. In other words, damage to Broca's area impairs fluent speech. Damage to the equivalent area on the right impairs emotionally intoned (**prosodic**) speech, which instead is said to be "aprosodic". More posterior right-sided damage (in regions roughly equivalent to Wernicke's area on the left side) can lead to difficulties in the interpretation of emotional tone. PET studies with normal individuals have also highlighted this double dissociation: speech production requiring emotional tone activates frontal regions on the right (Wallesch et al., 1985), whereas comprehension of emotionally intoned speech activates posterior regions on the right (Lechevalier et al., 1989). Obviously, the actual message may convey enough meaning to be understood without having to decode the emotional tone too, but sometimes appreciation of tone is critical in understanding the true message. "Thanks very much!" can mean "thank you" or "thanks for nothing" depending on the speaker's tone of voice. The right hemisphere's interpretation of "prosodic cues" appears to be closely related to more fundamental skills in detecting tonal differences, or changes to pitch, which are also mediated primarily by the right hemisphere: Stirling, Cavill, and Wilkinson (2000) reported a left ear (right hemisphere) advantage in normal individuals for the detection of emotional tone in a dichotic listening task (this sort of experiment is described in Chapter 9 and illustrated in Figure 9.1), a finding that reinforces the view that the processing of emotional voice cues may be preferentially a right hemisphere task.

There is growing evidence linking inferential skills (filling in the blanks, or "putting two and two

KEY TERM
Prosodic: An adjective to describe emotionally intoned language. (Aprosodic speech is devoid of emotional intonation, or monotone.)

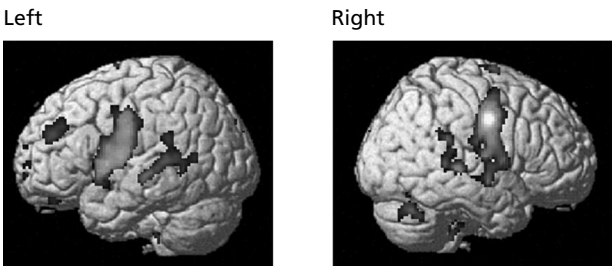


FIG. 6.6 Bilateral brain activations associated with speech production. This figure clearly demonstrates that some normal language functions rely on neuronal activity in both left and right hemisphere regions. We are very grateful to Professor Cathy Price of the Wellcome Trust Centre for Neuroimaging, London, for providing these images.

together") and even "sense of humour" to the right hemisphere too. Individuals with right hemisphere damage are less adept at following the thread of a story (Kaplan et al., 1990) or understanding the non-literal aspects of language, such as metaphors (Brownell, 1988). They also struggle to rearrange sentences into coherent paragraphs (Schneiderman, Murasugi, & Saddy, 1992). Functional imaging has revealed greater right- than left-sided activation associated with "higher-level" language tasks, such as understanding metaphors (Sotillo et al., 2005), detecting inconsistencies in stories (Ferstl, Rinck, & von Cramon, 2005) and drawing inferences from text (Mason & Just, 2004). The idea that the right hemisphere may be critically involved in more abstract aspects of language is one that is gaining ground and is, in certain respects, reminiscent of the idea (discussed in Chapter 3) that the two hemispheres have different processing styles. Jung-Beeman (2005) has proposed that the two hemispheres allow a two-pronged approach to the comprehension of natural language. The left hemisphere is involved in rapid interpretation and tight links, while the right hemisphere underpins broader meaning and recognition of distant semantic and conceptual relations.

A final interesting point concerning language lateralisation is that the right hemisphere can sometimes support the recovery of language function following brain damage. This is particularly true in children, as we discussed in Chapter 3. In fact, children who have had their entire left hemisphere removed to treat epilepsy can regain most language abilities (Vargha-Khadem et al., 1997) and this must be mediated by the right hemisphere. In some cases adults can also regain some degree of language function after left hemisphere damage, due to the corresponding region on the right taking over the function (e.g., Blank et al., 2003). One interpretation of these observations is that language areas exist on the right and, if necessary, these can become more finely tuned to perform tasks that are normally the province of left-lateralised regions.

CHAPTER SUMMARY

The classic neurological approach to understanding the role of the brain in language relied on case studies of people with localised damage, usually to the left hemisphere. Broca and Wernicke described differing forms of aphasia, the prominent features of the former being non-fluent agrammatical speech, and those of the latter being fluent but usually unintelligible speech. Their work led to the development of Lichtheim's "connectionist" model of language, which emphasised both localisation of function and the connections between functional areas. Connectionist models gained renewed impetus with the work of Geschwind in the 1960s.

Three new lines of inquiry—the cognitive neuropsychology approach, functional neuroimaging research, and the neuroanatomical work of Dronkers and colleagues—have prompted new ideas about the networks of brain regions that mediate language. The cognitive neuropsychological approach has underlined the subtle differences in cognitive processes that may give rise to specific language disorders. The functional imaging research has identified a wider set of left brain (and some right brain) regions that are clearly active as participants undertake language tasks. The newer structural imaging work has also prompted this conclusion, as well as necessitating a re-evaluation of the functional roles of Broca's

and Wernicke's areas. The emerging view from these diverse research approaches is that language is a far more complex and sophisticated skill than was once thought. Many left-sided cortical regions collaborate in a truly distributed network to facilitate receptive and expressive language functions. Their work is supplemented by right hemisphere regions with particular responsibilities for higher-level aspects of language processing.

CHAPTER 7

CONTENTS

7

Memory and amnesia

(contributed by Andrew Parker)

INTRODUCTION

Memory has been investigated extensively by those involved in neuropsychological research. This research has taken many forms encompassing practically all types of memory, ranging from information that is processed for the briefest of periods of time to memory across the lifespan. This chapter assesses the contribution that neuropsychologists have made both through the study of those individuals with brain damage and by use of neuroimaging procedures with healthy volunteers. Memory itself, at a most general level, refers to our ability to acquire, retain, and retrieve information (see Figure 7.1a). This information is stored in the brain, and thus analysis of those who have sustained damage to the brain, or techniques that allow us to image brain activity, provide us with means by which we can understand memory.

The fact that memories are stored somewhere in the brain, *and* that they consist of activities involved in acquiring, storing, and retrieving information, points to two general theoretical approaches that have provided guiding frameworks in the study of memory. The first approach has often been labelled the *systems* approach and takes the view that different types of memory are located within different regions of the brain (e.g., Cohen & Squire, 1980; Schacter & Tulving, 1994). The second approach has been called the *process* approach and takes the view that memory is composed of different processes that may recruit similar or different neural regions depending on the task facing the individual (e.g., Cermak, 1994; Roediger, Weldon, & Challis, 1989; Verfaellie & Keane, 2002). Of course this dichotomy simplifies many aspects of past and ongoing research; memory is likely to consist of multiple neural regions and multiple processes (Parkin, 1999). In light of this, the current chapter emphasises the idea that memory consists of both systems and processes and that both views are important for a comprehensive understanding of this topic.

The chapter starts with a consideration of short-term and **working memory** before moving onto long-term memory. This outline appears to emphasise the memory systems approach, and indeed in some ways it does. However, this is purely for the sake of exposition, as the reader will soon become aware of how

KEY TERM
Working memory: A form of short-term memory, first characterised by Alan Baddeley, which allows a person to hold "on-line" (and manipulate) a certain amount of information for a few seconds after it has been presented. For example, keeping a phone number in mind until you have dialled it.

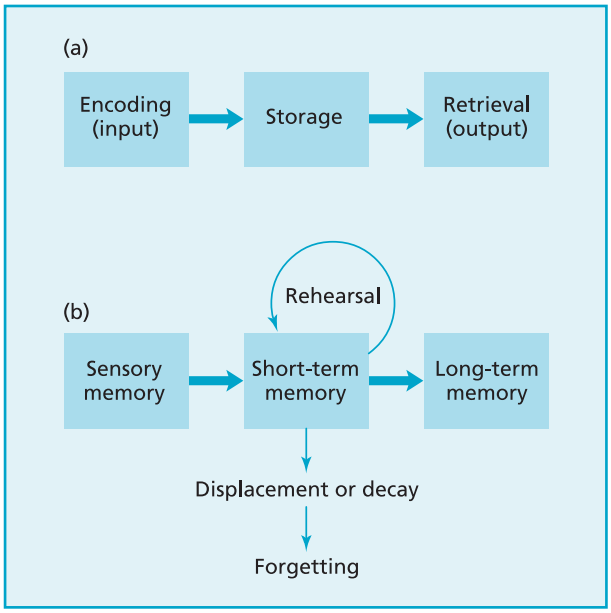


FIG. 7.1 (a) A generic model of the main information processing activities associated with memory. (b) A schematic diagram of Atkinson and Shiffrin's model of human memory. According to this model, sensory input was conceptualised as passing from a sensory register into short-term storage. If the material was rehearsed it would be consolidated into long-term memory. Otherwise it would quickly be forgotten.

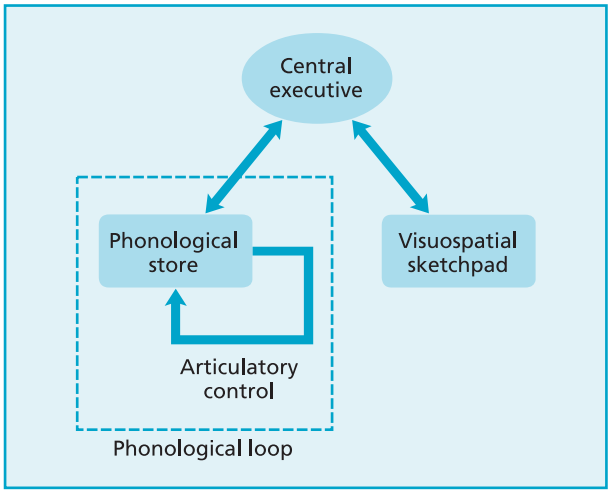


FIG. 7.2 The key components in Baddeley's model of working memory. The central executive coordinates activity in the two slave systems to keep in mind visuospatial or auditory-verbal information.

these "so-called" systems operate, and thus of the processing activities performed by these systems.

SHORT-TERM MEMORY AND WORKING MEMORY

The idea of short-term memory (STM) has a long history but its most influential form was developed by Atkinson and Shiffrin (1968). Their "modal model" of memory (see Figure 7.1) distinguishes between a sensory memory store (which stores sensory impressions for very brief periods of time), a short-term memory store (which can hold information over longer periods through mental rehearsal), and a long-term memory store (into which information is passed following processing by the short-term store). The model proposes that the memory stores (systems) are essentially unitary: that is, indivisible into separate subcomponents. However this notion has been subject to revision following empirical investigations into both short-term and long-term memory.

With respect to short-term storage, the concept of a unitary STM system presented a number of problems and has undergone subsequent revisions. These revisions eventually led to an alternative conception in which STM is composed of a number of subsystems. This multi-component model, referred to as working memory, is most closely associated with the work of Alan Baddeley and colleagues (e.g., Baddeley, 1986; Baddeley & Hitch, 1974). The structure of working memory is illustrated in Figure 7.2. It consists of a central executive whose function is to direct and regulate the flow of information, and allocate attention and processing operations within the two "slave" systems, so-called because they are essentially controlled by the central executive. These slave systems are the visuospatial sketchpad (which serves the function of integrating and processing spatial and visual information over short periods) and the phonological loop (which serves the function of storing and processing verbal auditory information over short periods). Although the model was initially proposed on the basis of research with individuals without brain damage, the study of both neuropsychological patients and the use of neuroimaging with healthy controls has been useful in its subsequent testing and development.

NEUROPSYCHOLOGICAL EVIDENCE FOR COMPONENTS OF WORKING MEMORY

The visuospatial sketchpad is the subsystem responsible for the temporary storage and manipulation of visual and spatial information. One particular neuropsychological test used to assess visuospatial memory is the Corsi block test (see Chapter 2). In this task nine identical blocks are arranged in front of the participant in such a manner that there is no apparent order or pattern to their placement. Following this, the experimenter taps the blocks in a particular sequence (e.g., touches block 3 followed by 5, 2, 8, etc.). The participant is then required to immediately reproduce this sequence. This measures visuospatial working memory, as the participant has to retain the spatial sequence in order to achieve accurate reproduction. DeRenzi, Faglioni, and Previdi (1977) found that patients with damage to the right posterior parietal region were significantly impaired on this task. However, the parietal regions do not act by themselves in terms of processing spatial information—the right frontal cortex is also important. For example, Pigott and Milner (1994) tested performance on a task that required short-term memory for chequerboard-like patterns. In this, participants were presented with a random array of black and white squares. After a short delay the participant was shown the same pattern with one of the squares missing. It was found that those with right frontal damage were impaired at remembering the spatial position of the missing square. Neuroimaging work also suggests a role for frontal regions in visuospatial working memory. For example, Smith, Jonides, and Koeppe (1996) presented to participants arrays of dots on a computer screen for 200 ms. Following a 3-second delay, a circle appeared either in the same or in a different location to one of the dots. Participants were asked to decide if the circle would have covered one of the dots if it had been present at the same time. It was found that this task led to activation in the right frontal lobe.

The label "visuospatial" suggests a combination of both visual and spatial processing. In everyday life most visual perceptions contain both visual and spatial information, which may in turn suggest that such features are processed together in the brain. However, it is now becoming clear that the visual and spatial components of working memory can be dissociated. For example, Owen et al. (1995) reported that damage to the anterior temporal lobes impairs visual working memory, while leaving spatial working memory intact. Conversely, Levine, Warach, and Farah, (1985) reported that damage to the parietal lobes selectively impairs spatial memory tasks. This double dissociation provides strong evidence that the visuospatial sketchpad needs to be subdivided into separate visual and spatial components. The visual component is important for processing the identity of the object, while the spatial component is important for processing the relative location of objects or features of object. Overall, these studies testify to the importance of neuropsychological research in advancing our understanding of this component of working memory.

Neuroimaging with healthy controls has also revealed that separate regions are implicated in the processing of visual and spatial information, with visual working memory associated with activations in inferior occipitotemporal regions and spatial working memory associated with activations in parietal regions (Courtney et al., 1996; Postle, Druzgal, & D'Esposito, 2003).

In Baddeley's model the phonological loop actually comprises a passive storage system called the phonological store and an active rehearsal mechanism

called the articulatory control process. The former is responsible for the temporary storage of speech-based sounds which decay rapidly unless refreshed by the articulatory control process. An everyday example of the phonological loop would be holding a phone number in one's memory just long enough for a call to be made; the number is held in the passive store in speech-based form and refreshed by subvocal rehearsal. Studies of brain-damaged individuals support the idea that the phonological loop consists of two components. For example, it is possible to observe patients with damage to the phonological store without damage to the articulatory control process (e.g., Caterina & Cappa, 2003; Vallar & Baddeley, 1984). Neuroimaging work also provides broad support for the model, as different activations are associated with the phonological store, in BA 40 on the left, and the rehearsal process, in BA 44/45 also on the left (Awh et al., 1996; and see previous chapter). However, the location of these subsystems is far from being resolved. For example, Chein, Ravizza and Fiez (2003) argued that the putative location of the phonological store around BA 40 may not be an accurate reflection of the functions of this region as it is often activated by non-verbal stimuli, which is inconsistent with its role in phonological processing.

Recent work in neuroimaging has revealed some interesting findings about auditory non-verbal working memory that are not encompassed by Baddeley's model. Arnot et al. (2005) found support for the idea that the neural processes that support working memory for the identity of a sound differ from those that support working memory for localising a sound. In their experiment, participants were presented with two sounds in succession and performed one of two tasks. In one task, participants were asked if the second sound was the same as the first. In the other task, participants were asked if the second sound was in the same spatial location as the first. Arnot et al. found that working memory for the identity of the sound activated a region in the left superior temporal gyrus. In contrast, working memory for spatial location activated parietal cortex, posterior temporal lobe, and the superior frontal sulcus. Thus the processing associated with auditory non-verbal working memory appears to be functionally segregated, with different processing requirements being performed by different neural regions or pathways. In some sense this finding is similar to the results obtained for visuospatial working memory in which the neural regions associated with the processing of object identity are different from those associated with object location (see Chapter 8 for a review of dorsal and ventral streams, and Box 7.1 for a description of a recent modification to Baddeley's working memory model: the episodic buffer).

Box 7.1 Additions to the working memory model: the episodic buffer

Although the working memory (WM) model has stood the test of time and received considerable support, a number of changes and adaptations have been made that further refine the original ideas about short-term storage and processing. One important change has been the addition of a new component called the episodic buffer (Baddeley & Wilson, 2002). This component was added for two main reasons: first, because of the need for WM to have some means of integrating visual and verbal codes (which, remember, are processed by separate

subsystems); second, because of the need for the temporary storage of information that exceeds the capacity of the two slave subsystems. The latter came to light from the finding that immediate memory span for prose passages is much greater than that for unrelated lists of words. Originally, this fact was attributed to long-term memory. However, Baddeley and Wilson (2002) reported a group of amnesic individuals who, despite having impaired long-term memory, displayed normal levels of prose recall if asked to remember the passages immediately without any form of interference or delay. If the superiority of prose recall is dependent on long-term memory, then the amnesic individuals should clearly be deficient when tested on this task. Baddeley and Wilson claimed that the reason for unimpaired recall of prose was due to the operation of the episodic buffer, which is able to hold and integrate relatively large amounts of information over short periods and act as an intermediary between the two slave systems and long-term memory. This conception of the episodic buffer is not without its critics. Gooding, Isaac, and Mayes (2005) point out that as a theoretical construct it is as yet somewhat underspecified and difficult to test. Also, there is currently no means of assessing the independent contributions of the episodic buffer and long-term memory to prose recall. As a consequence the validity of the episodic buffer awaits the test of time and future research.

The central executive is considered to be responsible for the attentional control of the other working memory subsystems as outlined above. It is thought to be primarily dependent on the dorsolateral prefrontal regions such that damage here impairs performance on experimental tasks that depend on executive control and processing (Stuss & Knight, 2002). Research has revealed that the executive may actually comprise a number of subprocesses, each associated with a different neural region (Baddeley, 2002; Shallice, 2002, 2004). More details on the frontal lobes and executive functioning can be found in Chapter 11.

INTERIM COMMENT

On the whole, neuropsychological research has provided good support for the idea that working memory comprises a number of subcomponents with each involved in the processing or storage of different forms of information. What is becoming increasingly clear is that these subcomponents are widely distributed across diverse neural regions. A challenge for future research is to answer the question of how these subcomponents interact in order to perform the everyday tasks in which working memory is so crucially important.

LONG-TERM MEMORY

GENERAL BACKGROUND

Amnesia refers to a particular cognitive deficit in which long-term memory is selectively impaired (Victor, Adams, & Collins, 1971). There are two broad

KEY TERM
Amnesia: General term for loss of memory. Anterograde amnesia is loss of memory following some trauma. Retrograde amnesia is loss of memory for a period of time prior to trauma.

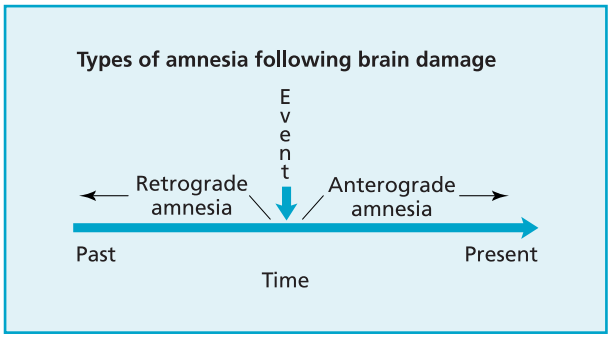


FIG. 7.3 A schematic diagram that illustrates the distinction between anterograde and retrograde amnesia. Anterograde amnesia refers to memory loss following the event that brought about the brain damage. Retrograde amnesia refers to memory loss of information that precedes the event that brought about the brain damage.

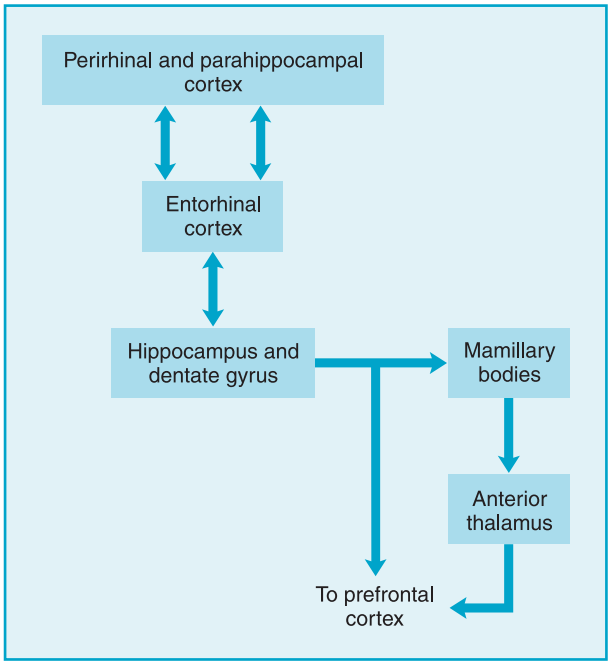


FIG. 7.4 The major structures and connections of the medial temporal lobes.

KEY TERMS
Anterograde amnesia: A form of memory loss where new events are not stored in long-term memory.
Retrograde amnesia: A form of memory loss where people are unable to remember events that happened before the onset of amnesia.

classes or subtypes of global memory impairments referred to as anterograde and retrograde amnesia (see Figure 7.3).

Anterograde amnesia is essentially a memory deficit for the acquisition of new information or new learning since the time of the brain damage. Thus those with anterograde amnesia will have problems remembering what they did the previous day or even a few moments ago. It can be considered a deficit in the ability to update memory, and in many respects those with this form of amnesia effectively live in the past as no (or very few) new memories are laid down. This type of amnesia is typically associated with damage to the medial temporal lobe (MTL) and associated structures, namely the hippocampus, the dentate gyrus, the entorhinal cortex, the perirhinal cortex, and the parahippocampal cortex (Zola-Morgan & Squire, 1993) (see Box 7.2 and Figure 7.4). Some of these structures are connected to other neural regions important for memory such as the thalamus, mamillary bodies, and prefrontal cortex.

Retrograde amnesia refers to an impairment in remembering information from the time prior to the onset of the damage. In terms of neuropsychological research, these two types of amnesia are often investigated separately, with theoretical emphasis and empirical studies designed to assess or characterise the nature of one or the other form. This chapter will deal with each in turn and attempt to consider how research with brain-damaged individuals and neuroimaging work has advanced what we know about the neural basis of long-term memory.

ANTEROGRADE AMNESIA AND NON-DECLARATIVE MEMORY

Perhaps the most famous case of anterograde amnesia is that of patient HM. He was unfortunate enough to suffer from severe epilepsy, and efforts to treat this conventionally (with medications) were unsuccessful. The decision was made to remove the focus of his seizures and this entailed the surgical removal of much of the medial temporal lobe regions in both hemispheres. The operation took place in the early 1950s and left HM with a very severe form of anterograde amnesia. As a consequence of being unable to update his memory, HM was mentally "stuck" in the 1950s (Corkin, 1984). Thus he failed to recognise people he had recently encountered even when these individuals had been in frequent contact with him. He also reread magazines and newspapers because he failed to recognise the fact that he had read them before. On several occasions he made his

Box 7.2 Causes of amnesia

A brief overview of some of the causes of amnesia is provided below. However the list is not exhaustive and memory loss is also known to be associated with electro-convulsive therapy (ECT), dementia, and epileptic seizures to name just a few. In spite of this, the causes outlined below are important as these have been the most informative in the neuropsychological investigation of memory.

The Korsakoff syndrome

Amnesia can actually result from nutritional deficiency that is often associated with chronic alcoholism. Alcohol interferes with the gastrointestinal transport of the vitamin thiamine. Thiamine itself plays an important role in cerebral metabolism and thus a reduction in the amount of thiamine reaching the brain has serious consequences for healthy neural functioning. The memory disorder resulting from thiamine depletion is called the Korsakoff syndrome or sometimes the Wernicke-Korsakoff syndrome (after the two researchers, Carl Wernicke and Sergei Korsakoff, who were initially involved in studying this disorder). The precise neuropathology associated with this syndrome is still the subject of investigation but research has implicated the neural structures within the diencephalon (including the mamillary bodies and the thalamus) and even the frontal lobes (Colchester et al., 2001; and see Box 7.3 later in this chapter).

Hypoxia

Hypoxia refers to an inadequate supply of oxygen to the tissues (including neural tissue). Hypoxia can result from heart disorders, carbon monoxide poisoning, arterial disorders, and impaired respiratory function. The neuropathology associated with hypoxia is variable and often widespread (Caine & Watson, 2000) but in terms of memory disorders the hippocampus, thalamus, and fornix are often implicated (Aggleton & Saunders, 1997; Kesler et al., 2001; Reed et al., 1999).

Vascular disorders

The brain needs a constant supply of blood and this is carried to the brain by a dedicated vascular system. This vascular system consists of a number of major arteries that branch outwards throughout the brain into smaller and smaller arteries, which eventually merge with veins that carry the blood back to the heart. Interruptions to the supply of blood can occur for a number of reasons, such as a blockage from a blood clot or *embolism*, or damage to the walls of the artery. In both these cases, the cessation of the supply of blood leads to the brain being deprived of oxygen and nutrients, and brings about cell death. Depending on which arteries are damaged or blocked, different neural regions or structures can be affected. With respect to memory disorders, the important arteries are those that supply the hippocampus, thalamus, mamillary bodies, and basal forebrain (O'Conner & Verfaellie, 2002; von Cramon, Hebel, & Schuri, 1985).

Viral infections

Infection with the herpes simplex virus can bring about memory disorders as a consequence of herpes simplex encephalitis. Neuropathological features of this disease include widespread bilateral temporal lobe damage (Colchester et al.,

2001). As structures important for memory reside in the temporal lobe regions (more specifically the medial temporal lobes) then it is not surprising that herpes simplex encephalitis can bring about severe memory impairments.

Head injuries

As the name suggests this form of injury results from a blow to the head in one form or another. The injury can be either penetrating (e.g., gunshot wound) or closed. In the case of closed head injury, diffuse damage across widespread neural regions can occur as a result of compression of the brain, the shearing of axons, and haemorrhaging. Closed head injuries can often bring about post-traumatic amnesia which can last from minutes, following very mild injury, to months, following more severe injury.

way back to a previous address following a move to a new house (Milner, 1966; Scovile & Milner, 1957) because he was unable to update his memory for his new address.

In spite of this impairment, HM's IQ was above normal, as were his language and perceptual abilities (Scovile & Milner, 1957). Furthermore, if asked to keep a string of digits in mind (such as a phone number) he was able to do so very successfully if allowed to make use of mental rehearsal. However if rehearsal was prevented, his performance dropped to almost zero (Milner, 1966). HM had some degree of retrograde impairment but this was small in comparison to the severity of his anterograde deficit. For example, he was able to recognise the faces of people who became famous *before* but not after his surgery (Marslen-Wilson & Teuber, 1975). However, it has recently been demonstrated that HM has acquired small amounts of new knowledge. For example, O'Kane, Kesinger, and Corkin, (2004) found that he knew a small number of facts about celebrities who had only become famous since his operation. In addition he was able to reconstruct an accurate floor plan of the house he moved into since the onset of the amnesia, presumably due to what amounts to thousands of learning trials (Corkin, 2002). In general, HM showed impaired abilities on recall and recognition memory tasks under conditions that do not allow for extended practice or learning. However he demonstrated intact abilities for perceptual and motor skills learning (Corkin, 2002).

The study of HM raises a number of questions relating to amnesia. Two of these are addressed below: (1) What are the patterns of intact and impaired performance in amnesia? (2) What precisely is the contribution of the medial temporal lobe (MTL) to memory? Although amnesic individuals such as HM are deficient in acquiring new memories they are not deficient in all aspects of new learning. By examining the patterns of performance across a wide range of experimental tasks, research into amnesia has been a valuable source of information with regard to unravelling the complexity of long-term memory systems and processes.

One way to think about this is the distinction made between declarative and non-declarative memory (Squire & Knowlton, 2000). Declarative memory (sometimes called explicit memory) refers to memory for events, episodes, and facts (see Figure 7.5). This type of memory is accompanied by conscious awareness that memory is being used in order to perform some task. For example, if someone is asked to recall a list of words, or what they did yesterday, then that person will be

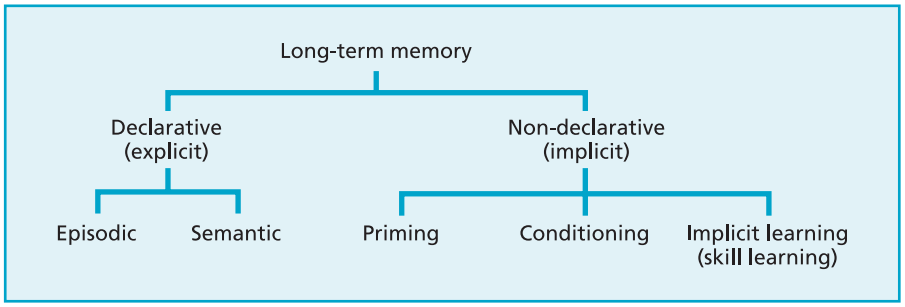


FIG. 7.5 A schematic diagram that illustrates the distinction between declarative and non-declarative memory (adapted from Squire, 2004).

aware that they are using memory in order to recall the information. Non-declarative memory (sometimes called implicit memory), on the other hand, is a form of memory that is observed and expressed though performance without any necessary dependence on awareness. In this case, the individual uses memory without any conscious awareness that memory is guiding or directing their performance. A typical example could be something like riding a bicycle. The ability to ride a bicycle is learned and then expressed through performance (actually riding it without falling off). This behaviour does not demand that the individual recall consciously the actual act of learning. Instead learning is expressed in an automatic fashion. Non-declarative memory comes in many forms and appears to be remarkably preserved in amnesic individuals (Squire 2004). Priming, classical conditioning and implicit learning are three examples of non-declarative memory, which are outlined below.

PRIMING

Priming refers to the influence of a previous study episode on current performance in terms of accuracy or speed of performance. When psychologists refer to implicit memory, more often than not they mean priming. Priming does not demand awareness of the study episode or the ability of the individual to remember any of the details of the study phase of the experiment. This fact makes it a form of non-declarative memory. For example, imagine a participant in an experiment being presented with a set of words (including, e.g., CHORD). Later they are given a set of word fragments (e.g., C H_ R _) and asked to say what word comes to mind when they read the fragments. Research has shown that participants are more likely to complete a word fragment with one presented earlier than an equally likely alternative such as CHARM, even though they do not consciously attempt to recall the studied words (Hayman & Tulving, 1989; Roediger et al., 1992). It is as if the words simply "pop into mind" in an automatic fashion. This popping into mind of previously studied stimuli is an example of priming. The same phenomenon can be observed in amnesic individuals. For example, Tulving, Hayman, and MacDonald (1991) studied priming in patient KC, who had very dense amnesia resulting from damage to the MTL. KC was presented with a list of words during the study phase of an experiment and then given a test of word fragment completion. Tulving et al. found that in spite of not being able to consciously remember any of the words, KC's performance was unimpaired on the word fragment completion task. Essentially, it was as if KC had

KEY TERM
Priming: The (possibly subconscious) influence of some preliminary event or stimulus on subsequent responding.

no deficit at all when memory was tested using an implicit test of memory—KC was just as likely as healthy respondents to complete word fragments with previously studied words. This suggests that whatever memory systems or processes are responsible for these priming effects, they are not dependent on the integrity of the MTL.

Cognitive research has indicated that the priming effects observed on tests such as word fragment completion are based on the perceptual characteristics of the word. Thus if the words are initially *heard* and then tested *visually*, priming is reduced (Rajaram & Roediger, 1993). This perhaps indicates that such priming effects are dependent on neural regions involved in vision and perception. Research with brain-damaged individuals and neuroimaging of healthy controls has provided broad support for this idea. For example, Gabrieli et al. (1995a) found priming effects to be reduced in a patient with damage to the right occipital lobes. Subsequent work has indicated that the left occipital lobe can also support priming (Yonelinas et al., 2001). With respect to neuroimaging research, priming effects on tasks like word fragment completion are associated with *decreased* activations in regions involved in perceptual processing, such as the occipital lobes and the ventral surface of the occipital/temporal region (Bäckman et al., 1997; Koutstaal et al., 2001). The fact that decreased activations were found may sound unusual but it is thought to be due to decreased metabolic demands or synaptic strengthening following the initial processing of the word during the study phase (Wagner, Bunge, & Badre, 2004).

Intact priming effects in amnesia are not limited to relatively low-level perceptual tasks as described above. In addition, performance on memory tasks that require conceptual or meaningful semantic processing is also spared. An example of such a task is word association. In this, participants are presented with words such as "belt" or "noisy". Later, during testing, they are presented with related words such as "strap" or "quiet" and asked to free-associate by saying whatever words come to mind. Participants without brain damage are more likely to respond with the meaningfully related words that were presented earlier in the experiment (e.g., strap – belt, quiet – noisy). Levy, Stark, and Squire (2004) assessed this form of priming, called conceptual priming, in amnesic patients and found it to be entirely intact in these respondents too, even when conscious recognition of the presented words was no greater than chance.

Again, this would appear to indicate that priming effects are not dependent on the medial temporal lobes but instead the contribution of some other neural region which has now been identified by neuroimaging. Wagner et al. (1997) found that when individuals were required to make conceptual or semantic judgements about words, the left prefrontal cortex became activated. Furthermore, when asked to make the same judgement to the words on a second occasion, a relative decrease in the activation was observed in this same area. This decrease in activation is considered to be the neural signature of priming effects, and parallels that found with perceptual tasks.

KEY TERM
Classical conditioning: A simple form of learning where a previously neutral stimulus (e.g., a light) becomes associated with a motivationally salient stimulus (e.g., food) through repeat presentation.

CLASSICAL CONDITIONING

Some recent work has focused on whether another form of non-declarative memory is also intact in amnesic individuals. **Classical conditioning** is a relatively simple form of associative learning that has been studied in humans using the eyeblink conditioning paradigm (see Figure 7.6). In its simplest form this involves present-

ing a conditioned stimulus such as a light or tone just before a puff of air, the unconditioned stimulus, is directed to the eye. The unconditioned stimulus automatically causes an eyeblink response. Following this pairing procedure, the light or tone alone also brings about an eyeblink response (the "conditioned" response). Gabrieli et al. (1995b) found that amnesic individuals with damage to the MTL had no difficulty in learning the conditioned eyeblink response in spite of profound declarative memory impairments.

The **cerebellum** seems to be the critical neural region for this type of non-declarative memory. For example, Woodruff-Pak, Papka, and Ivry (1996) found that patients with cerebellar damage were impaired at acquiring the classically conditioned eyeblink response. In addition, Coffin et al. (2005) noted that the cerebellum is particularly susceptible to the toxic effects of prenatal alcohol exposure. In line with this, they found that children with established prenatal alcohol exposure were also impaired at learning a classically conditioned eyeblink response. Neuroimaging research is supportive of the findings with brain-damaged patients. Using PET, Schreurs et al. (1997) found changes in cerebellar activity during the learning and extinction of classically conditioned responses.

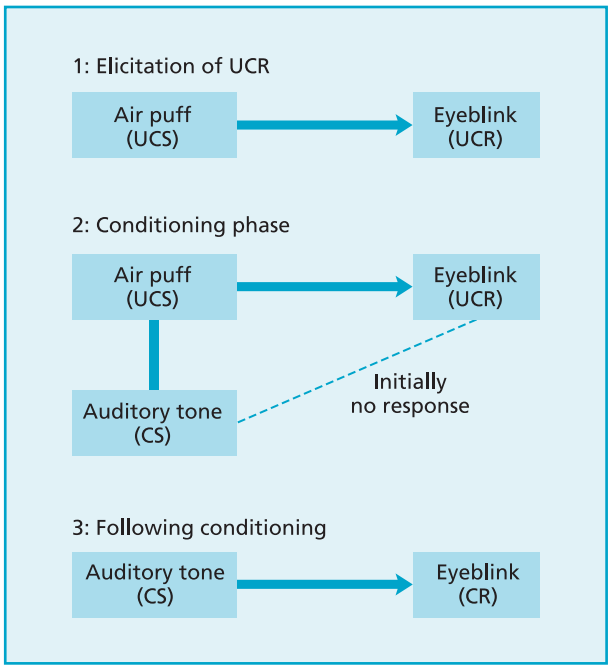


FIG. 7.6 The eyeblink conditioning paradigm, in which the unconditioned stimulus (UCS) is a small puff of air directed towards the eye. This elicits an eyeblink response. This response does not need to be learned and thus is called the unconditioned response (1). During conditioning (2), a conditioned stimulus such as an auditory tone is paired with the puff of air. Following this procedure the auditory tone comes to elicit the eyeblink response (3).

IMPLICIT LEARNING

Implicit learning is essentially learning without awareness. This form of learning has been assessed by a number of experimental procedures, one of which is the serial reaction time task. This may, for example, involve the presentation of a light in one of four horizontal locations. Each location is associated with a response button which respondents are required to press when the light flashes. The lights flash according to a particular sequence or pattern of which the participant is unaware. In spite of being unaware of this sequence, participants' reaction times become faster with practice. This is taken to indicate implicit learning of the sequence. Studies with amnesic individuals indicate that their performance on this task is spared despite profound recognition memory deficits (Reber & Squire, 1994). Another interesting task, developed only recently, is a variation of the radial arm maze initially used in rodent studies of learning. This task involves the presentation of a central circular area on a computer screen. Stemming outwards from this are a number of rectangular arms. A dot is presented at the end of one of the arms and the respondent is required to move the screen cursor down the arm using a computer mouse. Once this is done, a dot appears in another arm and the participant is required to trace the cursor back along the first arm and then down the arm that now has a dot within it. Again, unbeknown to the respondent, the appearance of the dot is not in fact random, but follows a predetermined sequence. Implicit learning is indicated by decreased reaction times to move

KEY TERM
Cerebellum: Region at the base of the brain that is important in sensory and motor functions.

around the maze. It has been demonstrated that those with selective damage to the hippocampus were able to acquire this skill in the absence of knowledge of how the skill was acquired (Hopkins, Waldram, & Kesner, 2004).

The above studies demonstrate that whatever neural systems underlie such learning abilities, they are not dependent on MTL structures. Instead, learning of this sort appears to be dependent on the striatum and substantia nigra: both components of the basal ganglia (see Chapter 5 for more details on this structure). Studies of individuals with damage to these structures, such as patients with Huntington's or Parkinson's disease, find impaired performance on such implicit learning tasks (Helmuth, Mayr, & Daum, 2000; Knopman & Nissen, 1991). The importance of the basal ganglia in implicit learning is backed up by neuroimaging research that demonstrates changes in basal ganglia activity over the course of learning structured, compared to random, sequences (Thomas et al., 2004).

INTERIM COMMENT

The research outlined above is broadly consistent with the idea that preserved memory functions in amnesia are of the non-declarative type. One of the main characteristics of non-declarative memory is that it is a form of non-conscious memory (Squire & Knowlton, 2000). For example most amnesic patients demonstrate priming effects, classical conditioning, and implicit learning without any form of conscious memory for the initial study or learning episode. This may appear to indicate that the primary deficit in amnesia is to conscious memory with all forms of non-conscious memory intact. However this may not be the whole story, as amnesic patients can sometimes show impairments in certain tasks of non-conscious memory. For example, they show impairments on a number of tasks including priming effects for fragmented pictures (Verfaellie et al., 1996), more complex forms of classical conditioning (McGlinchey-Berroth et al., 1997), and the later stages of skill learning (Knowlton, Squire, & Gluck, 1994). As a consequence the characterisation of intact learning abilities in amnesia as being one of non-conscious memory is likely to be too simplistic, and no generally agreed conclusions have yet been formed.

ANTEROGRADE AMNESIA AND DECLARATIVE MEMORY

The medial temporal lobes have been shown to be important for declarative memory. Damage to these structures brings about an anterograde deficit. Considered below are a range of neuropsychological investigations that add to our understanding of declarative memory and show how the study of the hippocampus can help to redefine the nature of conscious remembering.

EPISODIC AND SEMANTIC MEMORY

Declarative memory, as noted earlier, refers to memory for events and facts. Memory for events is often called episodic memory and memory for facts is often called semantic memory (Tulving, 1983). Some researchers claim that the amnesic

deficit is one that specifically pertains to episodic memory (Parkin, 1982). This is argued because amnesic patients have no problems with using language or answering general knowledge questions. As both of these depend on the use of semantic memory, it would seem reasonable to conclude that semantic memory is intact. However, when amnesic individuals are presented with a list of words to recall, or asked about what they did yesterday, then their performance is likely to be severely impaired. In both of these instances, the amnesic person is being asked to remember a specific event or episode. This, of course, depends on episodic memory. As amnesic individuals are clearly impaired on tasks of this kind, it would seem reasonable to conclude that episodic memory is impaired. In theoretical terms it could be said that amnesia provides support for the distinction between episodic and semantic memory.

Unfortunately this conclusion is somewhat premature and thought needs to be given to an alternative explanation. In the above example, the typical amnesic patient could be considered successful at retrieving information that was learned *prior* to the onset of the amnesia (this would be general world knowledge or semantic information learned earlier in their life) but unsuccessful at learning and recalling new information *after* the onset of amnesia. If this is true then the amnesia may simply be a new learning deficit rather than one that can be seen as supporting the episodic–semantic distinction. Support for the episodic–semantic distinction would be more conclusive if amnesic individuals were able to learn new semantic information in the absence of new episodic information. Current findings are somewhat ambiguous on this issue. An early study by Gabrieli, Cohen, and Corkin (1988) found HM to be severely impaired at learning new semantic facts and this does not support the episodic–semantic distinction (but see more recent research on HM by O'Kane, et al., 2004). However other research has demonstrated some degree of support. Tulving et al. (1991) and Westmacott and Moscovitch (2001) both found that new semantic learning could take place in amnesic individuals albeit at a rather slow pace. This conflict may have been resolved by Bayley and Squire (2005) who suggest that new learning of semantic information may take place but only if some of the structures in the MTL remain undamaged. When destruction is more widespread then new semantic learning is absent.

THE ROLE OF THE HIPPOCAMPUS

The role of the hippocampus has been extensively studied in both animals and humans and is known to be centrally important for declarative memory. However, declarative memory can take different forms and can be assessed by different means. One form is related to the recognition of a stimulus such as a word, picture, or face based on its overall familiarity. Another is often called recollection and is based on the retrieval of more detailed information, typically in the form of an association between two or more stimuli. Both types of declarative memory are accompanied by conscious awareness but differ in our experience of remembering. This distinction, between *familiarity* and *recollection*, can be easily illustrated. A typical example is to imagine seeing someone you recognise. Unfortunately you cannot remember their name or any other details about them—this represents *familiarity*-based recognition. Later, you recall their name and perhaps where you have seen them before. This is *recollection*-based memory. These two components of declarative memory can be measured in a number of ways. One technique

involves comparing item recognition memory (e.g., memory for a list of words) with free recall. The idea behind this is that item recognition can be based on familiarity (if a word on the test list seems familiar then respond "yes", i.e., I saw this word earlier). However free recall requires the retrieval of associations between the stimuli and cannot be based on familiarity alone. Another technique involves comparing item recognition and associative recognition. For the latter, rather than measuring memory for single stimuli, the experimenter presents pairs of words during the study phase (e.g., stay–pool; hall–thin; rage–firm). Later, during the recognition test, some of these pairs are presented again, in the same pairs as before (e.g., stay–pool), whereas others are re-paired (e.g., rage–thin; hall–form). The participant has to try to distinguish those pairs presented unchanged from those that have been rearranged. As a consequence, associative recognition, by its very nature, requires the retrieval (recollection) of associations.

The distinction between familiarity-based memory and recollection has become very important recently as neuropsychologists have attempted to uncover the neural regions responsible for each of these. Some argue that the hippocampus is important for all forms of declarative memory, both familiarity and recollection (Squire & Knowlton, 2000). However, others argue that the hippocampus is important only for recollection (Aggleton & Brown, 1999, 2006). These ideas can be examined in individuals with selective damage to the hippocampus. If the hippocampus is required for both familiarity and recollection then selective damage to this structure should impair both forms of memory. But if the hippocampus is required for only recollection, then it should be possible to observe dissociations between recollection and familiarity. Evidence in favour of the idea that the hippocampus is important for all forms of declarative memory was presented by Reed and Squire (1997). They tested a group of patients with selective bilateral damage to the hippocampal region and found impairments on tests of even single item recognition. More recently, Stark and Squire (2003) compared memory for single items and memory for associations between items in a group of patients with bilateral damage to the hippocampal region and found impairments on both types of test. Thus, on the basis of these findings it would appear that the hippocampus *is* needed for *both* familiarity and recollection, thus supporting the ideas of Squire and colleagues.

However, these findings have not gone unchallenged. For example, Mayes et al. (2002) and Holdstock et al. (2002) studied patient YR who, like the patients mentioned above, has bilateral damage to the hippocampus. YR was assessed across a range of tests designed to tap familiarity and recollection. The researchers found that her memory abilities were impaired when tested with recall-type tasks (recollection) but preserved on tests of recognition (familiarity). In addition Holdstock et al. (2005) tested patient BE, who also has selective bilateral hippocampal damage, and found his associative recognition and recall performance to be more impaired than single item recognition. Accordingly, both YR and BE provide evidence for the theory of Aggleton and Brown (1999, 2006).

INTERIM COMMENT

Theories about hippocampal function have been the focus of investigation in the animal modelling literature. Of course it is not possible to ask animals if they are

conscious of a specific event or are able to recollect details of some particular experience. As a consequence, understanding hippocampal functioning in animals has, of necessity, taken a different route. However, elements of both the human and animal research can be seen to map onto one another. For example, largely on the basis of work with rodents, Eichenbaum (2002) has advanced the idea that the hippocampus is important for the acquisition and expression of *relational* memories. An important property of relational memory is that associations are formed between multiple elements of an episode but, in spite of being associated, these elements maintain their own independent identity. Thus an association between A and B is not "fused" in some rigid and inseparable representation but rather stored in a manner that allows each element to be accessed, compared, and processed in relation to other elements. These relational representations can be altered, added to, and changed over time. Thus relational representations formed by the hippocampus are said to be flexible. For example, if A is related to B, and B is related to C, then a flexible representation of these pairings allows one to make an inference about the relationship between A and C even though they have never been paired together.

The research with brain-damaged individuals reviewed earlier provides some support for the relational account of hippocampal function, as do some recent neuroimaging studies that find greater hippocampal activation during the formation and remembering of stimulus pairings. In addition, it has been shown that solving problems of the type A–B, B–C, A–C also leads to greater activity in the hippocampus (Heckers et al., 2004).

So where do all these findings leave the debate regarding the functions of the hippocampus? Unfortunately, the picture is still unclear and only further research is likely to clarify it. In terms of research on amnesia this will be an interesting debate to keep an eye on, as it will help to sharpen our understanding of the precise functions of the hippocampus and the contribution it makes to declarative memory. (See also Box 7.3.)

Box 7.3 The diencephalon and amnesia

Damage to the diencephalon, which comprises the thalamus and hypothalamus (including the mamillary bodies), typically results in memory impairments. In part this is known on the basis of research with Korsakoff amnesia. However, as this syndrome produces pathology that is more widespread and not limited to the diencephalon, then the precise contribution of this structure remains uncertain. Of course what we need to do is to assess the memory performance of individuals with more circumscribed lesions. Kishiyama et al. (2005) presented a patient (RG) with bilateral damage to the thalamus following a stroke. Testing revealed impaired recognition memory across a range of materials including words, pictures, and faces. Theoretically, these results are of importance because they demonstrate that damage to the thalamus can bring about reductions in memory performance. More specifically, as the thalamus receives afferents from the hippocampus these two structures can be thought of as comprising a neural circuit in which damage to either component can bring about amnesia (Aggleton & Brown, 1999, 2006). As the thalamus itself comprises a number of distinct nuclei, it has been proposed that different mnemonic processes are subserved by

different nuclei. For example, Aggleton and Brown (1999, 2006) claim that the anterior nuclei are important for recollection, while the medial dorsal nuclei are important for familiarity-based recognition. Unfortunately this has yet to receive support from human studies and some evidence actually runs contrary to its proposal. In particular, Edelstyn, Hunter, and Ellis (2006) found that damage to the medial dorsal thalamic nuclei did not impair familiarity-based recognition.

MEMORY PROCESSES

So far, this chapter has dealt with research that provides broad support for the idea of memory systems. The notion that memory systems differ with regard to how they process information has been implicit in much of the foregoing, and research with brain-damaged individuals has highlighted the importance of component processes involved in different types of memory task. This section deals with the concept of memory processes in a more explicit manner and considers how such ideas from mainstream cognitive psychology have been integrated and advanced by neuroscience research. One of the most significant achievements of the cognitive approach to learning and memory relates to the development of theories and ideas about encoding and retrieval processes, and how these interact to influence memory performance. Functional imaging procedures have, in a sense, enhanced cognitive psychology by revealing the neural processes underlying memory formation and remembering. In other words, it is now possible to "see" the hypothetical processes postulated by cognition researchers.

ENCODING

Encoding refers to those cognitive activities or processes that are responsible for creating a representation of the event or episode to be remembered. Early work in cognitive psychology demonstrated that the manner in which a stimulus is encoded has direct implications for whether that stimulus will be remembered. For example, Craik and Lockhart (1972) found that performing "deep" meaningful processing on a set of words (e.g., Is a "cat" a mammal?) enhanced memory for those words compared to a condition where shallow processing was performed (e.g., Is the word "cat" printed in upper- or lower-case letters?). Craik and Lockhart claimed that memory was nothing more than the remnants of prior processing activity and that deeper processing led to more durable and robust memory traces. The idea of levels of processing has been advanced by neuroimaging studies in which participants perform either a deep or shallow processing task on a set of stimuli (e.g., words) while in the scanner. Collectively the results indicate that a number of areas are active in the deep processing condition compared to the shallow processing condition. These include the hippocampus and adjacent MTL regions and the left prefrontal cortex (see Cabeza & Nyberg, 2000, for a review). Some studies have found hemispheric differences such that greater left (vs right) activations are typical when the stimuli are words (vs patterns) (Wagner et al., 1998). Thus different encoding processes that are known to influence memory appear to be associated with different neural regions.

As deep processing is associated with both enhanced memory and enhanced activations in particular neural regions, it should be possible to predict the

memorability of a stimulus by the magnitude of these activations. For example, Fletcher et al. (2003) required participants to perform a deep or shallow processing task on a set of words while being scanned. Later, the participants were asked to recall as many of the words as possible. The researchers found a number of things: First, deep encoding led to greater activations in left medial temporal lobes and the left lateral prefrontal cortex. Second, the amount of activation in these areas actually predicted which words would be recalled; the greater the amount of activation, the more likely the word would be recalled.

Some more recent work indicates that successful memory encoding is related to the *interaction* between the hippocampus and other cortical regions to which it connects; greater interactions lead to greater probability of recall success (Ranganath et al., 2005). Other research has shown that not only can we predict which words will be recalled by monitoring neural activity during the encoding of the word, but the neural activations that occur milliseconds *before* a word is encoded can also predict memory success (Otten et al., 2006).

The focus so far has been on encoding. However, memory is as much about retrieval as it is about encoding (Tulving, 1983). What has neuroimaging research told us about the act of retrieving information from memory?

RETRIEVAL

Retrieval refers to accessing information stored in memory. In cognitive research, retrieval can be broken down into a number of subcomponents called retrieval mode, ecphory, and recollection (Tulving, 1983). For further details see Box 7.4.

Box 7.4 Components of memory retrieval

Retrieval mode refers to a form of "mental set" in which the individual directs attention to the act of remembering, and makes use of cues in order to recall information. For example, suppose someone asks me if Zack was at the fancy dress party I went to last week. The name "Zack", the event "party", and the time "last week" all act as potential retrieval cues. In attempting to answer the question I will put them all together and prepare to probe my memory of the event. Ecphory is the term used to refer to the interaction between the retrieval cue and the stored memory trace. For example, the stored memory trace of who was at the party will interact with the retrieval cues "Zack", "party", etc. and allow me to recover the stored information of who was at the party. Recollection is when the individual becomes aware of the information retrieved. In this case I become aware that Zack was indeed at the party, as I recall him swinging from the chandelier in an astronaut suit. As with encoding, these processes are unobservable but neuroimaging procedures may again allow us to "see" some of these activities and help to establish a neural basis for retrieval.

Retrieval mode was examined by Lepage et al. (2000). They found a number of regions to be activated, including the right prefrontal cortex (and to a much lesser extent the left prefrontal region), during retrieval. This was found whether or not retrieval was successful, and was taken to indicate the neurocognitive

processes underlying the establishment and maintenance of the "mental set" in which attention is directed to the act of remembering. The involvement of the right prefrontal region has taken on added significance given the fact that numerous studies appear to show similar activations during episodic memory retrieval (see below).

Distinguishing between ecphory and recollection is difficult, and research has tended to compare whether different areas of the brain are activated when retrieval is successful (in which case *both* ecphory and recollection have presumably taken place) to conditions in which the retrieval is unsuccessful (in which case ecphory and recollection have not taken place). For example, Stark and Squire (2000) compared which regions of the brain were active when participants recognised words (or pictures) presented earlier during the experiment, compared to words (or pictures) that were not presented earlier. The assumption was that stimuli presented earlier would lead to ecphory and recollection whereas new stimuli would not lead to such processes. Stark and Squire found significant activation in the left hippocampus during word recognition, and bilateral activation of the hippocampus during picture recognition. However, a potential problem with this study is that participants may not have recognised some of the words and pictures presented earlier. What is needed in order to "image" ecphory and recollection is to compare activations that occur when participants actually recognise the stimuli to activations in which participants fail to recognise the stimuli. This requires the use of event-related fMRI (see Chapter 2). Using this method Dobbins et al. (2003) found that correct recognition responses were associated with enhanced activations in the left hippocampus and the parietal cortex. The finding of enhanced neural responses in the hippocampus is to be expected on the basis of work with brain-damaged individuals. However the significance of the parietal activations is somewhat unclear even though it has been observed in a number of experiments (McDermott & Buckner, 2002; Rugg, 2004).

ENCODING AND RETRIEVAL INTERACTIONS

On the basis of the previous discussion it may be thought that encoding and retrieval are two entirely separate processes. However, cognitive research has come to place emphasis on how these two processes interact with each other in order to enhance memory. The manner in which encoding and retrieval processes interact has been the focus of much research and forms the foundation of a particular framework called *transfer appropriate processing* or TAP for short. TAP has its roots in memory research dating back to the 1970s but has been more formally specified by Roediger and colleagues (e.g., Roediger et al., 1989). Basically, TAP states that the most important factor determining successful memory is the extent to which encoding and retrieval processes overlap. If retrieval processes overlap or recapitulate the same mental processes that occurred during encoding, then memory will be successful. For example, Morris, Bransford, and Franks (1977) presented participants with words such as EAGLE and asked them to perform one of two tasks on these words: a semantic-meaningful task (e.g., Is an eagle a large bird?) or a rhyming task (e.g., Does eagle rhyme with legal?). Later, participants were given one of two tests of memory: one presumed to rely on meaning (a recognition test) and one thought to rely on the sounds of the words (deciding if the test words sounded similar to the studied words). It was found that

performance on the test that depended on meaning was enhanced by the earlier meaning-based encoding task, while performance on the sound test was enhanced by the earlier rhyme-based encoding task.

Presumably, the reason why encoding–retrieval overlap is important is that retrieval reflects the recovery or reactivation of the memory trace laid down during encoding. This idea has been assessed by neuroimaging research. Vaidya et al. (2002) made use of fMRI in order to examine whether the cognitive/neural processes used to encode pictures of objects into memory were also active when retrieving this information. Participants were scanned while encoding words and pictures into memory and also later while retrieving this information. It was found that during the encoding of pictures a number of neural regions became activated, including the fusiform gyrus and inferior temporal gyrus bilaterally, and the left mid-occipital gyrus. During retrieval a subset of these regions became active once again, most notably in the left hemisphere. These regions are known to play a role in aspects of object recognition and Vaidya et al. speculated that during retrieval these regions became reactivated as information about an object's shape and its meaning was being processed.

INTERIM COMMENT

Research with neuroimaging has revealed that encoding and retrieval processes may be implemented in different hemispheres of the brain. The so called HERA (hemispheric encoding and retrieval asymmetry) model was originally proposed by Tulving et al. (1994) and Nyberg, Cabeza, and Tulving (1996) and was meant to summarise a number of findings indicating that the left prefrontal region showed greater activation during encoding while the right prefrontal region showed greater activation during retrieval. Although subject to some criticisms (Lee et al., 2000) these findings have been shown to be remarkably robust (Habib, Nyberg, & Tulving, 2003). It would seem that although encoding and retrieval processes do activate similar neural regions, as predicted by TAP, the extent of overlap is partial. Some of the differences are related to the manner in which processing activity is lateralised.

RETROGRADE AMNESIA AND AUTOBIOGRAPHICAL MEMORY

As mentioned earlier, retrograde amnesia refers to an impairment in remembering information from the time prior to the onset of the disorder or injury to the brain. Although it often co-occurs with anterograde amnesia (Kapur, 1999) it can also occur in relative isolation and is then called focal retrograde amnesia (e.g., Kapur et al., 1989). Most often, impairments are greatest for more *recent* events leading up to the injury or disease (Squire, 1992). This produces a situation in which memory for more distant events, such as those in childhood, is actually better than memory for more recent events. This is the reverse of what is found in those without retrograde amnesia, who display superior memory for more recent events. The temporal extent of the retrograde impairment can vary quite widely. For some individuals the impairment may be for the previous few months or years. For very

severe cases, the extent of impairment can be across the whole lifespan (Cermak & O'Connor, 1983).

In addition, individuals with retrograde amnesia can often display a range of deficits in recalling pre-morbid memories. These can include: (1) memory for personal episodes and events from their lives such as a birthday party or holiday, (2) personal semantic information such as who they are, their characteristic traits and preferences, (3) public and news events, such as who won the general election on some particular date, and also famous people and personalities, such as politicians and TV stars. Interestingly, on some occasions deficits can be more severe for certain types of memory. For example, Manning (2002) examined patient CH who had retrograde amnesia resulting from hypoxia following a cardiac arrest. Testing revealed that CH had relatively preserved new learning abilities (i.e., limited anterograde amnesia), however memory for autobiographical information was particularly impaired, and more so for personal events and episodes.

When asked to recall an autobiographical memory many people report recalling visual images of the event or seeing what happened (Brewer, 1995). It is now thought that visual imagery may play an important role in the retrieval of memory for personal events and experiences (autobiographical memory) and that it enables us to mentally relive and re-experience our past (Rubin, Schrauf, & Greenberg, 2003). If this is true, then individuals who are deficient with respect to processing visual information may also have impaired access to their autobiographical memories and feel unable to relive those memories. Recent studies are consistent with this idea. Greenberg et al. (2005) studied patient MS, a man with a visual processing deficit (agnosia) who had sustained damage to a number of regions including the temporal and occipital lobes. Not only did MS display a severe retrograde deficit, but the autobiographical memories he did manage to recall were unlike those of control participants in a number of ways. For example, when rating his memories in terms of how real or vivid they felt, MS was significantly impaired. His memories were simply lacking in the types of detail and recollective experience that make our memories of incidents and events so compelling.

Why should visual imagery play such an important role in the retrieval of our past? A neuroscientific explanation relates to the way in which memories are stored and retrieved. Memories, especially autobiographical memories, are complex and often involve the interplay of a number of different senses such as vision, audition, olfaction, etc. (Hodges, 2002). Damasio (1989) advanced a theoretical account that argued that the processing and storage of such a variety of information takes place not in one neural region but across multiple regions, with each involved in processing a different aspect of the original event. For humans at least, the visual sense is particularly important. When it comes to retrieving autobiographical memory then multiple neural regions become activated and provide the basis of our re-experiencing the event. These interacting regions can be seen as being dependent on one another and, as a consequence, damage to one region can effectively disrupt the activation process from spreading to other neural regions. This may either prevent memory retrieval, or at least disrupt the retrieval of some of the details of the experienced event. Damasio's theory has been used on a number of occasions to account for aspects of the retrograde deficit (e.g., Hunkin, 1997) and, in relation to patient MS, the explanation could be that damage to the regions of brain responsible for visual processing (e.g., occipital lobes) disrupts

retrieval processes and prevents access to either autobiographical memory or to the types of details that lead to vivid recollection (Greenberg et al., 2005). Interestingly, the MTL would still appear to be important for more vivid and detailed recollection. For example, Steinvorth, Levine, and Corkin (2005) found that patient HM, although able to retrieve distant memories, often substituted gist for specific details. Thus the ability to recall personal experiences and almost "relive the moment" depends on the intact functioning of multiple neural regions.

NEUROIMAGING OF AUTOBIOGRAPHICAL MEMORY

The idea that autobiographical memory is dependent on a diverse set of interacting neural regions has received some support from neuroimaging research. In a review, Maguire (2002) reported that autobiographical retrieval leads to the activation of a network of areas including temporal and parietal regions, the medial frontal cortex, the cerebellum, and the hippocampus. However, different experimental studies often reveal different activations. Maguire claims that this is likely to be due to a number of factors such as the variety of means by which autobiographical memories are elicited, the relative recency of the memories, differences in the amount of effort required to recall a memory, and the amount of time allowed for each recall and response. All these differences make comparisons and generalisations quite difficult and clearly much research needs to be carried out in this important and interesting area.

As mentioned earlier, patients with retrograde amnesia often display a temporal gradient of memory loss affecting more recent (vs more distant) memories. According to some researchers, the reason for this is that following the encoding of an event, memories undergo a slow consolidation process and this is dependent on the hippocampus (Squire, 1992; Teng & Squire, 1999). Thus, initially, a newly formed memory is actually quite unstable. Consolidation processes work to make the memory stable and increase its strength and resistance to forgetting. More specifically, it has been proposed that the hippocampus is responsible for retrieving only relatively recent memories. Following the passage of time, and the consolidation process, it becomes possible to retrieve memories independently of the hippocampus. This idea has received support from research with animals and humans. For example, Zola-Morgan and Squire (1990) trained monkeys to discriminate between a set of different objects over a period of weeks. Following lesions to the hippocampus the monkeys were tested on their memory for the previously learned objects. If the hippocampus is required for the retrieval of more recent memories, then lesions to this structure should produce a greater impairment for the most recently acquired objects. This was indeed the case: memory was most impaired for the objects learned a few days before and was best for those acquired weeks before. In humans, Bayley, Hopkins, and Squire (2003) presented amnesic individuals, whose pathology was limited to the hippocampal region, with the cue-word autobiographical memory test. They were asked to recall memories from the first third of their lives prior to the onset of their amnesia. Compared to control participants, the quality and details of the memories retrieved were virtually identical. Thus it would appear that the recall of more distant memories is not dependent on an intact and fully functioning hippocampus.

The idea that the hippocampus is not required for more distant memories is not without its dissenters. For example, Nadel and Moscovitch (1997) and Moscovitch and Nadel (1998) propose that the hippocampus is required for the retrieval of both recent *and* remote memories. They note that the temporal gradient of memory loss in some retrograde amnesia cases extends back decades, sometimes up to 30 years. They suggest it is implausible that any form of physiological consolidation process would take this amount of time, extending sometimes over the entire life of the individual. Their alternative hypothesis is that the hippocampus is always involved in the encoding and retrieval of memories. Over time, memories are subject to reactivation with older memories, acquiring a greater number of reactivations. The reactivation process leads to multiple memory traces being formed within the hippocampus and surrounding cortex. When damaged, older (vs more recent) memories are more likely to be recalled because they are more resistant to loss as they possess multiple retrieval routes. Some recent neuroimaging work is consistent with the predictions of this theory: Bosshardt et al. (2005) found that recall of more distant memories resulted in the *increased* activity of the hippocampus. The consolidation theory of Squire and colleagues would predict a *smaller* amount of activation over extended periods of time because older memories are hypothesised to be less dependent on the hippocampus. As a consequence, it is not clear how the findings of Bosshardt et al. could be accounted for by the consolidation theory. (See Box 7.5 for a summary of the neurobiological events thought to underpin consolidation of memories at the cellular level.)

Box 7.5 Long-term potentiation and consolidation

Although the consolidation theory of Squire and colleagues has met some challenges, very few researchers would seriously question the idea that for memories to become stable they must undergo some form of consolidation process. Presumably this process takes the form of cellular and molecular changes at the synaptic level. In spite of being beyond the scope of this chapter, the molecular and cellular basis of memory consolidation has been the object of intensive research and is worth mentioning here. One candidate mechanism thought to be responsible for the consolidation of memories is called long-term potentiation (LTP). The process underlying LTP is complex but, at the risk of oversimplifying matters, it refers to the increased magnitude of the response of the postsynaptic neuron following stimulation by the presynaptic neuron (in experimental animals the action of the presynaptic neuron is mimicked by an electrical impulse). This increased response can be shown to last for hours or months (Barnes, 1979) and thus represents the record of *previous* neuronal activity. The reason for this is an increase in protein synthesis in the postsynaptic neuron (Bourne et al., 2006; Fonseca, Nagerl, & Bonhoeffer, 2006). Effectively, this leads to a modification or strengthening of the synapse (Martin & Morris, 2002). LTP has been shown to occur in the hippocampus and in the cortex (Bear & Kirkwood, 1993; Ivanco & Racine, 2000) and thus provides a molecular basis for plastic changes in these regions. Linking LTP to overt behavioural changes (learning and memory) has been demonstrated by findings that indicate impaired

learning following drug-induced blockade of LTP (Davis, Butcher, & Morris, 1992) and that learning can bring about LTP-like changes (Mitsuno et al., 1994; Tsvetkov et al., 2002). As a consequence, LTP represents a potential mechanism for the enduring cellular and molecular changes underlying consolidation processes in learning and memory. Exactly how these cellular and molecular changes are reflected in the types of memory considered in this chapter is as yet unknown and represents a pressing challenge for neuroscientific research.

CHAPTER SUMMARY

This chapter has considered what neuropsychological research has told us about the *systems* and *processes* underlying short-term/working memory and long-term memory. Through the careful analysis of individuals with brain damage, and with the use of neuroimaging procedures, it will be appreciated that the concept of memory does indeed encompass and support the idea of multiple memory systems and sub-systems with multiple component processes. It is now clear that the human brain possesses the capacity to represent many different forms of information and that different neural regions performing different cognitive processes are responsible for this capacity. With respect to short-term memory, broad support has been gathered for the idea that multiple systems and processes are responsible for the maintenance and manipulation of information currently being processed. Neuroscientific research has assisted in the development and refinement of models of short-term and working memory. By the careful analysis of those individuals with brain damage, the idea of a unitary short-term memory does not stand up to scrutiny: Different regions of the brain are, for example, responsible for maintaining and manipulating verbal information and visuospatial information. Neuropsychological work has also provided the impetus for revisions of the working memory model and the incorporation of the so-called episodic buffer.

With respect to long-term memory, the idea of declarative and non-declarative memory has received considerable support. Furthermore, the precise nature of the subsystems and processes underlying these forms of memory is being worked out in ever finer detail. For example, non-declarative memory comprises a number of subsystems that dissociate from one another and are located in different neural regions. Declarative memory comprises a number of processes that enable conscious remembering of past events, and research suggests that these processes may be differentially dependent on different neural systems and pathways. Conscious recollection appears to be crucially dependent on the hippocampus, and vivid memories may require the additional involvement of neural regions involved in perception. However, this does not mean that our understanding of memory is complete—rather, that it is continuing to develop. Further growth will depend in part on the theoretical frameworks and ideas that we bring to bear on the empirical data, and on the discovery of new findings that may challenge these frameworks and preconceptions.

CHAPTER 8

CONTENTS

8

Visual object recognition and spatial processing

INTRODUCTION

The primacy of the visual system in humans is reinforced by the observation that up to half of the cerebral cortex is directly or indirectly involved in visual processing. It is important at the outset to try to distinguish between sensory mechanisms of vision and perceptual processes that permit recognition of the visual input. Essentially, visual sensation is about input "getting registered" in the brain. Perception is concerned with interpretation of that input (Mesulam, 1998). The latter is what principally concerns us here, and we will consider research findings from case studies of people who have lost certain perceptual functions, usually after damage or disease to key cortical regions, as well as findings from functional brain imaging.

Although the distinction between "sensation" and "perception" sounds clear-cut, it is, to some extent, artificial, because a good deal of "processing" of visual input takes place almost as soon as light enters the eye. In the retina, a network of cells interacts to provide the brain with evidence of contrast, colour, and boundaries (edges). Retinal output, in the form of millions of nerve impulses, travels via the optic nerve and tract to the lateral geniculate nuclei (one on each side) of the thalamus. Here, information from the two eyes begins to coalesce, with input from the central fovic retinal regions being separated from peripheral retinal regions. Most lateral geniculate output is relayed on to the primary visual cortex where two vast "sheets" of cells (in the left and right occipital lobes) map out the entire visual field (see Figure 3.4). Cells in this region are arranged in columns and respond preferentially, and in some cases exclusively, to particular types of visual input, such as the orientation of lines, colour information, and so on. Thanks in no small part to the pioneering work of Hubel and Weisel in the 1960s and 1970s, the route from eye to brain is reasonably well understood. We do not intend to provide detailed coverage of it in this chapter—readers wishing to learn more should refer to one of the many excellent reviews of this research area, such as Chapter 5 of Gazzaniga, Ivry, and Mangun (2002).

Neuropsychologists tend to be more interested in the processes after sensory registration that lead to perception. In order to begin to understand these stages of processing, we need to look beyond V1 and V2 of the occipital lobe to other cortical regions that are implicated in the interpretation of visual sensation. Separate cortical regions deal with colour and movement, and coordinate higher-order perceptual processes such as reading, object recognition, and facial recognition. In fact, "visual" areas exist throughout the occipital, parietal, and even temporal lobes.

There is substantial evidence that these areas divide (to some extent) into two separate processing streams, commonly referred to as the "what" and "where" streams (Ungerleider & Mishkin, 1982). Later in the chapter we introduce some brain disorders that seem to be anatomically and functionally linked to one or other stream. These are of interest in their own right, but they also provide clues about the sort of visual perceptual processing that must occur in "intact" brains. Normal visual perception can be studied more directly using functional imaging and we will also review some of this literature. However, we start with a brief review of Ungerleider and Mishkin's model of parallel, but functionally distinct, visual processing streams.

THE "WHAT" AND "WHERE" STREAMS AND VISUAL PERCEPTION

In the mammalian brain there is extensive output from the occipital lobes to other cortical regions that is carried primarily by two major pathways. The inferior route follows a ventral course (round the side and particularly underneath) into the temporal lobes, whereas the superior route takes a dorsal course (over the top) into posterior regions of the parietal lobes. In 1982, Ungerleider and Mishkin suggested that these anatomically distinct routes could also be distinguished in terms of the types of "processing" they mediated. On the basis of data gleaned largely from lesion studies and electrical recording in monkeys, they proposed that the ventral stream is specialised for object recognition and perception, whereas the dorsal stream is specialised for spatial perception—i.e., for determining the locations of objects and their positions relative to one another and to the viewer. The two streams operate in parallel to allow us to address the fundamental questions of "what" we are looking at, and "where" it is located in our field of vision (see Figure 8.1).

Pohl's (1973) discrimination learning study is typical of the research from which Ungerleider and Mishkin developed their model. It had two conditions: in the landmark task, monkeys learned to associate the presence of food in one of two food wells with a landmark such as a cone, which was always positioned near the baited well. After a period of learning the rule was reversed so that food now only appeared in the well farthest away from the cone. In the object discrimination condition, there were two landmarks such as a cone and a cube. In the training phase, food was only hidden in the food well near to one particular landmark, then when this had been learned, the relationship between cue and food was reversed. Pohl found evidence of a double dissociation: performance on the "spatial" landmark task was disrupted by parietal but not temporal lesions, whereas performance in the object discrimination was impaired by temporal but not parietal lesions (see Figure 8.2).

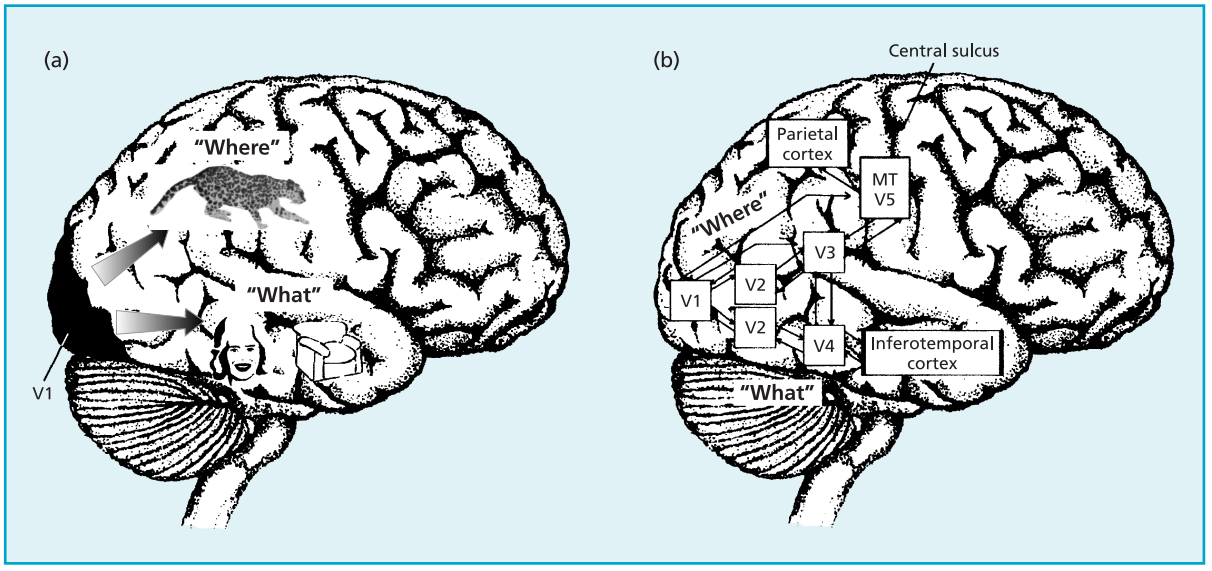


FIG. 8.1 The "what" and "where" streams of visual perception. (a) Ungerleider and Mishkin's "what" and "where" streams, and (b) a slightly more detailed flow diagram of some of the cortical regions implicated in these two processing streams.

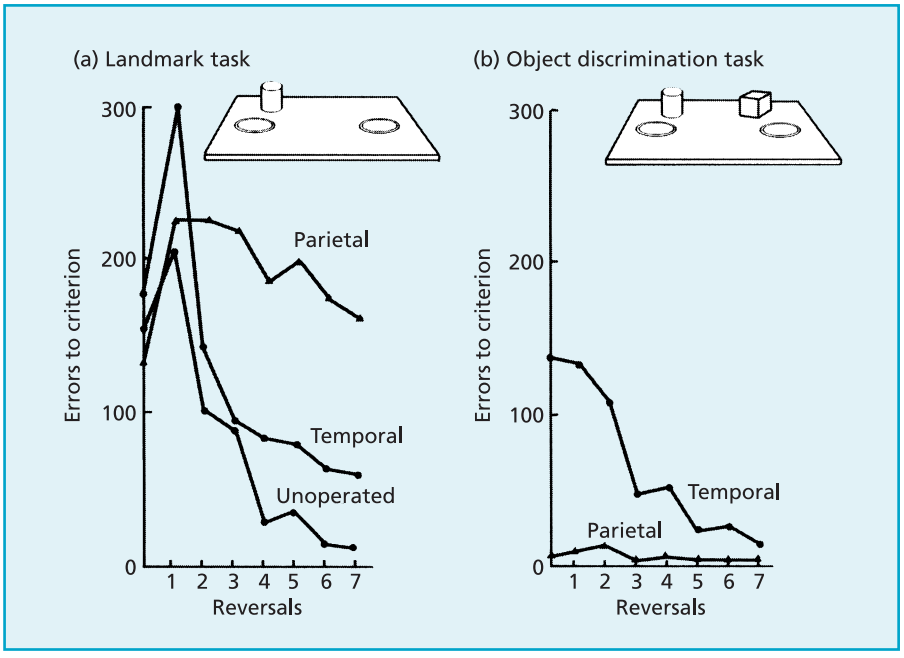


FIG. 8.2 Pohl's double dissociation study. In the landmark experiment, monkeys learned to associate the presence of food in a well identified by a particular marker (in this case, a cylinder). Once learned, the rule was reversed so that now the food was in the well farthest away from the marker. Although control animals and those with temporal lesions quickly learned the reversal, animals with bilateral parietal lobe lesions failed to improve. In the object discrimination experiment, monkeys learned to associate the presence of food with one of two markers (say, the cube). Once learned, the rule was reversed and the food was now associated with another object (the cylinder). Monkeys with parietal lesions were untroubled by this reversal, whereas those with bilateral temporal lobe lesions took several trials to learn the new association. The former experiment relies on processing in the "where" stream; the latter relies on processing in the "what" stream. Adapted from Pohl (1973).

Ungerleider and Mishkin's model has been largely supported by anatomical and lesion data in humans (e.g., Farah, 1990) as well as functional imaging (e.g., Haxby et al., 1991, 1994). For example, patient DF (reported by Milner & Goodale, 1995), who had incurred damage to the ventrolateral region of her occipital lobe as a result of carbon monoxide poisoning, had a profound difficulty in recognising and discriminating between simple objects such as different-sized cubes. However, her visually guided action towards an object (to grasp it for example) was normal. Conversely, patients with **optic ataxia** have preserved object recognition but cannot use visual information to guide their actions, leading to grossly defective grasping/reaching skills. This condition is almost always associated with damage to the superior parietal lobule (Battaglia-Mayer & Caminiti, 2002).

However the details of the model have been amended as our knowledge of cortical functions has increased. Anatomically, it is clear that more cortical modules are involved in the two streams than was initially thought. Moreover, modules within the two streams appear to interact with one another (i.e., send and receive projections) more extensively than Ungerleider and Mishkin anticipated (see below). Goodale and Milner (1992) mooted the possibility of a third pathway, projecting into the superior temporal sulcus area (STS) which contains many **polysensory** neurons (meaning that they respond to inputs from multiple sensory channels). It is therefore possible that this route would be important in the integration of perceptual information about stimuli arising from different sensory inputs, such as hearing and touch (Boussaoud, Ungerleider, & Desimone, 1990). Recent functional imaging studies support this notion (e.g., Taylor et al., 2006), but cross-modal integration remains incompletely understood.

Conceptually, the main challenge to the model has concerned the nature of information processing in the dorsal stream. Originally, Ungerleider and Mishkin proposed that this stream was dedicated to the identification of object location in space. But Goodale and Milner (1992) suggested that the real purpose of the dorsal stream was to guide an individual's on-line control of action. In other words, while knowing about the location of objects is an important component, some neurons in this pathway become particularly active only when a visual stimulus prompts a motor response, such as reaching for an object. This observation has led to the idea that the dorsal route really serves "how" rather than "where" functions (Milner & Goodale, 1995), and it is of interest to note that a major projection from the parietal lobe is to frontal areas, which, as we mentioned in Chapter 5, are critical in planning and controlling purposeful actions.

Yet another modification to Ungerleider and Mishkin's model was proposed by Turnbull, Beschin, and Della Sala (1997) and elaborated by Creem and Proffitt (2001). These authors argue that although there is good support for Milner and Goodale's re-labelling of the dorsal "where" stream as the "how" stream, it is important to recall that this route terminates in the *superior* parietal lobe and is primarily related to "egocentric" (viewer-centred) visually guided action. The *inferior* parietal lobule, on the other hand, is known to be associated with a range of visuospatial skills (some of which we describe later in this chapter) *not* directly concerned with action, such as mental rotation and 3D construction. Creem and Proffitt have characterised these as involving the manipulation of non-egocentric spatial representations. In other words, in humans (and it is important to

KEY TERMS
Optic ataxia: A deficit in reaching under visual guidance that cannot be explained by motor, somatosensory, or primary visual deficits.
Polysensory: Responsive to input from several modalities.

emphasise species-specific distinctions here given that Ungerleider and Mishkin's model was derived from primate studies), the parietal lobe may actually subserve both "how" and "where" functions in the superior and inferior regions respectively. Moreover, the latter may represent a point of interaction between Ungerleider and Mishkin's dorsal and ventral streams in situations where recognition of an object would be facilitated by knowledge of its visuospatial properties (see Figure 8.1b).

While debates about, and refinements of, the model are likely to continue for some time, the basic principle of separable dorsal and ventral processing streams for visual perception, specialised for what and where (or how), has become accepted as a tenet of brain organisation. In fact, recent evidence suggests that the same what/where segregation may be an organisational principle that extends to other perceptual domains such as audition (Alain et al., 2001) and touch (Reed, Klatzky, & Halgren, 2005).

INTERIM COMMENT

Ungerleider and Mishkin's model is accepted as offering a heuristic framework for understanding the lines of demarcation between object recognition and spatial processing. However, many neuropsychologists anticipate further revisions to the model as more is learned about the nuances of visual perception. The question of laterality, for example, is one unresolved issue: primate studies show that although both pathways receive bilateral inputs—because primates (including humans) tend to scan the visual field with both eyes—callosal lesions induce a greater impairment for ventral stream (what) processing than dorsal stream (where/how) processing. This suggests that processing in the latter pathway is somehow "more segregated" within each hemisphere. Confirmation of this distinction in humans is currently lacking although anecdotal evidence from cases of "hemineglect" (see Chapter 9) is broadly consistent with it, despite additional evidence for the "primacy" of the right hemisphere in these cases. We return to consider spatial processing in the dorsal stream later in this chapter. For the time being, we need to consider some of the characteristics of the ventral stream, and the effects that damage to different components of it can have on object recognition.

THE VENTRAL STREAM AND OBJECT RECOGNITION

Although we humans are inclined to take visual perception for granted, it is in fact an astonishingly complex process, or, more accurately, collection of processes, involving multiple computations, reconstructions, and integrations. For example, 3D objects in our field of vision are projected onto our retinas, which only work in 2D. So the brain must "reconstruct" a third dimension in order for us to see in 3D. Second, objects must be recognised as such irrespective of where their image falls on the retina, their distance from the viewer, and their orientation. For example, a tree is still usually *perceived* as a tree whether it is close to you or on the distant horizon. Third, you must also be able to recognise objects when they are moving in

different directions. A horse moving across your line of vision projects a quite different image from one galloping directly towards you. Finally, your brain must be able to link the percept (of the horse for example) with stored representations of horses in order for you to make the semantic leap towards recognition of the object as a horse.

The ventral stream runs bilaterally from area V1 of the occipital lobes via areas V2 and V4 into the inferior regions of the temporal lobes (see Figure 8.1). If we examine the response characteristics of neurons in this stream, three clear trends emerge. First, neurons in posterior regions (at the beginning of the stream) fire in response to relatively simple stimulus characteristics such as width, shading, and texture, whereas neurons later on in the stream only respond to much more complex visual stimuli. Remarkably, some cells in anterior temporal regions only respond to very specific shapes of stimuli such as a hand, or even particular faces (Gross, Rocha-Miranda, & Bender, 1972). A second feature is that neurons further forward along the stream are less concerned with the physical position of objects in the visual field. We could describe cells in these forward regions as having large **receptive fields**, and in the case of some anterior temporal neurons almost the entire retina appears to be covered. So, no matter where the object falls on the retina, cortical cells will respond to an object to which they are tuned. A final point is that cells in this stream make considerable use of colour. This attribute is tremendously important for object recognition, not least because it often allows us to distinguish **figure** from **ground**, providing additional clues about the edges (and thus the shape) of objects (Zeki, 1980).

CLASSIC DESCRIPTIONS OF VISUAL AGNOSIA

In order to better understand the sort of processing that occurs in the ventral stream, it is helpful to consider classic neurological disorders that appear to stem from dysfunction or damage to it. In the 1890s, on the basis of a small number of detailed case studies, Lissauer described two forms of object recognition failure which he called apperceptive and associative agnosia. Today, we think that the two disorders are linked to damage at different stages in the ventral stream, and reflect different types of perceptual disturbance. Lissauer's binary classification of agnosias oversimplifies the true diversity of these conditions. However, the distinction at least provides a useful starting point for our consideration of visual agnosia.

KEY TERMS
Receptive fields: The area of external influence on any given internal sensory element. Typically, for example, cells in your fovea (central field of vision) have much smaller receptive fields than those in the periphery.
Figure: (As in figure and ground.) The figure is the prominent or core feature of an array.
Ground: (As in figure and ground.) The ground is the background or peripheral element of an array.

Apperceptive agnosia

When shown a photograph of a cup, someone with this type of agnosia will probably be able to describe some of the physical features of it such as its size, colour, the presence of a handle, and so on. However, they will be unable to identify the object. In the most severe cases, when damage to occipital and surrounding posterior regions (especially in the right hemisphere) is widespread, patients with apperceptive agnosia cannot even copy simple shapes, match them, or discriminate between them. A case in point is Mr S (studied by Benson & Greenberg, 1969) who had become agnosic following accidental carbon monoxide poisoning. Although he clearly had some rudimentary impression of form, describing a safety-pin as "*silver and shiny like a watch or nail clippers*", he could

not recognise objects, letters, numbers, or faces. He could, however, recognise objects from touch. Moreover, there was no evident deficit in his speech, memory, or comprehension.

People with apperceptive agnosia are described as being unable to put individual parts of a visual stimulus together to form what psychologists call a **percept**. The problem is regarded as "perceptual" rather than "sensory" because patients with apperceptive agnosia can usually describe individual elements of an object. They can see an object's form and features but they seem unable to "bind" individual components together into a meaningful whole.

Associative agnosia

Individuals with this form of agnosia can copy objects relatively well, and detect similar items from a visual display. In some cases they may even be able to sort items into groupings (animals, items of cutlery, tools, etc.). The problem in associative agnosia is an inability to identify (and name) specific objects. Consider the following situation: a patient is shown an assortment of cutlery. He picks up a fork and, when asked, draws a recognisable sketch of it. This shows that perception of the item is relatively complete, and therefore that the individual does not have apperceptive agnosia. He may, if asked, be able to find another similar item from the cutlery drawer. However, he would still be unable to identify the item as a fork. Moreover, if later asked to draw the object from memory, he might be unable to do so, although if actually asked to draw a fork, he probably could. Even at this point, he might not realise that the object he was holding and the drawing he has just made were of the same item. This problem is not necessarily related to general deficits in semantic memory because individuals with this form of agnosia can sometimes describe in great detail functional (or other semantic) information about objects from memory. One associative agnosic patient (MS) was unable to draw an anchor from memory, but was nevertheless able to define the item as "a brake for ships" (Ratcliff & Newcombe, 1982).

On the other hand, some people with associative agnosia *do* have problems with their semantic memory. Patient AB (studied by Warrington, 1975) could match objects and distinguish shapes, and he could also match different views of faces reasonably well. However, he was unable to name any of a series of 12 common objects shown to him. He could determine whether photographs depicted animals or objects, but he was unable to name or distinguish between different types of animal, suggesting some form of semantic memory deficit.

Insight into the nature of the cognitive deficit found in associative agnosia is provided by McCarthy and Warrington (1986). Their patient FRA suffered a stroke that affected left occipital and temporal regions. Amongst other "spared" perceptual skills such as being able to point to "named" objects, he could, additionally, colour in overlapping line drawings of objects (something that patients with apperceptive agnosia cannot do). However, he was unable to name any of them, and could provide only partial semantic information (at best) about just a few of them. This suggests that the core problem in associative agnosia is one of linking percepts to meaning. Object recognition is certainly more complete than for someone with apperceptive agnosia. However, the remaining problem is one of forming links between the "percept" and stored semantic information about such items.

Key Term
Percept: The "whole" that is perceived by putting together the constituent parts.

INTERIM COMMENT

Historically, a key distinction between apperceptive and associative agnosia has been whether or not individuals can copy drawings; generally people with associative agnosia can, but those with apperceptive agnosia cannot (but see below). Lissauer's distinction between the two forms can be related to processing in the ventral stream. Apperceptive agnosia occurs because of damage at an early stage in the ventral stream, and although many people with this form of agnosia have bilateral damage, cases of people with unilateral damage suggest that it is the right hemisphere that is most critical. People with this form of agnosia have only the most rudimentary visual perceptual functions, and damage to the occipital lobes and adjacent cortical regions such as the occipitotemporal border is often apparent. Associative agnosia is related to a somewhat later stage in perceptual processing in the ventral stream. The percept is relatively complete, but there is a problem linking it with relevant stored semantic information. This form of agnosia is much less common than apperceptive agnosia. However, rare instances indicate underlying damage either to semantic systems in posterior regions of the left hemisphere, or to the pathways connecting the occipito-temporal border regions of the right and left hemispheres (Janowiak & Albert, 1994; and see Figure 8.3).

RECENT CONCERNS ABOUT UNDERSTANDING VISUAL AGNOSIA

One unresolved problem concerning the classification of visual agnosia is a consequence of the inherently non-specific nature of brain damage. In Lissauer's original characterisations, both apperceptive and associative agnosia were considered to be "post-sensory" disorders. Yet the reality is that many people with visual agnosia have sensory impairments such as colour blindness or small blind spots (scotomas) *in addition* to their perceptual problems. This is particularly so in apperceptive agnosia, which is frequently associated with accidental carbon monoxide poisoning (see the case of Mr S discussed earlier). The poisoning also leads to widespread but minor lesions (sometimes called "salt and pepper" lesions) in posterior regions that are linked to sensory impairments such as those mentioned above. Clearly, it is important to ensure that the apparently perceptual deficits seen in agnosia are not, after all, caused by more fundamental sensory impairments as some writers have suggested (e.g., Bay, 1953).

However, the main problem with Lissauer's classification of visual agnosia is that it is too simple, and therefore fails to distinguish satisfactorily between subtly different forms of deficit. Consider first apperceptive agnosia: although the classic description emphasises the failure to bind together individual elements into a perceptual whole, cases have recently come to light where correct perception of the whole appears to depend on the orientation of the objects, the shading or shadowing that is apparent, or even the extent to which images are degraded. Some agnosic patients may, for example, be able to identify an object when viewed in a normal (standard) orientation, yet be unable to identify the same object if it is shown end-on, upside-down, or in some other unusual orientation. Patient JL, studied by Humphreys and Riddoch (1984), struggled to match normal views of

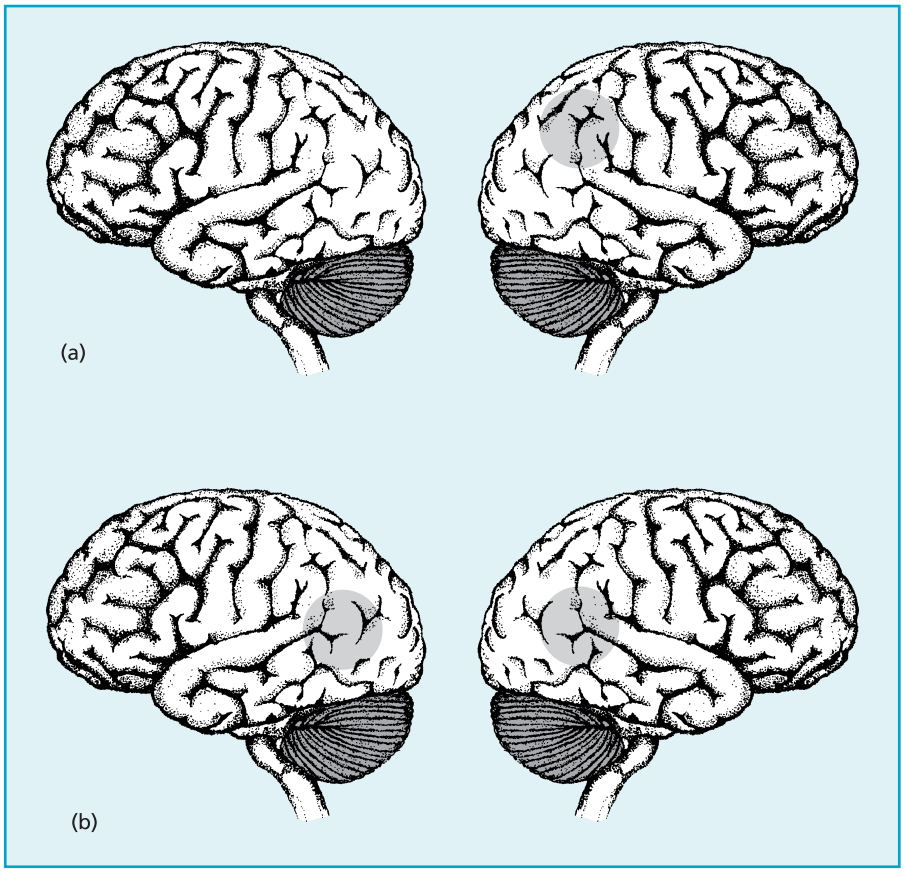


FIG. 8.3 Cortical regions typically damaged in apperceptive and associative agnosia. (a) Unilateral damage in posterior regions of the right hemisphere is more likely to be associated with apperceptive agnosia than equivalent damage on the left, although damage is, in fact, often bilateral. (b) In associative agnosia damage can be to either hemisphere, although the location is typically more ventral than that seen in apperceptive agnosia (in the vicinity of the occipital-temporal boundary).

objects with foreshortened views (end-on) (see Figure 8.4a). Moreover, when shown items from the Gollin picture test (1960), which comprises intact and partially degraded line drawings of familiar objects, some agnosic patients can identify the intact drawings but not the degraded ones (Warrington & Taylor, 1973, and see Figure 8.4b).

Associative agnosia also seems too simple a concept to account for the subtle differences in deficit that are observed in this condition. As we have seen, patient AB, studied by Warrington (1975), could draw and match objects, and was good at recognising unusual views of objects. However, he was profoundly impaired at object or picture naming, and was equally poor at describing functions of objects when given their names aurally. HJA, studied by Humphreys and Riddoch (1984), on the other hand, could define a carrot when asked to do so verbally, yet failed to identify a picture of one, guessing that it was a sort of brush. Moreover, he could often name objects by touch (when blindfolded) that he could not identify visually. These two examples illustrate that similar perceptual frailties may, on closer observation, take subtly different forms, and be related to different cognitive

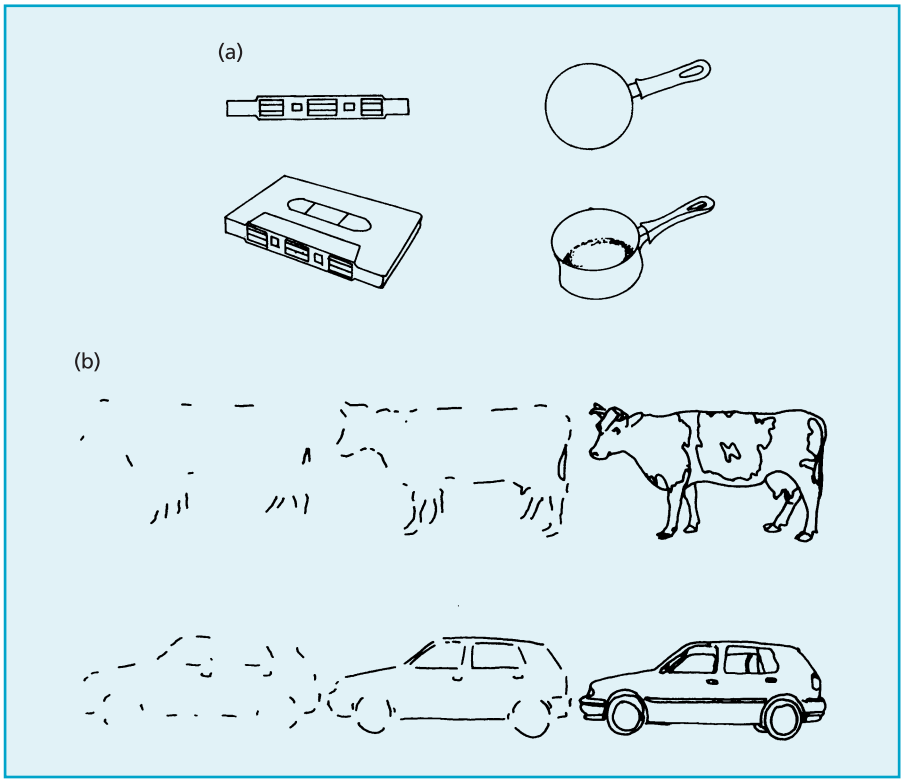


FIG. 8.4 Unusual views of objects. (a) All people find it easier to recognise objects when viewed from a "normal" angle. However, some people with agnosia cannot recognise objects at all when shown an "unusual" view. (b) The Gollin figures also present particular difficulties for some agnosic patients, although recognition of complete figures may be unaffected.

processing impairments. AB's problems involved semantic memory deficits, whereas HJA had an intact memory but seemed unable to access it from visually presented material.

Another problem is related to the question of how complete the percept actually is for individuals who would otherwise receive a diagnosis of associative agnosia. Recall that the acid test of this form has, historically, been whether or not the person can copy whole drawings. HJA, mentioned earlier, was able to produce an accurate copy of an etching of London, but the process took 6 hours and he completed the exercise in a laborious, slavish, line-by-line manner, which seemed to be independent of any "knowledge" of the actual form of objects in the sketch. Humphreys and Riddoch acknowledged that HJA was an unusual case. They argued that he had a particular problem in the integration of overall form with local detail, and other test findings showed that HJA was often "thrown" by the presence of detail in drawings or pictures that he was trying to copy or recognise: for example, he found silhouettes easier to recognise than line drawings. Of course, it is likely that normal individuals make extensive use of their semantic memory (which HJA could not do) when copying a drawing. This may make the copy less accurate, but a lot faster. The point is that, whichever way we look at it, HJA does not fit conveniently into either of Lissauer's agnosic types.

MODERN IDEAS ABOUT VISUAL AGNOSIA

Most researchers now acknowledge that Lissauer's classification is in need of revision and/or expansion. Farah (1990), for example, has proposed that visual object agnosia needs to be considered in relation to deficits in both word and face recognition (see below). Warrington has emphasised the importance of perceptual categorisation as a stage in object recognition that may be impaired in patients with apperceptive agnosia (Warrington & Taylor, 1978). Humphreys and Riddoch (1987, 2001) have argued that there are at least five subtypes of agnosia, and Ellis and Young (1996) also found it necessary to disaggregate Lissauer's two forms into several subtypes.

Riddoch and Humphreys' (2001) cognitive neuropsychological model of object recognition is an attempt to integrate case study reports (from their own patients, and those of Warrington, Farah, etc.) with an influential theory of visual perception proposed by Marr (1982). Although the details of his model need not concern us, it broadly comprises three sequential stages. The first is the generation of a unified "primal sketch" from the two 2D retinal images. It includes information about boundaries, contours, and brightness fluctuations, but not overall form. The second stage involves the generation of what Marr called a 2.5D image. This is viewer-centred (from the viewer's perspective), and contains information about form and contour, but neither object constancy (recognising an object as such whether it is near or far away, or even upside-down) nor perceptual classification. The final stage is the 3D representation. This is a true object- (rather than viewer-) centred mental representation. It is independent of the viewer's position, and specifies the real 3D shape of an object from any view, enabling true object recognition. Riddoch and Humphreys' model of object recognition is shown in Figure 8.5. For simplicity we have identified the stages sequentially:

- The initial parallel visual processing of objects is along the basic dimensions of colour, depth, and form. Motion features may also be processed if appropriate (if the object is moving). This stage of processing (motion excepted) essentially corresponds to Marr's primal sketch.
- The next stage involves grouping by colinearity (meaning identification of the edge of the object by dint of it having a common boundary).
- Then comes feature binding/multiple shape segmentation. This involves combining object features to form shapes, or breaking up compound images into component objects. Problems at this stage are more likely with overlapping or "busy" images where recognition depends on the correct binding of elements into a coherent image: see Figure 8.6a and b for examples of stimuli that may cause recognition difficulties at this stage.
- The next stage is equivalent to converting Marr's 2.5D sketch into a true viewpoint-independent 3D image. This stage is about the formation of constancy (see above), and remains somewhat controversial because some people with agnosia seem able to recognise objects despite being unable to match together conventional and unusual views of the same object.
- The next stage is a full structural description, tested by asking respondents whether or not presented pictures/drawings are of real objects. Some patients perform poorly on this task even though they may be good at matching different views of objects (see previous stage).

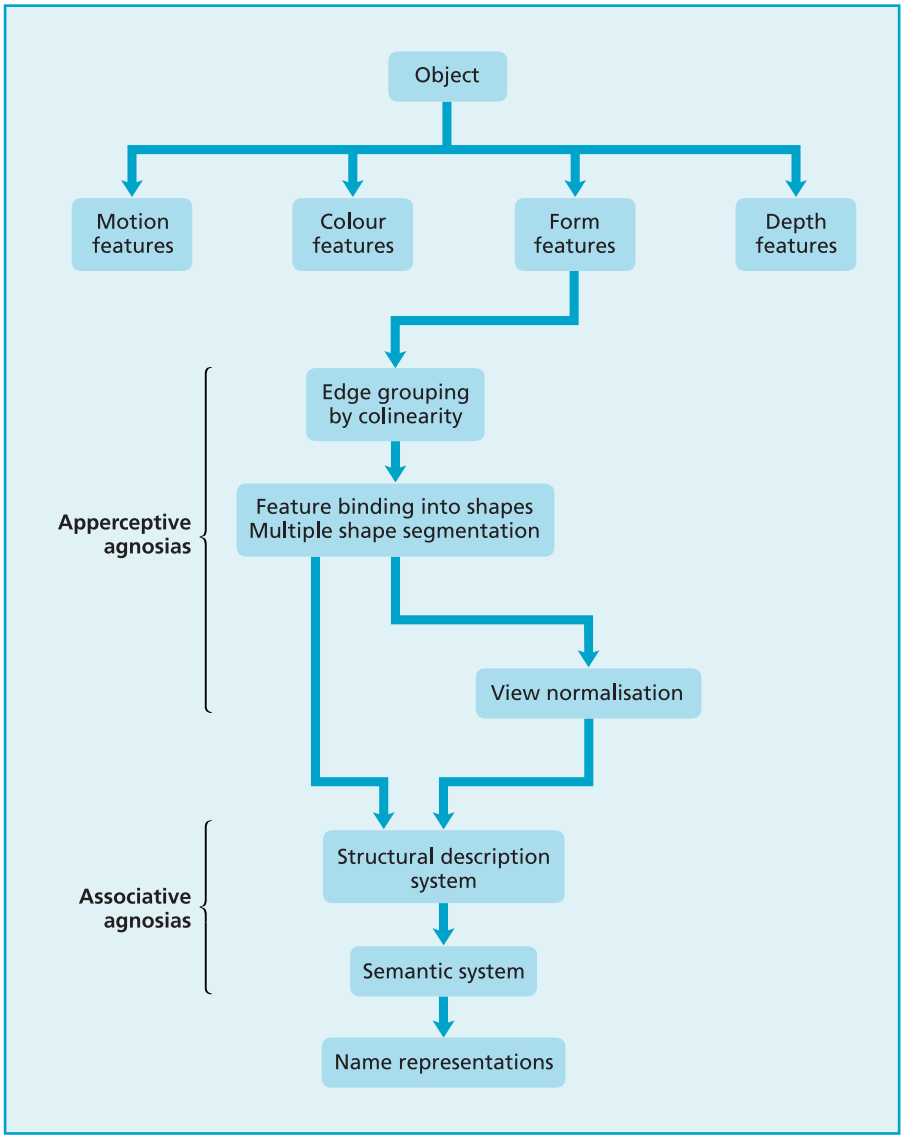


FIG. 8.5 Riddoch and Humphreys' (2001) model of visual object recognition. The model describes the component processes (and their connections) assumed to underpin normal and faulty object recognition. Adapted from Riddoch & Humphreys (2001) in B. Rapp (Ed.), *Handbook of cognitive neuropsychology*. Hove, UK: Psychology Press.

- In reality, the full structural description quickly meshes into the semantic system stage: individuals may be able to distinguish real from imaginary objects yet be unable to say which two items in an array of three (for example, hammer, nail, spanner) "go together". Some individuals with this problem can nevertheless provide detailed semantic information about the same objects if told their names, indicating that the problem is one of accessing the semantic system from the visual image.
- For other patients with agnosia, especially with category-specific semantic problems (see below), the basic deficit may either be loss of specific access

(from the essentially intact visual image) or a semantic deficit, in which case the patient would not be able to elaborate on an item even when *told* what it was.

- The last stage in the model (name representations) is necessary to accommodate a small number of agnosic patients who clearly have semantic knowledge of objects but still cannot name them when they see them; a condition called **optical aphasia**.

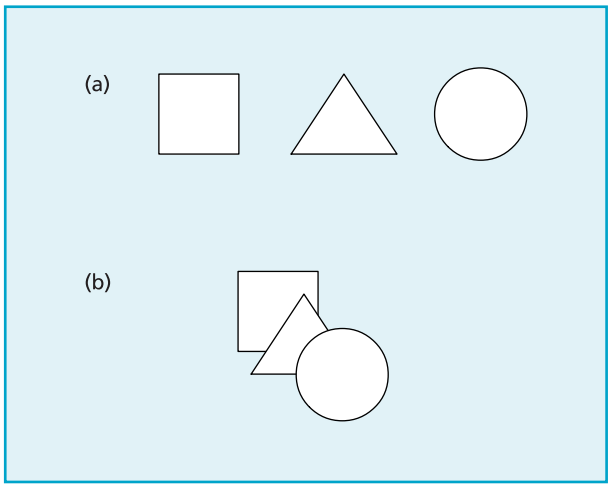


FIG. 8.6 Binding elements into a coherent image. Some apperceptive agnosic patients can recognise simple shapes when they are separate (a) but not when they overlap (b).

Riddoch and Humphreys' modification and extension of Marr's model serves as a useful template for understanding the various forms of agnosia that have now been described in the literature and, inter alia, provides a heuristic model for visual object recognition in the intact brain. For example, Lissauer's apperceptive agnosia actually encompasses a series of disorders linked to failures (early) in the processing stream up to and including an inability to form either a primal sketch or a 2.5D viewer-centred image (e.g., Mr S). An inability to recognise degraded objects or unusual views of objects with preserved ability to recognise form (e.g., JL) may be specifically related to a failure, at the view normalisation stage, in forming a 3D object-centred image. Associative agnosia may occur either because of problems in accessing semantic memory despite the formation of an intact object-centred image (e.g., FRA), or because of impairments to semantic memory itself (e.g., AB).

INTERIM COMMENT

Riddoch and Humphreys have offered a dynamic multi-stage scheme of visual object recognition that accounts for many of the apparent contradictions or inexactitudes of earlier models. However, the authors acknowledge that much more research is required to resolve remaining uncertainties about agnosic disorders and, in the process, about normal object recognition. One example relates to the formation of a true object-centred image. Recall that the copying style of agnosic patients like HJA, though accurate, was painstaking and laborious. Humphreys and Riddoch have taken this as an indication that HJA did not, in fact, have normal form recognition, because of his problems in integrating fine detail into the global form (a problem at the feature-binding stage in their model). This in turn implies that normal object recognition involves both the encoding of a global form and the integration of fine detail into that form. Humphreys and Riddoch coined the term **integrative agnosia** to describe HJA's deficit and suggested that such a "processing" failure was, in fact, a hallmark of many agnosic patients.

KEY TERMS
Optical aphasia: A deficit in naming objects viewed visually in spite of intact semantic knowledge of them.
Integrative agnosia: A condition characterised by impaired object recognition due to problems in integrating or combining elements of objects.

FUNCTIONAL IMAGING OF OBJECT RECOGNITION

PET and fMRI have provided us with the tools to examine the neural substrates of object recognition in normal people. Farah and Aguirre (1999) reviewed the results of 17 early imaging studies and their conclusions were somewhat disappointing. The meta-analysis revealed a lack of internal consistency and showed only that the posterior part of the brain was involved in object recognition. Farah and Aguirre argued that in spite of their uninspiring findings, imaging was a potentially exciting tool for exploring category specificity. This prediction has been borne out since, with a wealth of informative imaging results that are revolutionising our understanding of category-specific organisation at the neural level. We will review this literature later in the chapter.

fMRI has also provided evidence about other aspects of object recognition. For example, Bar and colleagues (Bar, 2004; Bar et al., 2006) have explored the role of the prefrontal cortex in exerting top-down control over object recognition. They suggest that very early in object recognition, prefrontal regions use coarse shape information to narrow the range of candidate objects, facilitating object recognition (see Figure 8.7). Carlson, Grol, and Verstraten (2006) have explored the temporal dynamics of object recognition, revealing multiple unique stages in the process, including support for Bar's top-down modulation. Thus, fMRI is providing evidence about the details of object recognition that classic neuropsychology simply cannot access. Imaging studies have also suggested that the neural basis of object recognition can be altered. Behrmann et al. (2005) performed lengthy training on a subject with long-standing agnosia and succeeded in improving some aspects of his object recognition skills. fMRI revealed that behavioural improvement was accompanied by functional reorganisation in the fusiform gyrus, part of the visual recognition system. This raises the possibility that some of the anomalies in the classic neuropsychological studies of agnosia may represent individual differences in the extent to which dynamic functional reorganisation occurs.

CATEGORY SPECIFICITY

Prior to the advent of functional imaging, an outstanding issue for the understanding of object recognition was that of category specificity. For some agnosic patients (for example, AB, whose case was reviewed earlier), impairment is linked to general deficits in semantic memory and inability to make intra-class distinctions. However, cases have come to light suggesting that category-specific semantic impairments may also occur in agnosia. A seminal series of papers by Warrington, Shallice, and McCarthy (Warrington & McCarthy, 1983, 1987; Warrington & Shallice, 1984) described a small number of agnosic patients with category-specific semantic deficits. For example, some had a naming deficit for living things, and others had a deficit for inanimate objects (see also Table 6.1). Other studies have since confirmed the existence of category specificity in patients. There have been various attempts to explain this phenomenon (see Caramazza & Mahon, 2003). One suggestion is that naming living things depends more on visual/perceptual information, while naming inanimate objects depends more on functional/associative information. There is some empirical support for this theory, but also evidence that is problematic (Caramazza & Shelton, 1998). We will return to this theory later when we review neuroimaging data. Although

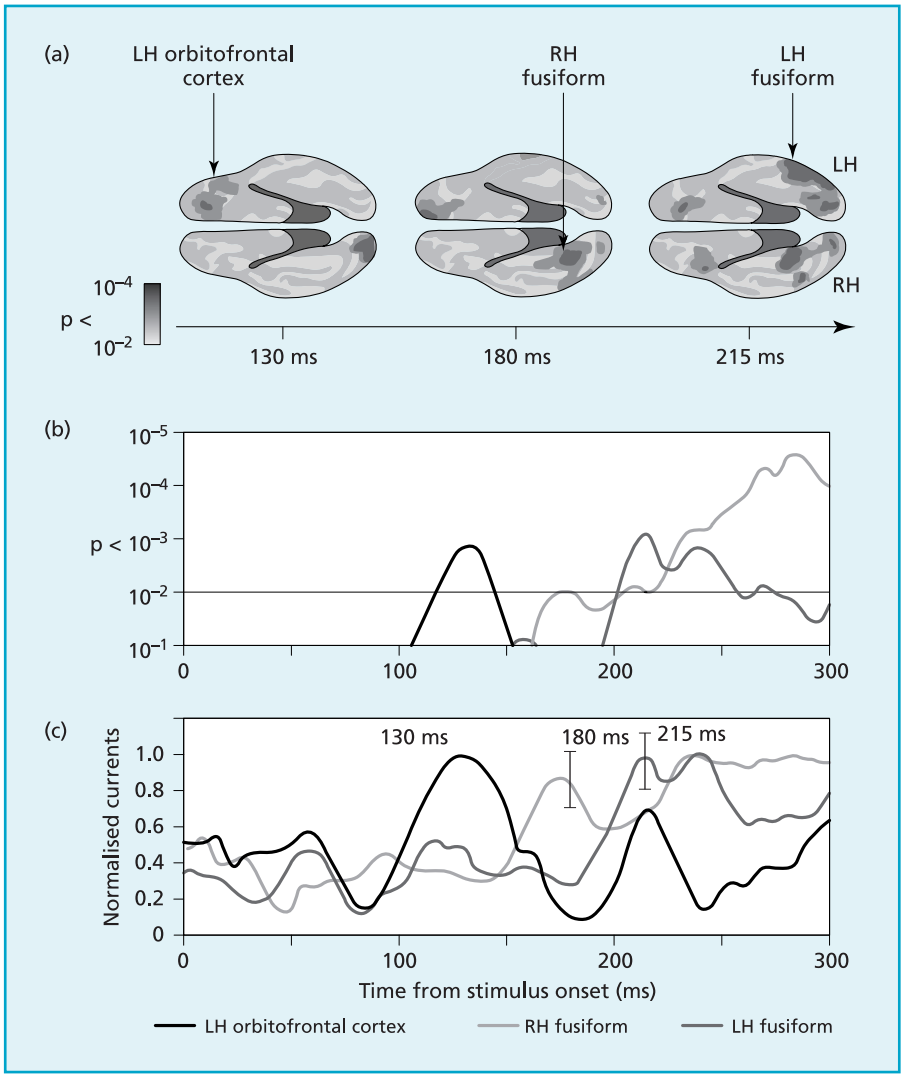


FIG. 8.7 Top-down control of object recognition. Orbitofrontal activity precedes temporal cortex activity. Source: Bar, M., et al. (2006). Top-down facilitation of visual recognition. *Proceedings of the National Academy of Sciences*, *103*, 449–454. Reproduced with permission.

convincing evidence for category-specific deficits has only really emerged since the 1990s, one class of objects has always been considered special and distinct in the field of object recognition: faces.

RECOGNITION OF FACES AND PROSOPAGNOSIA

The ability to recognise faces is a skill that has long intrigued psychologists, partly because humans are so good at it. Consider the following lines of evidence. First, humans have a phenomenal memory for faces. Most readers will be aware of that "striking" moment of recognition when spotting the face of someone not encountered for many years. Second, research indicates that humans can

memorise face information very quickly and with very little effort. People tested on Warrington's facial memory test, in which they look briefly at 50 anonymous black and white photographs of people, can correctly recognise most (or even all) of them in a later test. Third, although the distinctions between faces are subtle (all humans usually have two eyes, a nose, and a mouth), humans are able to scan large numbers of photographs very quickly to find one famous face. This last observation is a reminder that the key to effective face processing is "individuation"—that is, being able to distinguish between the subtle variations in form, size, shape, and alignment of the components of a human face.

A small number of people suffer from a specific form of agnosia that involves the inability to perceive faces. In **prosopagnosia** (as it is known) the degree of impairment is, as with object recognition, variable. In some cases, people may be unable to match pairs of faces, or say whether two photographs are of the same individual. In other cases, recognition of particular individuals such as film stars or members of the person's own family may be affected. In the most extreme and perplexing form of the disorder, the person may even lose the ability to recognise themselves from photographs or in the mirror.

Consider the following cases: Soldier S was studied by Bodamer (1947). Despite making an otherwise reasonable recovery following head injury, he was unable to recognise once-familiar faces. He could differentiate between faces and other objects, although he was prone to errors in recognising animals from photographs of their head, once misidentifying a dog as an unusually hairy person! When it came to humans, he complained that all faces looked very much alike, describing them as routinely flat white ovals with dark eyes. He was unable to interpret facial expressions although he could see movements (of a face) that led to changed expressions. He was unable to recognise his own face in a mirror.

Now consider Mr W, who was studied by Bruyer et al. (1983). He developed prosopagnosia in middle-age following a period of illness. He retained the ability to copy line drawings of faces, and he could match photographs of faces taken from different perspectives. He could also select faces correctly when given a verbal description, and his performance on this task deteriorated (as it would for normal subjects) if the faces were partly obscured. His particular problem only became apparent when he was asked to identify faces of either famous people or people he knew personally. For example, he identified only one of ten photographs of famous people. He also failed to recognise any familiar acquaintances from video vignettes, although he could recognise them from their names or even from hearing their voices. This showed that Mr W had "semantic knowledge" of these acquaintances, so his prosopagnosia was not simply an amnesic condition. Ellis and Young (1996) suggested that his problem was one of accessing memories about the person (including his/her name) from the image of the face. A fault in the operation of "facial recognition units" (the facial equivalent to object recognition units in their model of object recognition) would account for Mr W's prosopagnosia.

Prosopagnosia is a rare condition with a variable presentation. However, the deficits of Soldier S and Mr W suggest the existence of (at least two) different forms: Soldier S's problems are, in certain respects, analogous to the object recognition deficits seen in apperceptive agnosia; his basic perception of faces is impaired. Mr W's prosopagnosia, on the other hand, parallels the object recognition deficit of associative agnosia. His face perception seems relatively intact but

KEY TERM
Prosopagnosia: The form of agnosia in which the ability to perceive faces is affected.

he is unable to recognise (or in other ways semantically process) faces (a comparable vignette is presented in Box 8.1).

Box 8.1 A case study of prosopagnosia (adapted from Stirling, 1999)

Therapist: (shows patient a picture of a cow and horse) "Which is the horse?"
Patient: "That's easy . . . the one on the right without horns."
Therapist: (shows photograph of Elvis Presley) "Do you know who this is?"
Patient: "Is it a famous person?"
Therapist: "Yes."
Patient: "Is it the Pope?"
Therapist: "No, this person is no longer alive . . . Describe the face to me."
Patient: "Well, he's tall, and has got black hair swept back with lots of grease . . ."
Therapist: "Does he have a moustache?"
Patient: "No, but he has long sideburns . . . and a guitar."
Therapist: "It's Elvis Presley!" (Patient nods, but doesn't appear to connect the face to the name.)
Therapist: "Now, who's this?" (Shows photograph of patient's wife.)
Patient: "I dunno . . . some woman . . . about my age with grey hair and nice eyes . . ."
Therapist: "It's your wife." (Patient once again seems unable to connect the picture to the identification.)
Therapist: "OK. Who's this?" (Shows photograph of patient.)
Patient: "No idea . . ."
Therapist: "Describe him . . ."
Patient: "Well, he looks quite old, and has lost a lot of hair. He looks like he needs a holiday, with those bags under his eyes . . . A good long rest . . ."
Therapist: "It's you!"
Patient: "No . . . you are kidding me! It's a very poor photograph. I don't look a bit like that!"

CO-OCCURRENCE OF DIFFERENT FORMS OF AGNOSIA

Many people with prosopagnosia also show other abnormalities of object recognition, and when these conditions coincide the prosopagnosia is, typically, more severe. This has led to the suggestion that prosopagnosia is just a particular type of object recognition failure involving a breakdown of within-category recognition. However, the test of this hypothesis is not the number of individuals who show both forms of agnosia, but whether individuals can be found with one but not the other form. Cases of specific prosopagnosia have been well documented, although cases with impaired object recognition but intact face recognition are much rarer. However, they do exist; for example, patient CK studied by Moscovitch, Winocur, and Behrmann (1997) had profound object recognition but intact face recognition. This suggests a dissociation between object

recognition and facial recognition, indicating that facial recognition is a separate skill that *need not* overlap with object recognition. Another case was reported by Assal, Favre, and Anders (1984). Their patient MX developed a marked agnosia for livestock (he was a farmer), places, and faces. Within 6 months his prosopagnosia had disappeared although he remained agnosic for animals. Prosopagnosic patient WJ (McNeil & Warrington, 1993) showed almost the exact opposite pattern of deficit. His performance on a version of the famous faces recognition test was at chance level, although his ability to recognise objects such as cars, breeds of dog, or flowers was normal. After developing the disorder, he acquired a flock of 36 sheep which could be identified by number. On a series of recognition tests WJ clearly retained his knowledge of individual sheep despite his profound prosopagnosia for human faces!

Farah (1990) has conducted a meta-analysis of the coincidence of object agnosia, prosopagnosia, and **acquired alexia** (inability to recognise written words after brain injury/damage) by reviewing every published study detailing cases of any of these disorders between 1966 and 1989. She hypothesised that alexia and prosopagnosia could be linked to fundamentally different deficits in analytical and holistic processing respectively, whereas object agnosia could result from deficits in either system. One prediction from this intriguing hypothesis is that object agnosia should not occur independent of either alexia or prosopagnosia (one or other must be present). The results of her analysis are shown in Table 8.1. Clearly, many people have deficits in all three areas. Numerous instances of alexia alone and prosopagnosia alone were also identified. But the most interesting findings were that only a single case of object agnosia alone could be identified, and there was one possible case of alexia and prosopagnosia without object agnosia. Since publication of this research a small number of additional "exceptions" have been reported, casting doubt on Farah's hypothesis. Nevertheless, the co-occurrence (and mutual exclusivity) of different forms of agnosia merits further investigation.

TABLE 8.1 THE RESULTS OF FARAH'S META-ANALYSIS

Deficits in	Number of patients
Face, object, and word recognition	21
Faces and objects	14
Words and objects	15
Faces and words	1?
Faces only	Many
Objects only	1?

PROSOPAGNOSIA AND THE BRAIN

If we consider the question of location of brain damage and prosopagnosia, the following picture emerges: many cases have bilateral damage, and this is predominantly to occipital or temporal lobes. Of those people with prosopagnosia who have unilateral lesions, the vast majority have right hemisphere damage, again mainly to ventral occipital and/or temporal regions (DeRenzi et al., 1994). In fact Farah (1990) could find only four cases (6% of her sample) of prosopagnosia following unilateral left-sided damage. Overall, this is quite strong evidence of a specialised role for the right hemisphere in face recognition. This view is further supported by data from a small number of imaging case studies of prosopagnosia reported by Sergent and Signoret (1992). For two prosopagnosic patients with

KEY TERM
Acquired alexia: Loss of reading ability in a previously literate person.

problems similar to Soldier S (see above) but no object agnosia, damage was localised to occipital and medial temporal regions of the right hemisphere. For two additional prosopagnosic patients with intact face perception but impaired access to memory (like Mr W), damage was found in more anterior regions of the right temporal lobe.

INTERIM COMMENT

In summary, the available neuropsychological evidence suggests that face recognition is more than just a sophisticated form of object recognition. Prosopagnosia also seems to be linked to damage to brain regions that may be specialised to deal preferentially with faces. These areas include ventral regions of the occipital and temporal lobes on the right side. One interpretation of these data is that posterior regions (early in the ventral stream) deal with the integrative process of putting together the face from its component parts, whereas areas further forward, but still on the right side, are concerned with identification, and linking this with other semantic and biographic information about the person. fMRI has provided a wealth of evidence about category specificity generally and face specificity in particular, which we will review in more detail below.

IMAGING CATEGORY SPECIFICITY

As we have indicated earlier, category specificity is the area of visual recognition where functional imaging has been most useful (so far). fMRI has shown quite clearly that distinct regions of the brain show a selectively enhanced response to objects within a visually similar class. As with the classic neuropsychology evidence, the fMRI literature has been particularly strong in identifying faces as a "special" class of objects. A small region of the fusiform gyrus (dubbed the "fusiform face area") is activated when respondents view faces but not non-face objects (Kanwisher, 2000). fMRI has also identified regional specificity in response to other object categories including such diverse examples as body parts (Downing et al., 2001), cars (Xu, 2005), and birds (Gauthier et al., 2000).

Debate continues about the extent to which these neural substrates for different objects overlap. The data suggest that some of the selective responses co-locate, although it has been argued that this represents a failure of spatial resolution of the technique. fMRI data in group studies have always undergone a degree of spatial "smoothing" and therefore studies may not have the sensitivity to distinguish regions that are small and closely adjacent. Perhaps more interestingly, the abundance of neuroimaging data has sparked theoretical debate about why category specificity might occur. In a series of experiments by Gauthier and colleagues, fMRI responses have been studied in subjects with a particular expertise in identifying a certain type of object (for example, birdwatchers or car buffs). These subjects were found to have a shift in levels of processing and category-selective regions, compared to non-expert subjects (see Figure 8.8). Further, Gauthier showed that similar shifts could be observed in non-expert subjects after a period of intensive training on a particular category. For these

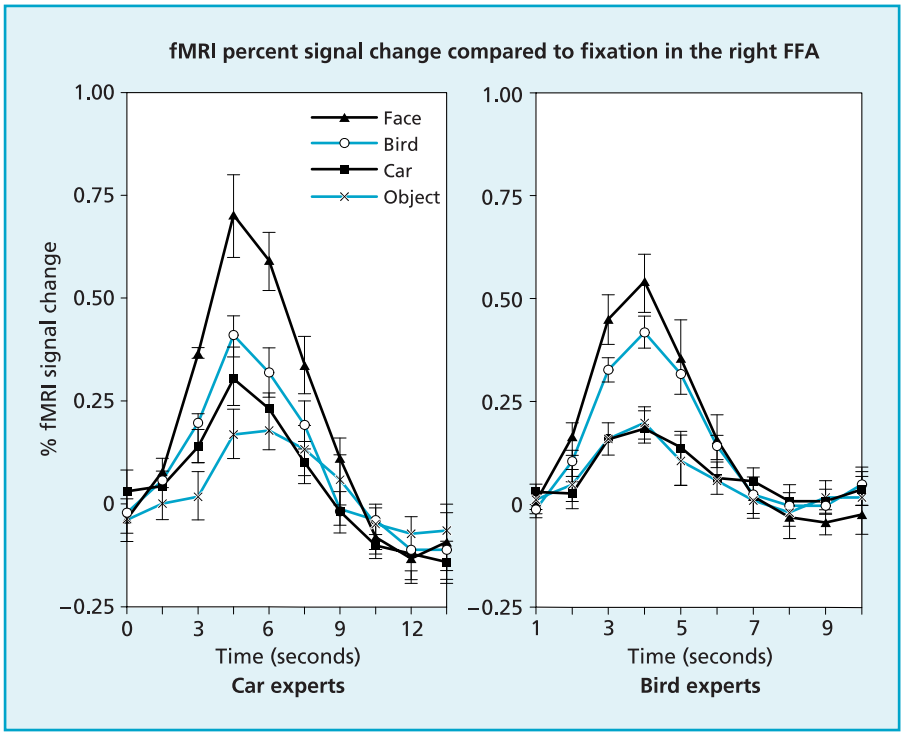


FIG. 8.8 Imaging modification of object recognition signal strength in expert subjects. Source: Xu, Y. (2005). Revisiting the role of the fusiform face area in visual expertise. *Cerebral Cortex, 15*, 1234–1242. Reproduced with permission.

expert and highly trained individuals, other classes of objects have acquired the "special" status that faces have for all of us—we are all experts at recognising faces (Tanaka, 2001). Gauthier and colleagues suggest that normal face recognition involves a different level of recognition from that of other objects, and thus the fusiform face area is not specific to faces but to the type of processing we normally apply to faces.

Other theories have focused on the computational requirements of recognising different classes of objects. For example, Malach, Levy, and Hasson (2002) argued that recognising stimuli like faces requires analysis of fine details and this is best served by regions that represent information from the central visual field. By contrast, identifying houses or places requires large-scale integration and this is best served by regions that represent peripheral visual field information. He suggested that certain types of category selectivity can be explained by these basic perceptual requirements.

Although theories are starting to emerge from the neuroimaging literature, it is an area that can still be characterised as involving "too much data but too few models" (Peissig & Tarr, 2006). In some ways, this is the complete reverse of the situation before functional imaging, when it could be argued there were not enough data but too many models. Now that we are not relying on extremely rare neuropsychological cases with unusual object recognition deficits, it seems reasonable to assume that our understanding of object recognition will continue to develop over the next few years.

SPATIAL FUNCTIONS AND THE "WHERE" STREAM

Earlier in this chapter we reviewed some of the evidence that led to Ungerleider and Mishkin's proposal of separate "what" and "where" visual processing streams. The agnosic conditions described earlier illustrate the effects of disturbances to functioning at different stages of the "what" (perhaps it should be what and who) stream, but we now need to consider the other stream, which is concerned with a range of spatial functions.

The "where" stream runs from the occipital cortex into the parietal lobe (see Figure 8.1). Output travels via V2 and V3 into area V5 (also known as the mid-temporal sulcus or MT). From there, it is channelled into various modular regions within the posterior parietal cortex. In V5, for example, we find cells that are exquisitely sensitive to stimuli moving in a particular direction irrespective of their exact location in the visual field. Cells in a parietal region known as V7 have even more extensive receptive fields and are selectively responsive to objects moving in particular directions at particular speeds. Other cells in the parietal region are responsive to a combination of input signalling spatial location of objects in the viewer's field of vision and the position of the viewer's own head and eyes. This is important because it allows the viewer to reference object location in space regardless of head or eye position or orientation. So, for example, you do not "see" the world as tilted when you bend your head to the left or right (Motter & Mountcastle, 1981).

As we mentioned in Chapter 3, the right hemisphere is often referred to as the spatial hemisphere although the left hemisphere also engages in spatial processing. The available evidence leads to the intriguing possibility that the left and right hemispheres may actually have complementary responsibilities when it comes to dealing with spatial information, and we revisit the question of "laterality" effects in spatial processing towards the end of the chapter. First, however, we need to consider briefly some basic spatial processes related to perception. Then we review some of the more integrative skills that nevertheless make substantial demands on spatial processing, such as constructional skills and negotiating routes. Finally, we consider briefly the general role of the left and right hemispheres in spatial memory.

BASIC SPATIAL PROCESSES

LOCALISING POINTS IN SPACE

Individuals with damage to superior regions of parietal cortex have difficulty reaching towards a visual stimulus (see our reference to optic ataxia earlier). Left-sided damage affects ability to reach towards the right side, and vice versa. If we remove the movement component, and simply measure perception of left- or right-side space (i.e., detection of stimuli in the left or right visual fields), we find that unilateral damage to the right parietal regions is most likely to adversely affect this ability.

DEPTH PERCEPTION

Local depth perception, meaning the ability to detect depth of close objects because of the different images falling on each eye (binocular disparity), can be

disrupted by both right and left hemisphere lesions (Danta, Hilton, & O'Boyle, 1978). Global depth perception, which refers to detection of depth (as in a landscape) where binocular disparity for individual items is not helpful, appears to be disrupted by right hemisphere damage (Benton & Hecaen, 1970).

LINE ORIENTATION AND GEOMETRIC RELATIONS

The ability to judge angles or orientations of lines is affected following right (but not left) parietal damage (Benton, Hannay, & Varney, 1975). Similarly, the ability to remember novel complex shapes of geometric patterns (especially those that cannot be named) is also affected after right parietal damage.

MOTION

It is very rare for humans to lose their ability to detect motion yet retain other perceptual abilities. In the handful of well-documented cases, there is usually damage to both left and right parietal lobes. Patient MP, reported by Zihl, von Cramon, and Mai (1983), had extensive damage that included areas of the mid-temporal gyrus and adjacent regions of the parietal lobes on both sides. She described her motion blindness as like seeing movements as a series of jerky still photographs (similar to what we might see in strobe lighting conditions). Interestingly, other spatial skills such as localisation of objects in space were relatively spared, which supports the idea of distinct movement-processing modules in each hemisphere. Motion perception has also been studied using neuroimaging techniques and area V5 has been identified as particularly important. This region is also activated by illusory motion (Zeki, Watson, & Frackowiak, 1993) and the motion after-effect (Tootell et al., 1995) suggesting a role in the processing of perceived as well as actual motion. Conversely, in a recent study Moutoussis and Zeki (2006) showed V5, as well as parietal cortex, activation when motion occurred, regardless of whether or not respondents were consciously aware of it. So V5 processing may proceed even when participants are not aware of motion.

ROTATION

PET imaging research, both with normal participants engaged in tasks that involve mental rotation and analysis of the performance of brain-damaged participants on similar tasks, once again points to the involvement of the right parietal lobe. In a classic study by Deutsch et al. (1988) participants had to decide which hand a "cartoon man" was holding a ball in. The cartoon was shown in various orientations, and in front and rear view. Patients with right hemisphere lesions made more errors and had slower reaction times on this task. More recent fMRI studies have confirmed the importance of right parietal regions in mental rotation tasks, although some studies have suggested that the activation is more bilateral. One reason for this discrepancy may involve individual differences. An intriguing recent fMRI study has found sex differences in the neural basis of mental rotation. Hugdahl, Thomsen, and Ersland (2006) reported more parietal activation in male participants and more inferior frontal activation in female participants, potentially suggesting a systematic difference in how the task was performed.

CONSTRUCTIONAL SKILLS

The skills involved in completing constructional tasks are more complex than those needed to undertake the spatial-perceptual tests mentioned above. They involve spatial perception, but in addition require the production or generation of some tangible output. There are several standard neuropsychological assessments of these skills and evidence suggests that right parietal damage is most likely to impair performance on them. However, some caution is required in interpreting test results because, in moving away from the purely perceptual, we introduce other psychological factors. The following two tests certainly involve hand–eye coordination and attention, and arguably even memory (which depends on other cortical functions), in addition to spatial skills.

The Rey-Osterrieth complex figure is a detailed line drawing that looks a little like the Union Jack flag, with other elements such as extra triangles and lines attached (see Figure 8.9a). Participants simply have to copy the figure. Normal individuals often complete this task almost faultlessly within a few minutes. However, it presents major difficulties for some patients with damage in the right temporo-parietal region (Benton, 1967). Damage here also adversely affects individuals on the block design test (a test taken from the WAIS; see Chapter 2) in which participants have to copy a simple pattern by assembling coloured blocks (see Figure 8.9b). Right hemisphere patients sometimes even fail to appreciate that the configuration of the nine blocks must be 3×3. Left hemisphere damage can also affect block design performance but in this case the basic configuration is usually correct, and it is more likely that individual blocks will be incorrectly oriented.

Constructional skills are one of the areas where functional imaging has been of relatively little use. fMRI in particular does not lend itself to the study of these processes for simple mechanical reasons. When people are enclosed in an fMRI scanner, they cannot see their hands and the range of possible movements is extremely limited. Therefore, it is difficult to assess tasks depending on hand–eye coordination or complex manual construction.

ROUTE FINDING

Researchers have developed a number of tests to assess route finding. They range from simple **finger mazes** (where a blindfolded participant has to learn a route by trial and error, usually by guiding his/her finger through a small maze) to following directions using standardised maps. As with the construction tests mentioned earlier, in interpreting results we must be aware that the different tasks assess other skills in addition to basic spatial ones. Moreover, depending on the particular task, it may be possible to use non-spatial strategies as well as, or even instead of, spatial ones, which further complicates interpretation. An additional complication is that some people struggle with certain types of route-finding tasks and not with others. This has necessitated a distinction between those measures that tap perception of spatial relationships in extra-personal space (like finger mazes) and measures that require respondents to guide *themselves* in three-dimensional space.

KEY TERM
Finger maze: A piece of apparatus in which the (usually blindfolded) respondent must negotiate a route from A to B. Typically the maze comprises a grooved piece of wood with one correct route and a series of blind alleys. The respondent pushes their finger along the "correct" path.

Performance on variants of the finger maze is compromised following damage to the right parietal lobe (Milner, 1965), but in addition, where there is a significant memory demand (a complex maze for example), performance can be affected

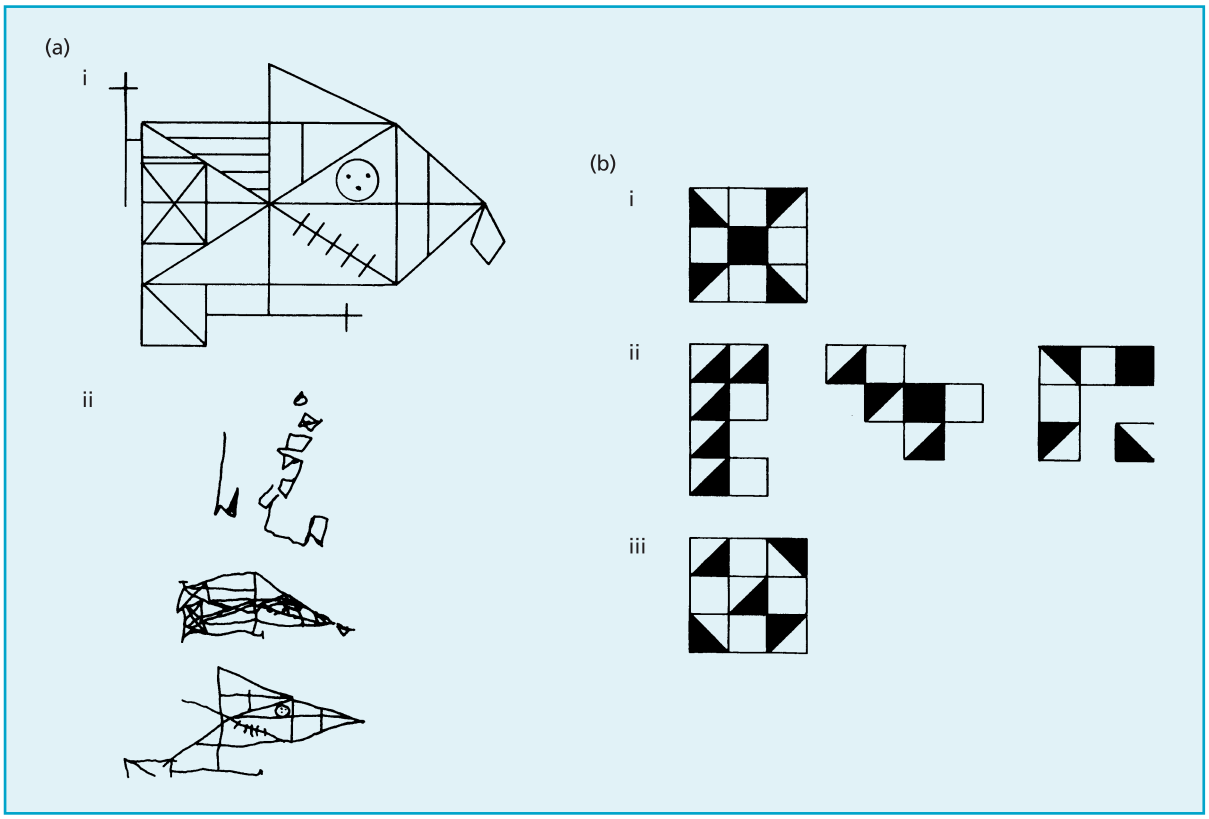


FIG. 8.9 Rey-Osterrieth figures and WAIS block design test. (a) This apparently simple copying task (i) is difficult for some patients with right temporal-parietal damage (ii). (b) In the WAIS block design test, respondents must "construct" the nine-square pattern (i) using individual blocks. Patients with right hemisphere damage (ii) are prone to errors in which they ignore the overall form of the pattern. Left hemisphere patients (iii) may get the overall form correct but get the detail wrong.

by damage to right temporal or frontal areas. A variant of the finger maze is where the participant has to find their way through a proper maze. In Semmes et al.'s (1955) maze test, nine dots are placed on the floor of a large room and participants are given a plan of the route (via the dots) to follow. For reference, one wall of the room is designated "north" and the person is not allowed to rotate the map as they follow the route. Typically, right parietal damage affects performance on this test (Semmes et al., 1963), although Ratcliff and Newcombe (1973) only found marked impairments in individuals with bilateral damage. A possible explanation for this is that in this type of task respondents can adopt different strategies. A "spatial" strategy is one way, but a verbal strategy (*turn right . . . go straight on . . . turn right again . . .*) can also be employed.

In Money's (1976) standardised road map test, participants are given a fictitious map that shows a route marked on it. At every junction they must "say" which direction (left, right, straight on) to go in. This test requires planning and memory as well as spatial skill, and performance is affected by damage to the frontal areas of the right hemisphere in addition to the more posterior parietal regions. Finally, there is even some evidence that basic geographic knowledge about entire countries can be adversely affected following right-sided damage.

Functional imaging has been widely used to study spatial navigation. Although parietal cortical regions have been shown to be involved in topographic processing, the main focus of imaging research has been on the hippocampus. This is a region that seems to be critically involved in complex route-finding tasks, whether using mazes or map-based navigation (see Figure 8.10). Indeed, structural imaging has suggested that individuals who have developed unusually acute navigational skills (London taxi drivers) actually have altered structure of the hippocampus (Maguire et al., 2000). A recent study has distinguished between route following (following well-learned paths between locations) and way finding (finding novel paths between locations) and has shown that they are associated with distinct neural substrates (Hartley et al., 2003). Way finding specifically activated right hippocampus in participants who navigated successfully. Posterior perceptual regions, including posterior parietal cortex, were also activated during way finding, regardless of performance.

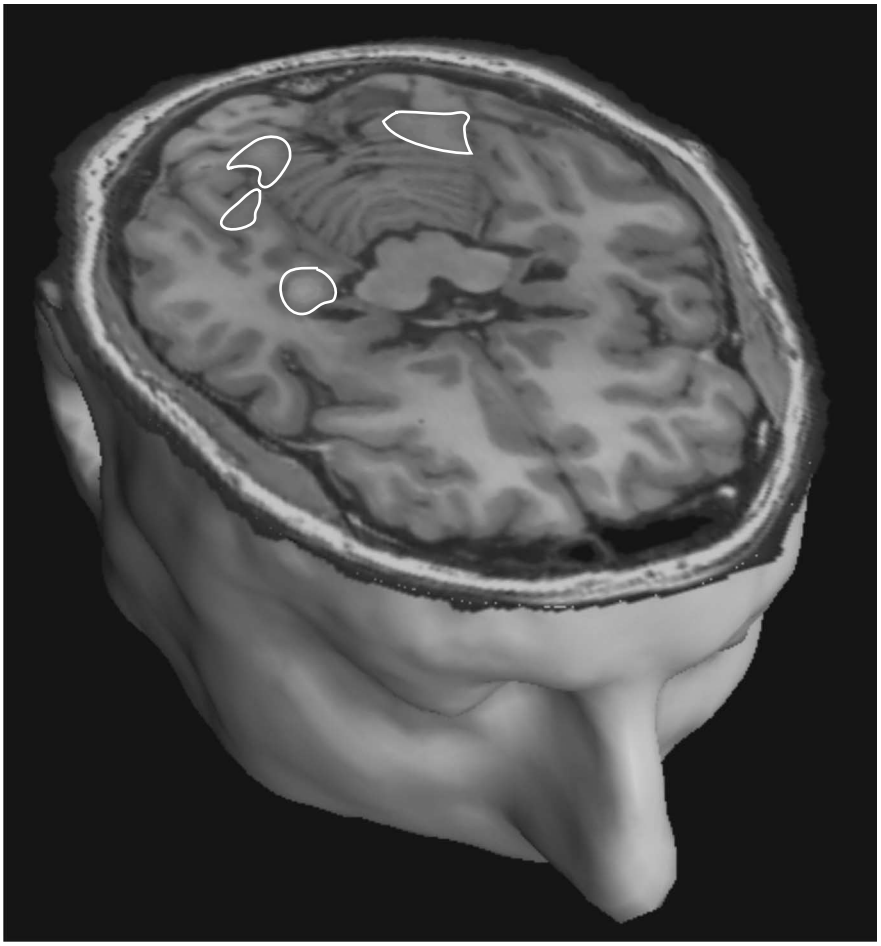


FIG. 8.10 Brain activations associated with spatial navigation. This image shows the brain responses in London taxi drivers when planning a route in virtual reality to deliver a (virtual) customer to their desired location. We are grateful to Dr Eleanor Maguire of the Wellcome Trust Centre for Neuroimaging, London, for providing this image [see Spiers, H. J. & Maguire E. A. (2006). *Neuroimage*, *31*, 1826–1840].

INTERIM COMMENT

Taken together, these observations illustrate the range of spatial perceptual abilities that humans possess, and which we tend to take for granted until a problem arises. Spatial perception depends on the ability to form an internal representation of the outside world, and sometimes to locate oneself in it. The formation of that internal representation, and the ability to manipulate it or "mentally" move around it, depends on effective processing in the "where" stream.

SPATIAL MEMORY

Spatial memory span can be assessed using Corsi's block-tapping test, which we introduced in Chapter 2. The wooden blocks are conveniently numbered on the tester's side, but the side facing the participant is blank. The experimenter taps a sequence of blocks, which the respondent must immediately duplicate. The experimenter increases the length of the sequence (in the classic manner) in order to establish spatial memory span. DeRenzi and Nichelli (1975) have found that patients with posterior damage on either side have a reduced span. Tests that assess spatial working memory appear to tap right hemisphere function, and usually present particular difficulties for respondents with right frontal damage. Recall from the previous chapter a study by Smith et al. (1996) in which normal participants were shown a brief array of dots (for 200 ms) then 3 seconds later a circle appeared on the screen. Respondents had to decide whether (or not) the circle would have surrounded one of the dots. PET activation during this test (when compared with a non-working memory condition) was most marked in the right frontal lobe. When we move beyond short-term retention, we find evidence of marked impairment in people with more posterior right hemisphere damage. For example, if recall on the Corsi tapping test is delayed by as little as 16 seconds, patients with right temporal and parietal hemisphere damage show the largest deficits. A recent study by van Asselen et al. (2006) considered stroke patients with different lesion foci. It suggested that patients with right posterior parietal or right dorsolateral prefrontal lesions were impaired at keeping spatial information in memory over short time periods, while those with lesions to either right or left hippocampus were impaired at longer time intervals.

Spatial working memory could be considered a form of higher-level processing that is critically dependent on visual perception and visual experience. However, Vecchi et al. (2004) have shown that although they do not have normal visuospatial abilities, patients who are congenitally blind are capable of performing spatial working memory tasks. An fMRI study by Ricciardi et al. (2006) showed that the parietal and prefrontal regions activated during a visual and a tactile spatial working memory task were extremely similar. This suggests that aspects of spatial working memory depend on higher-order representations that are independent of basic sensory processes. Figure 8.11 shows right-lateralised brain responses associated with a visual spatial working memory task.

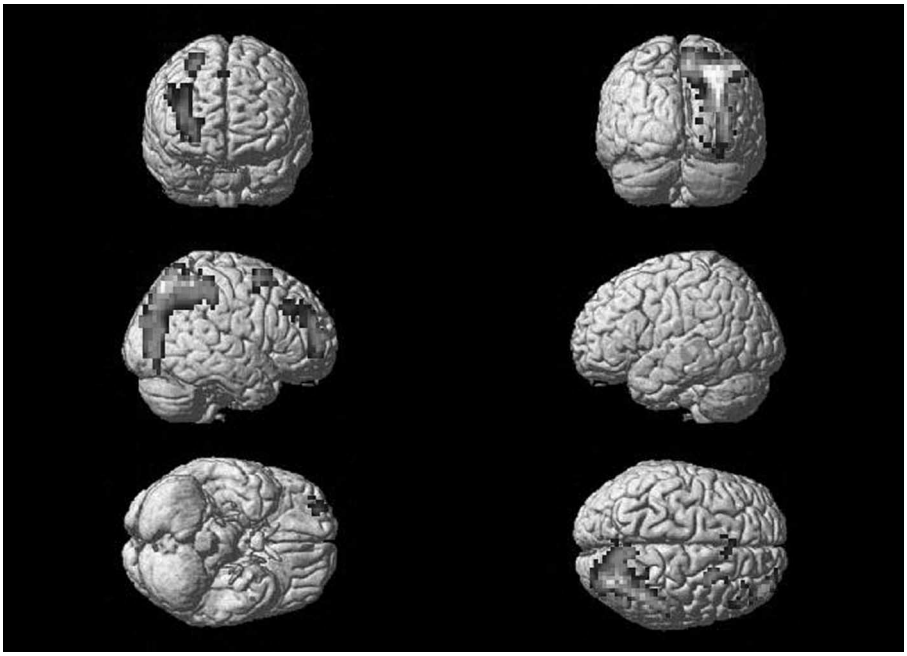


FIG. 8.11 Brain activations associated with spatial working memory. This image shows fMRI responses associated with the performance of an abstract spatial working memory task based on the CANTAB spatial working memory paradigm. Participants must search for coloured tokens in a spatial array, remembering where tokens have previously been found. We are grateful to our colleague Emma Pegg of the for providing this image.

THE LEFT HEMISPHERE AND SPATIAL PROCESSING

The fMRI literature on spatial processing has suggested that while right hemisphere structures may be predominantly involved, left hemisphere activity is also apparent. An insight into the operation of the left hemisphere in spatial tasks can be gleaned from observing the compensatory procedures adopted by individuals who have incurred right-sided damage. A classic case study of one such individual was reported by Clarke et al. (1993). Despite an extensive right-sided lesion resulting from a brain tumour, the Swiss woman in question hoped to become an architect, and the researchers were able to observe her as she tried to overcome (or circumvent) her spatial deficits by making greater use of left-sided functions. When copying arrays like the Rey-Osterrieth figure, she used a piecemeal strategy (akin to HJA's copying strategy described earlier). As a result, although basic elements of the figure were included, fine detail was often misplaced or omitted. She also used a feature-by-feature (as opposed to holistic) strategy in trying to recognise a series of Swiss towns from photographs. This worked well if a town had a distinctive or unique feature, but broke down when she tried to identify towns with similar but spatially distinct features. Related to these problems, her geographic knowledge and route-finding skills were also impaired, and in order to get around she developed a verbal point-by-point (landmarks) strategy. An fMRI study by Slotnick and Moo (2006) adds weight to these observations. They compared participants performing a categorical and a coordinate spatial memory task. The categorical task involved judgements like "one item is above another"

while the coordinate task involved judgements like "one item is near another". Categorical spatial memory recruited left prefrontal cortex while coordinate spatial memory recruited right prefrontal cortex. This is evidence for hemispheric specialisation for different aspects of spatial memory, both of which may be recruited in the spatial processes we employ in everyday life.

INTERIM COMMENT

The weight of evidence considered in the previous sections underlines the importance of right hemisphere structures in processing all kinds of spatial information. However, we also saw that once we moved away from purely perceptual types of task it became possible to solve or complete tasks using various strategies—essentially spatial, verbal, or perhaps a combination of both. Studies such as that reported by Clarke et al. remind us that both hemispheres can participate in spatial processing. Spatial skills are not the exclusive preserve of the right hemisphere. We might describe the processing responsibilities of the left and right hemispheres as verbal and spatial respectively, but this confuses the issue in view of the fact that we have been talking about how each hemisphere contributes to dealing with spatial tasks. We might, alternatively, invoke the idea of processing styles (see Chapter 3), by comparing the holistic approach of the right hemisphere with the analytical style of the left. Once again, this does not entirely work because some of the spatial skills that are affected by right hemisphere damage (such as spatial location) make no particular demands on holistic skills. Kosslyn (1987) has suggested a cerebral division of labour such that the right hemisphere is specialised for dealing with "coordinate" spatial relations whereas the left is specialised for "categorical" spatial relations. fMRI has provided some support for this view.

CHAPTER SUMMARY

Visual perception of objects depends on activity in two parallel but separate processing streams. The "what" stream deals with object recognition and links with stored memories of related objects. The "where" stream deals with various aspects of spatial processing, both of perceived objects and of the individual in space. This distinction is apparent if you consider the situation of reaching to select a particular object from a group of items: the "where" stream guides your hand to the object, and the "what" stream allows you to select the correct object. The visual agnosias appear to result from disturbances to different stages of processing in the "what" stream. Lissauer's original distinction between apperceptive and associative agnosia is now considered an oversimplification of the true diversity of (object) agnosic conditions. Riddoch and Humphreys' model of object recognition is better able to explain many of these subtly distinct conditions.

Prosopagnosia often co-occurs with object agnosia, but the weight of available evidence suggests that it is a distinct condition that is linked anatomically to ventral regions in the right hemisphere. In fact, many neuropsychologists think that it actually comprises at least two disorders: one related to a failure to construct the facial image from its component parts, and a second concerned with an inability to

relate facial images with semantic information about the person in question. fMRI studies of category specificity have identified distinct regions for the recognition of many different classes of objects. However, a coherent theoretical framework for understanding *why* these specialisations occur has yet to emerge.

Spatial processing is subserved by a dorsal stream that terminates in the parietal lobes. Damage to this stream affects the perception of objects in space, detection of motion, and mental rotation. This stream interacts with other cortical regions to mediate spatial constructional skills, route finding, and spatial memory. The hippocampus is also a crucial structure in route finding. Although available evidence tends to emphasise the importance of the right hemisphere for spatial processing, the left hemisphere can make important contributions to the overall processing effort through the employment of complementary processing styles.

CHAPTER 9

CONTENTS

9

Attention and consciousness

INTRODUCTION

We intuitively know what it means to "attend" to a particular event, process, or stimulus sequence. We cannot pay attention to every item of input so we have to be choosy. In this sense, attention refers to selecting, focusing, and homing in on certain things, and ignoring, filtering out, or inhibiting others.

The concept of an "attentional spotlight" has often been mooted as a metaphor for this process (in the visual modality at least) but, as we shall see, it is only approximate. For example, although we usually look directly at whatever we are trying to attend to, it is possible to attend to an area of space that we are not directly gazing at (essentially looking out of the corner of one's eye; a phenomenon demonstrated by von Helmholtz over 100 years ago). A second problem is that it has now been demonstrated quite convincingly that, under certain circumstances, we can actually track several moving targets (up to four) at the same time (Cavanagh & Alvarez, 2005), raising the possibility of multiple spotlights, albeit ranging over a limited angle of visual field (i.e., close to one another). A third problem illustrated by LaBerge (1983) is that the attentional spotlight can be shown to have a narrower or wider "beam" depending on task requirements (respondents could be "pre-cued" to focus on a five-letter word or on the central letter of the same word)—an observation that led him to suggest as an alternative metaphor the "attentional zoom-lens".

LaBerge's work illustrates a further complication that must be taken into consideration in our efforts to understand the parameters of attention—that it can clearly be guided/directed by both task requirements and the goal(s) of the perceiver. A real-world example of this can be seen in the card game of "snap", in which the players attend to each card as it is dealt to see if it matches one of theirs, or the top card in the "pool". Some neuropsychologists have called this "endogenous" attention because "the spotlight" is being driven internally. Yet, conversely, our own experience tells us that no matter how hard we may try to focus our attention on one thing, we can easily be distracted by an unexpected but salient event or stimulus occurring elsewhere. When attention is disrupted or even re-directed by external influences, a sudden loud noise for example, neuropsychologists refer to this as exogenous attention (or orienting; see below). In

other words, attention can be directed by both deliberate and accidental processes. Finally, under certain circumstances, attention can be directed to internally generated ideas, thoughts, or plans. This may involve nothing more sinister than day-dreaming, but it can quite easily merge into more pathological processes if it involves rumination or obsessive/recurrent thoughts. Conditions such as post-traumatic stress disorder, morbid jealously, and even depression have been linked to dysfunctional processing of this sort.

In the first edition of this book we bemoaned the absence of a unified theory of attention. In the intervening 5 years, psychologists have continued to work on the development of models to explain how different aspects of attention may work in "intact" individuals (e.g., Duncan, 2006). And neuropsychologists have focused on trying to unravel the brain regions that may be involved in attention, often through detailed investigations of individuals with neurological disorders in which attentional mechanisms seem to be damaged or impaired. Both these lines of inquiry are reviewed here. Functional imaging and ERP studies have also been informative, and these too are reviewed. Yet despite this valuable and often intriguing work, a unified theory arguably remains elusive. Nevertheless, Corbetta and Shulman's (2002) neuropsychological model (essentially, a development and elaboration of an earlier proposal from Posner, 1980) has attracted considerable attention (see also Corbetta et al., 2005) and we review it later in the chapter.

Then we briefly consider the vexed question of consciousness—an area of investigation "off-limits" for most psychologists and neuropsychologists for the last 100 years or so, yet in truth a nettle that just had to be grasped sooner or later. We consider some recent research and thinking about consciousness, and how it relates to attention, and even working memory. However, it is important to stress that in so doing, we are interpreting consciousness in a narrow sense, relating to conscious awareness, rather than in the broader sense which encompasses awareness of subjective experience and self-awareness.

TYPES OF ATTENTION

We start on a point of consensus: there seems to be broad agreement that the general domain of attention needs to be subdivided into at least four more specific areas—vigilance, arousal, divided attention, and selective attention (LaBerge, 1990).

Vigilance is about sustaining attention over time. Whenever you go to a lecture your vigilance is put to the test as you try to stay "on track" with the lecturer right to the end of the class. Exceptional vigilance skills are regarded as a prerequisite for air-traffic controllers, whose job involves the monitoring of plane movements depicted on a computer screen (Molloy & Parasuraman, 1996). Impairments in vigilance skill have been linked to neurological disease and possibly psychiatric disorder too. Vigilance involves selection, but the emphasis is on maintaining this focus for minutes or even hours, something that may require prolonged conscious effort. Neuropsychologists have referred to this as a "top-down" influence (endogenous, if you like) to distinguish it from the attention-grabbing effect of an unexpected loud noise which, in this taxonomy, would be a "bottom-up" (or exogenous) influence.

Arousal and *alertness* are terms that have usually been linked to physiological states that may vary in relation to attention. Consider your own circadian pattern

of alertness for example. Every 24 hours you experience 6–8 hours of sleep during which time you are relatively unresponsive to external stimuli, although a clap of thunder or a loud firework may nevertheless disturb you. During your waking hours, you are more alert at some times than others. Research has shown that alertness generally improves through the day, reaching a peak in early evening, and then diminishing towards bedtime. Sudden unexpected events can interfere with your level of alertness when you are awake, just as they can when you are asleep. Researchers refer to the response that ensues as "orienting", and as we shall see, the evoking of an **orienting response** has been used as a research paradigm by psychologists trying to understand this aspect of attention

Divided attention would be addressed in tasks where there are at least two channels of input and the respondent has to try to "attend" to each one. Studies of divided attention have been useful in establishing an individual's processing capacity and limitations. That is to say, to what extent can an individual do two things at once? Practice and automaticity, task similarity and difficulty not surprisingly all affect dual-task performance.

Selective (*focused*) *attention* refers to the phenomenon alluded to at the start of the introduction. Our sensory apparatus is constantly bombarded with input, yet we more or less automatically seem able to invoke a process (the attentional spotlight?) that allows us to focus on one channel at the expense of others. As you read this page, we hope you are attending sufficiently carefully not to be distracted by the noises coming from outside, the smells wafting up from the kitchen, or the dull pain from that tooth that needs filling—not, at least, until we point them out to you. As we will see, understanding the mechanisms of selective attention has been a major goal of neuropsychologists, and we will inevitably focus on this work in the present chapter. Researchers have made extensive use of experiments in auditory selective attention and the related field of visual search to learn more about the way these attentional processes operate.

ISSUES IN PSYCHOLOGICAL INVESTIGATIONS OF ATTENTION

EARLY OR LATE SELECTIVE ATTENTION?

Most people will be aware of the effort required to converse with someone in a noisy and crowded room, and of suddenly becoming aware of a salient word or term used by another speaker on the far side of a room (Cherry, 1953; Moray, 1959). This apparently innocent experience (sometimes referred to as "the cocktail party phenomenon") shows that "unattended" material can, under certain circumstances, attract our attention. In the 1950s the pre-eminent model of attention held that "attended" material is selected at a very early stage of information processing (Broadbent, 1958), but the cocktail party phenomenon confounds this "early selection" model because the so-called unattended input must have undergone a certain amount of processing (up to semantic analysis) in order to cause a shift of our attention. If it had been subject to early selection, we might simply not have "heard" it.

An effective way of investigating selective attention experimentally is to use the dichotic listening paradigm. In a typical variant of this procedure a participant may be presented with two simultaneous streams of auditory (often verbal) input

Key Term
Orienting response: A spontaneous reaction to a stimulus in which the head and/or body are moved so that the source of the stimulus may be examined.

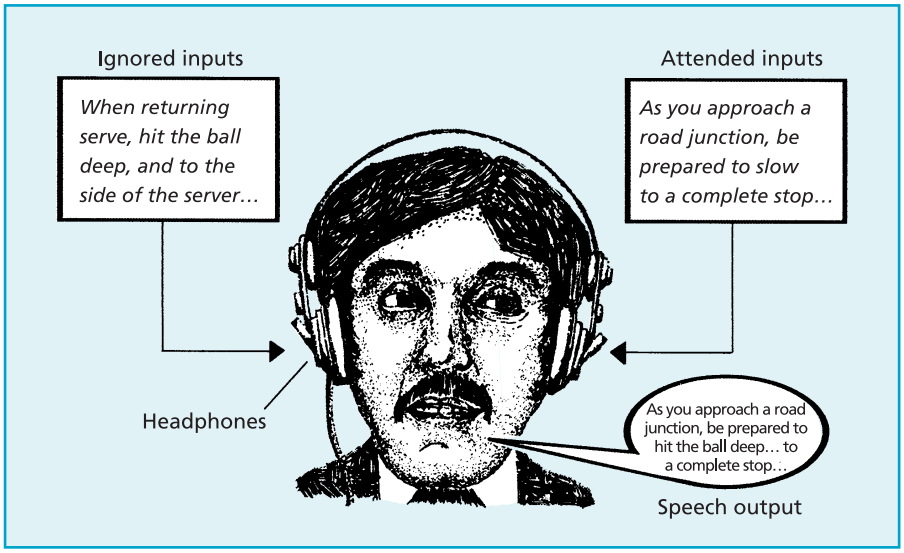


FIG. 9.1 A typical dichotic listening experiment. The respondent hears two verbal messages simultaneously but must repeat aloud only one of the "channels". Respondents usually notice little or nothing about the unattended input, but occasionally salient or personally significant material is recognised and sometimes even intrudes into the speech output. (Adapted from Gazzaniga et al., 2002.)

(one to each ear). By requiring the listener to "shadow" one channel (i.e., repeat aloud the stream of words in the "attended" channel, and thus have to attend to it) the experimenter can assess the extent to which information in the unattended channel "gets through", by later asking whether anything could be recalled from it. Not surprisingly, there is nearly always much better recall from the attended than the unattended channel, but in situations where the unattended channel material is "salient" or semantically related to the material in the attended channel, it is often recalled, and sometimes described (erroneously) as having been presented in the attended channel (Gray & Wedderburn, 1960). Like the cocktail party phenomenon, this suggests that material in the unattended channel may actually undergo quite extensive processing. Note that material would be presented too quickly for the result to be explained simply on the basis of rapid switching of attention (see Figure 9.1).

Although the evidence from dichotic listening experiments clearly supports some sort of selecting of attended over unattended material (because relatively little of the unattended message is recalled) it does not fit well with a strict "early selection" model of attention like Broadbent's, because some processing of the unattended material *does* take place. An alternative model was proposed by Treisman (1964) who argued that although a particular channel might be selected early on in the processing stream, the unattended channel, rather than being shut down, was "attenuated", meaning it received less attentional effort than the attended channel. Thus, salient or personally relevant material in this channel would not necessarily be lost and may undergo semantic processing, at which point a shift in attention to the unattended channel may occur. Treisman's model has received widespread support, even from Broadbent (1970), and is the dominant theory for selective attention in the auditory modality. Figure 9.2 illustrates the differences between the models of selective attention.

In studies of visual attention, the evidence also suggests that selection may occur relatively early in the processing stream, especially when attention is directed towards stimulus location. The logic of visual search studies is that the more "distractor" items present in a visual field, the longer it should take to identify the particular target. Consider, for example, a study by Treisman and Gelade (1980). Participants viewed a series of visual arrays comprising red Os and green Xs, and they had to identify the presence (or absence) of a red X. For such "conjunctive targets" (targets combining stimulus attributes shared by non-targets), the time taken to identify presence/absence is proportionate to the number of non-targets shown, because attention must be directed around the array item-by-item until the target is found. This shows that attention to a spatial location precedes identification, supporting the idea of early selection of location. A conjunctive search array similar to Triesman and Gelade's is shown in Figure 9.3a. This finding should be contrasted with the situation when the target is distinguishable on the basis of one solitary attribute: "*Find the Y among an array of Ks*". Now, the number of distractors is largely irrelevant, and participants describe the target as "popping-out" from the array (see Figure 9.3b). This process has been called "pre-attentive", which is taken to mean that attention is not needed to find the target (although it is obviously invoked once the target has been found).

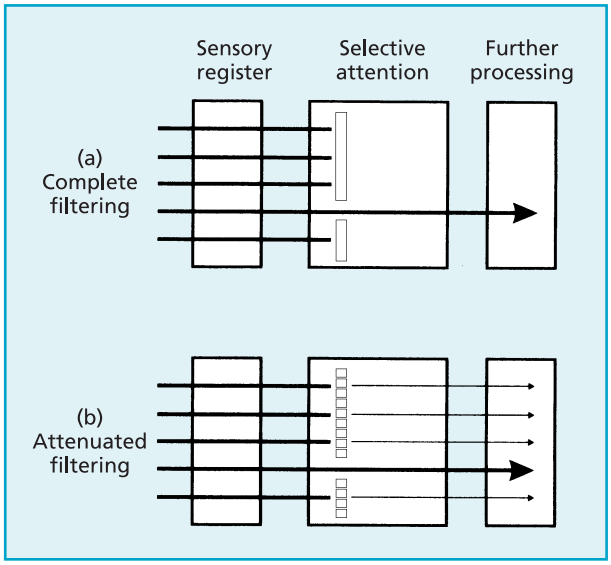


FIG. 9.2 Two filtering models of attention. (a) Following sensory registration, only one channel of input is selected for further processing. This is akin to Broadbent's model of early selective attention. (b) One channel is selected for "priority" processing. However, the other channels of input are not filtered out; rather they are attenuated. This is similar to Treisman's attenuation model of selective attention.

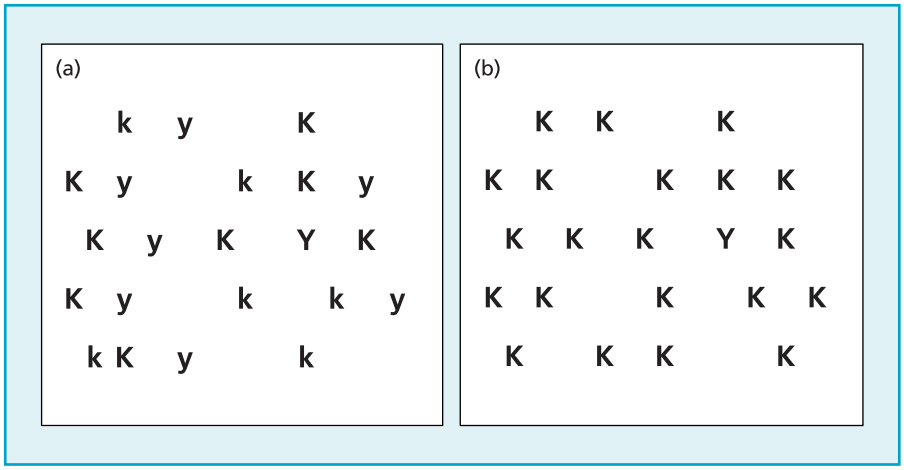


FIG. 9.3 The type of array used in visual search studies. (a) The "odd one out" target is a conjunctive one combining attributes of other targets. Visual search proceeds in a place-by-place manner until the target (upper case Y) is found. (b) The target (upper case Y) almost jumps out of this array. Little conscious effort is required to locate it, giving rise to the expression "pre-attentive" to characterise the processing requirements of the task.

Data from studies comparing these two experimental paradigms (with different numbers of distractor items, and more or fewer shared features between target and distractors) prompted Treisman and Gelade to propose that the "pop-out" phenomenon depended on parallel search, whereas conjunctive arrays relied on a serial search. Essentially, the argument went that the former task, being pre-attentive, is effortless and automatic, whereas the requirement to combine features (colour, shape, orientation, etc.), sometimes called feature binding, requires attentional effort, and probably early selection. Treisman developed her "feature integration theory" (FIT) to account for these findings. This theory has undergone various reformulations (Treisman, 1992, 1993, 1999) none of which entirely satisfies all critics (such as Duncan & Humphreys, 1992, and Wolfe, 1998). Among other concerns, researchers have questioned the assumption that pre-attentive stimulus coding (in the pop-out condition) can actually occur without any attentional effort. And they have pointed out that the degree of similarity among distractor items does, in fact, affect visual search times, contrary to FIT.

Arguably, a similar attentional process to that seen in "pop-out" can also be observed in studies of involuntary visual orienting (Posner & Cohen, 1984). In a typical experiment "irrelevant" visual stimuli (such as brief light flashes) would be presented to different locations in the visual field, interspersed with target stimuli to which the participant should respond. When a target stimulus falls in a similar location to a previous irrelevant light flash, reaction time to it is faster, indicating that the irrelevant stimulus somehow directed (researchers say "primed") attentional mechanisms to that particular spatial location, albeit involuntarily. However, this effect is only observed if the interval between irrelevant and target stimuli is brief (less than 300 ms). With longer intervals the effect is reversed leading to slower reaction times. This paradoxical effect is known as **inhibition of return** and serves a vital role in automatic visual orienting. If such a mechanism did not exist, we would probably find it difficult to attend voluntarily to anything for any period of time, being constantly distracted by new but irrelevant stimuli. The distinction between deliberate and incidental attentional processes appears critical, and we return to consider it later in this chapter.

A final twist in the "early versus late selection" debate comes from studies of "negative priming" (Tipper, 1985; Tipper, Weaver, & Houghton, 1994). In this paradigm, respondents view compound images (say, a red line drawing of a hammer on top of a second blue drawing of a cat) and have to name the blue object (and ignore the red one). If the ignored object then becomes the attended object on the next trial (i.e., a blue hammer appears superimposed with some other red object), participants are slower in naming it (the negative priming effect). This strongly suggests that the non-attended item was in fact meaningfully processed, not ignored as the FIT would predict. This, of course, implies that late selection is operating.

KEY TERM
Inhibition of return: When attention is directed to a location, there is a brief period when processing at that location is facilitated. Following facilitation, there is a period during which attention is inhibited from returning to that location. This is inhibition of return (IOR).

We revisit the question of early versus late selection when we review the concept of attention as a resource, and the question of "perceptual load" below. First, however, we consider whether attention is space- or object-based.

SPACE- OR OBJECT-BASED SELECTION?

Visual search studies such as Treisman and Gelade's show that voluntary attention can operate effectively when it is directed to particular points in space. Posner (1980) reported a classic study illustrating the advantage of space-based attention.

In this experiment, participants fixated on a central point on a computer screen with an empty box to the left and right of the fixation point. After a short delay, one of the two boxes briefly became illuminated. Then, after a further variable delay, a stimulus was presented either in the box that had been illuminated or in the other box. Reaction times to the stimulus were consistently faster when it appeared in the "cued" box than the "non-cued" one, a finding interpreted as showing how shifting attention (from the expected cued box to the non-expected uncued one) takes time. It is important to note that in this paradigm, participants fixated gaze on the central point at all times, so covert mechanisms rather than overt eye movements were responsible for this voluntary orienting effect (see Figure 9.4).

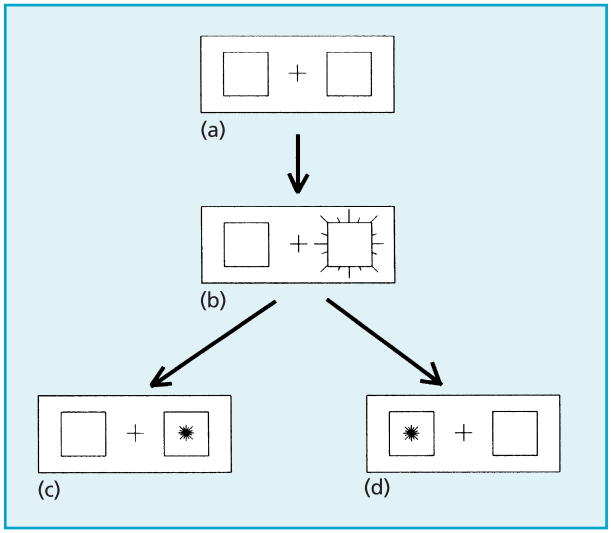


FIG. 9.4 An illustration of Posner's (1980) study. A participant fixates his or her gaze on the cross in between the two squares. One of the boxes is then "cued" (more brightly illuminated) for a brief period. The respondent knows that the cue usually correctly predicts the subsequent presentation of a target stimulus (an asterisk). Response speeds (reaction times) are significantly faster when the cue correctly predicts the location of the stimulus (c) than when it predicts the incorrect location (d).

On the other hand, as we saw above, object-based attention is apparent in studies of negative priming (Tipper, 1985; Tipper et al., 1994). A further illustration of object-based attention comes from a study by O'Craven, Downing, and Kanwisher (1999). Their participants viewed compound images of overlaid drawings similar to those in Tipper's study, except that one of the images was stationary and the other was moving slightly. They were told to attend either to the direction of the motion of the moving image, or to the stationary one. If attention is location based, participants would have to attend to both images because they are in the same location. If object-based attention operates, the attended item would receive more processing than the unattended one. Functional MRI of brain regions that became more active during this task supported the latter account: there was more activity in the fusiform face area (referred to in Chapter 8 as part of the temporal lobe associated with processing faces) when a face stimulus was attended to than ignored, and more activity in the para-hippocampal "place" area when a picture of a house had to be attended to than when it was ignored.

We might add that several observations from individuals with the neurological disorder "unilateral neglect", which we consider later in this chapter, support the ideas of both spatial- and object-based attention. Thus, overall, it seems that humans may deploy either attentional strategy in the visual modality, depending on the task requirements, including how easy or difficult it is. Indeed, looking beyond visual attention again, there appear to be several ways of directing (biasing) attention in the face of competing targets (location, feature, category, set, etc.) (Duncan, 2006). However, attention takes up "effort", which is not unlimited. We now consider the idea of attention as a resource.

ATTENTION AS A RESOURCE

Resource theory approaches to attention (Kahneman, 1973; Wickens, 1980) sidestep many of the arguments introduced thus far by proposing that there is a finite central pool of information-processing capacity available to the individual, which

is allocated according to demand. At one extreme, stimuli may be so simple or infrequent that only a fraction of the resource is "used", and attention (as we have conceptualised it) is not really an issue, though vigilance may be. At the other extreme, tasks may be so complex or demanding that the entire resource is "used up" by just part of the input invoking attention to this material at the expense of the remainder. Thus, the greater the effort needed to attend to target material, the less likely non-target material is to be processed. It follows that the greater the similarity between competing tasks (as in the dichotic listening studies) the greater the likelihood that such inputs will, by competing for the same resource, induce interference and errors.

A key question in this approach is whether the resource base is a single reservoir available to the individual irrespective of stimulus characteristics on a "first-come, first-served" basis, or whether there are separate reservoirs set aside for different types of input. Wickens' model envisages several separate resource domains with distinct pools: early versus late processing, verbal versus spatial processing, auditory versus visual processing, and even in terms of the nature of the required response (for example, manual versus vocal). It would be true to say that while the question of a single or multiple resource pool(s) has yet to be resolved, the experimental evidence tends to support separate pools. For example, in dual-task studies (see our earlier reference to divided attention) in which respondents try to complete two tasks simultaneously, there is less interference and hence fewer errors when the tasks or responses involve different stimulus modalities. McLeod (1977) required participants to engage in a tracking task (performed manually) and simultaneously to undertake a tone identification task that, in one condition, required a vocal response and, in another, a manual one with their other hand. Performance on the tracking task was worse in the latter condition. Moreover, the ERP research (which we review below) shows that different brain regions seem to be involved in early and later stimulus processing.

Yet it is also true that there is nearly always *some* interference effect in dual-task studies, prompting Baddeley (1986) to suggest that there may be separate resource pools at subordinate processing levels, but at the highest processing level "the central executive" represents a non-specific attentional resource. Indeed, proponents of resource-based theories of attention have argued that information-processing capacity limitations (in attention) *are determined* by working memory capacity limits. The overlap between attentional and working memory systems is the subject of ongoing investigations (Kastner & Ungerleider, 2000), and we briefly revisit this issue later in this chapter (in the section *Attention and the brain)*. For the time being we might simply note that overlapping cortical regions are active in both processes.

A slightly different take on this issue is represented in the work of Lavie and colleagues (Lavie, 1995, 2005; Lavie & Fox, 2000). She has argued that the critical consideration in allocating what is a finite attention resource is related to the perceptual "difficulty" or "complexity" of the task in hand—or the amount of perceptual "*load*", to use her term. In other words, with a very simple task plenty of attentional resource will be left over, permitting processing of other irrelevant or peripheral stimuli (in fact, this re-allocation happens automatically in her scheme). However, with more demanding tasks (big arrays, crowded images, and so on; an intrinsically heavy perceptual load, etc.) allocation of resource will dictate focused attention, early selection, and little or no processing of non-attended channels.

The effects of "perceptual load" intrinsic to a core task on distractor processing were illustrated in a functional imaging study by Rees, Frith, and Lavie (1997). Respondents had to monitor a string of words and decide either whether they were presented in upper or lower case (lower load), or how many syllables they contained (higher load). Irrelevant background motion evoked activity in motion-sensitive brain regions (area MT in particular) in lower- but not higher-load conditions. In other words, increasing the load of the core task led to less processing of the distractor stimuli. This effect has subsequently been found to hold in cross-modal situations where the load task is auditory but the irrelevant task is in the visual modality. However, and consistent with Baddeley's ideas outlined above, if *executive* control functions such as working memory are "loaded" by requiring the respondent to memorise six digits immediately before the target-detection task (as opposed to "loading" the core task itself), irrelevant low-priority distractors increase the interference with the target-detection task, leading to a consequent drop in performance (Lavie, 2005). So, it would appear that cognitive control is needed to maintain the distinction between targets and distractors, and if this is otherwise "engaged", performance on the core task will be adversely affected.

The "perceptual load approach" to understanding the allocation of attentional resources circumvents many of the earlier concerns about early/late filtering of unattended material or the operation of visual search strategies. However, the concept itself remains somewhat vague, and its relation to "the slave" and "central executive" components of working memory needs to be clarified.

INTERIM COMMENT

We know what we mean when we talk about attention, and there seem to be several ways of measuring it or invoking it. The process itself involves a biasing in favour of some particular aspect or feature of a stimulus at the expense of others: "biased competition" in Duncan's words. What we feel less sure about are its parameters—the extent to which it overlaps with alertness or working memory for instance. The material introduced in the previous section amply illustrates *the continued absence* of a cohesive framework on which to build psychological models of attention. Studies of selective attention lead to the conclusion that unattended material is not so much "filtered out" as "attenuated". In studies of visual search, attention may be "location" or "object" based, and we must also distinguish between voluntary and involuntary attentional mechanisms. Resource-based models raise the possibility that attentional mechanisms overlap closely with working memory systems, or at least that full effective deployment of an attentional resource depends on an unencumbered working memory system.

ATTENTION AND THE BRAIN

The psychological approach has provided a lot of data, but no truly unifying ideas about attention. In fact, it seems to have raised as many questions as it answers. In this section we consider contributions to our thinking about attention gleaned from more neurobiological approaches. Can an examination of brain structure and functioning inform our understanding of how attention operates?

BRAIN ACTIVATION AND ATTENTION

We can examine attentional processing in the nervous system by recording ERPs to attended and non-attended material. In a typical ERP study, the respondent may be instructed to attend to inputs to one ear and ignore those to the other. (At a later stage, the instructions can be reversed to avoid the possibility of differential ear sensitivity affecting results.) Typical findings from this type of study are illustrated in Figure 9.5. They suggest that the ERP to the attended channel begins to differentiate itself from the ERP to the unattended channel about 80 ms after stimulus onset (Andreassi, 1989), as indicated by a markedly enhanced N_1 wave. More recently, Woldorff and Hillyard (1991; Woldorff et al., 1993) found evidence of earlier cortical waveform changes in the 20 to 50 ms latency range. This means that attended material is being "treated" differently by regions of sensory cortex very soon after stimulus presentation.

With ERP studies in the visual modality it becomes possible to investigate "spatial" attention. In order to do this, researchers have adapted the paradigm developed by Posner, Snyder, and Davidson (1980) in which participants fixate on a central point but are cued to expect stimuli to the left or right of that point (see Figure 9.4). The ERP wave shows characteristic changes in amplitude which start about 70–90 ms after stimulus presentation (known as the P100 wave) when the stimulus appears in the "cued" location. The response is greater than when the same stimulus is presented but attention is focused elsewhere, suggesting an attentional amplification for the attended stimulus.

By combining ERP and ERF (event-related field) procedures (see Chapter 2), Mangun, Hillyard, and Luck (1993) have confirmed that the enhanced ERP is *cortical* in origin. In other words, by voluntarily directing attention towards particular stimuli, changes in ERP waveform (reflecting enhanced cortical activity)

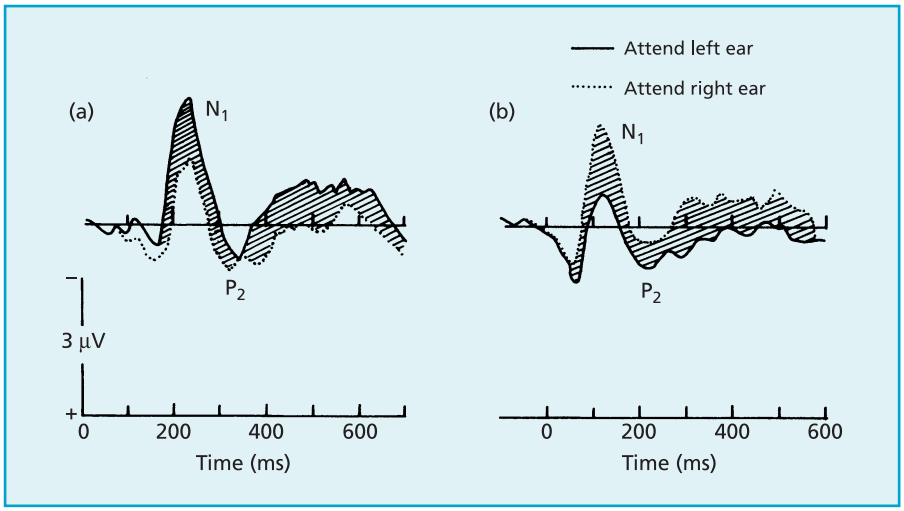


FIG. 9.5 Auditory ERPs to attended and non-attended stimuli. (a) The amplitude of the N_1 peak of the ERP is greater to a tone presented to the left ear when the respondent is attending to inputs to the left ear, than when the same tone is presented but the respondent is attending to inputs to the right ear. (b) This is not related to auditory acuity because the reverse effect can be observed if tones are now presented to the right ear. Adapted from Andreassi, J. L. (1989). *Psychophysiology: Human behaviour and physiological response* (2nd edn.). Hillsdale, NJ: Lawrence Erlbaum Associates Inc. Reproduced with permission.

can be seen well within one-tenth of a second. Interestingly, this technique can also be used to see if "involuntary" shifts in attention activate the same mechanisms. Hopfinger and Mangun (1998) have shown that when an unexpected and irrelevant sensory cue (which draws attention to part of the visual field) precedes the target stimulus by up to 300 ms, the ERP to the target stimulus is enhanced, but with longer intervals between the cue and target the effect is reversed (see our earlier reference to "inhibition of return"). This study strongly suggests that certain attentional processes evoked by voluntary cues are also evoked by involuntary ones. It is also a reminder that any effective model of attention must accommodate both deliberate and incidental influences on the direction of attention. We return to this matter later.

Several additional components of the ERP waveform, related to quite specific higher-level attentional processing, have also interested researchers. In chronological order, the N170 (a negative peak with a latency of between 170 and 200 ms) is strongest over right posterior temporal sites (Bentin et al., 1996) to facial images in general (including animal and cartoon faces). This is quickly superseded by a slightly later negative peak, the N250 (with a latency of about 250 ms), if the face is "meaningful", famous, or familiar (Herzmann et al., 2004). However, the most extensively researched such peak is the P300, a positive wave occurring roughly one-third of a second or later after stimulus presentation. This "late" wave seems to be related to the contextual meaning of the stimulus, and shows that attention can modify the brain's response for some time after a stimulus has been presented. A typical P300 study might require a respondent to listen out for infrequent high tones (so-called "odd-balls") presented in a series with more frequent low tones. The ERP to the "odd-ball" tones will show the typical positive shift (about one-third of a second after the stimulus is presented), while the non-salient low tones will not evoke this response. One crude way of distinguishing between ERP components is to envisage the early changes in terms of physical relevance, and the later ones as linked to semantic relevance (see Figure 9.6).

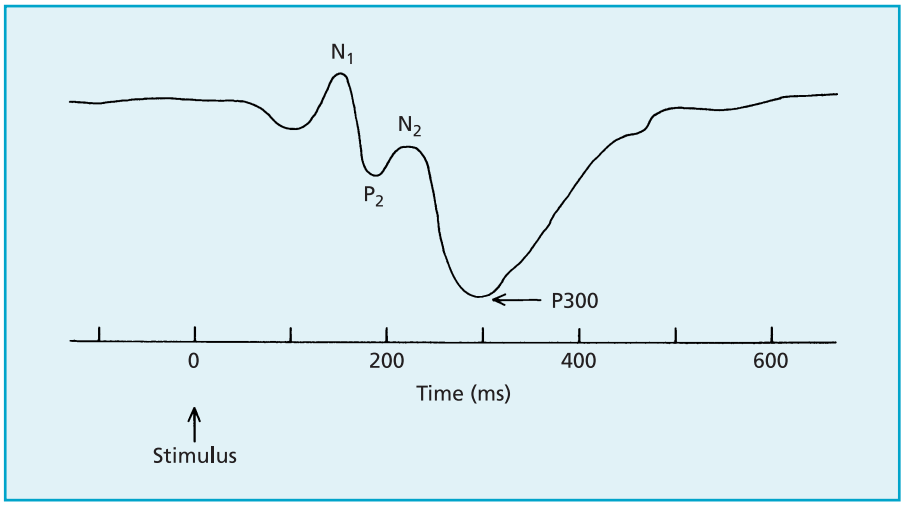


FIG. 9.6 Early and late components of an auditory ERP. The early components (up to about 200 ms) are thought to reflect cortical processing of relatively simple stimulus attributes such as intensity or pitch. Later components such as the P300 wave vary in relation to "significance" of stimuli and are thus thought to reflect higher-level (semantic) processing of stimuli.

Functional imaging has been less extensively used than ERPs to map brain attentional processes, mainly because of its comparatively poorer temporal resolution (see Chapter 2). Progress has nevertheless been made, and an fMRI study of object-based attention by O'Craven et al. (1999) was described earlier. You may recall that participants in this study viewed compound images of overlaid photographs in which one was stationary and the other was moving slightly, and they were told to attend either to the direction of the motion of the moving image, or only to the stationary one. Functional MRI of brain regions that became more active during this task indicated increased activity in the fusiform face area (referred to in Chapter 8 as part of the temporal lobe associated with processing faces) when a face stimulus was attended to than ignored, and more activity in the para-hippocampal "place" area when a picture of a house had to be attended to than when it was ignored. This study suggests that attention operates by facilitating the processing of the attended image rather than by inhibiting the unattended one.

An ingenious study by Egner and Hirsch (2005) has confirmed this facilitatory effect. The researchers used a version of the Stroop test in which images of famous actors or politicians were superimposed with the name of another either well-known actor or politician. In some trials the image and name were congruent (for example, both actors); on other trials they were incongruent (an image of an actor plus the name of a politician). Egner and Hirsch focused on trials that immediately followed an incongruent trial, when top-down attentional influences would be most pronounced. They recorded activity in the prefrontal cortex and fusiform face area on these trials, both when the face was the target (attended) stimulus, and when it was the distractor. Results indicated that fusiform activity was significantly enhanced on these attentionally "loaded" trials if participants were attending to faces, though not if the target was the name. Fusiform activation was clearly correlated with activation in the prefrontal cortex, suggesting that the former structure was receiving top-down control from the latter. (See also Nieuwehhuis & Yeung, 2005.)

Although, for reasons already explained, fMRI does not readily lend itself to the exploration and measurement of rapid brain activations associated with attentional processes, it has contributed, along with other methods described in Chapter 2, to the identification of key elements in an attentional circuit in the brain, which we now consider.

BRAIN STRUCTURES AND ATTENTION

There is no single attention "centre" in the brain. Instead, several regions are thought to form a distributed neural network that is collectively responsible for the attributes of attention considered so far. The network comprises brainstem, midbrain, and forebrain structures, and impaired attention may result from damage to any of these. However, as with most neural networks, it is also possible to predict the particular attentional dysfunction most directly linked to each component part of the system.

The ascending reticular activating system (ARAS)

This is a brainstem structure (actually a diffuse network itself) comprising neurons whose axons ascend through the midbrain to influence forebrain

structures including the cortex. The system was once thought to be unitary, but is now known to involve several distinct neurotransmitter systems (groups of neurons that release different chemical messengers to influence other neurons). It includes a cholinergic (acetylcholine-releasing) pathway, a noradrenergic (noradrenaline-releasing) pathway, a dopaminergic (dopamine-releasing) pathway, and a serotonergic (serotonin-releasing) pathway. The axons of most of these neurons divide many times en route to the cortex, and the upshot of this cortical innervation is that a relatively small number of brainstem and midbrain neurons can affect the excitability of virtually every cortical neuron. Not surprisingly, this system has long been implicated in arousal and the sleep–wake cycle. Damage to the ARAS will profoundly disrupt circadian rhythms and can result in coma, or chronic vegetative state. Stimulation of the ARAS will, conversely, quickly wake a sleeping animal. Moreover, drugs such as amphetamine, which are known to be CNS stimulants, are thought to have particular influences on the neurons in the ARAS and the pathway from it to the cortex. These findings suggest at least two roles for the ARAS in the control of attention. Tonic (background) influences will affect vigilance performance, while phasic (brief) changes will be important in orienting.

The superior colliculi

These are two modest bumps on the dorsal side of the brainstem in the midbrain region. They appear to play a key role in controlling a particular but vital type of eye movement in which objects initially in the peripheral field of vision "capture" attention. Their role in visual attention is thus self-evident. The eye movements controlled by the superior colliculi are called express saccades—the eyes jump from their old focus of attention to a new one in one jerk rather than a smooth arc. Damage to these structures interferes with express saccades but not other slower eye movements. In **supranuclear palsy**, a neurodegenerative disorder that affects several subcortical regions including the superior colliculi, patients are unable to direct their gaze in the normal way, not looking at someone who is speaking, or turning to greet an approaching friend. This deficit has been referred to as a loss of "visual grasp", and a similar temporary effect can be induced by local administration of drugs that block the action of neurotransmitters in the superior colliculi (Desimone et al., 1990). Incidentally, the inferior colliculi (two additional bumps just beneath the superior colliculi) are thought to play a similar role in orienting the individual towards "salient" auditory stimuli.

The pulvinar region of the thalamus

This appears to play a vital role in filtering material to be attended to from the vast amounts of sensory input that the brain actually receives. The thalamus as a whole acts as a relay station for almost all sensory inputs en route to the cortex, and is therefore ideally situated to serve as a filter. This idea was supported in a study by LaBerge and Buchsbaum (1990). In one condition, participants had to attend to the presence/absence of a single letter. In a second condition, participants had to "look out" for the same letter embedded among other letters. The second task required more "attention" than the first because there was now a requirement to filter or sift through the array to find the target letter. Sure enough, the second condition brought about greater PET activation of the pulvinar than the first, even

Key Term
Supranuclear palsy: One of the so-called subcortical dementias in which there is progressive tissue loss in the basal ganglia and midbrain structures such as the superior and inferior colliculi.

when stimulus complexity was accounted for. The application of drugs that interfere with pulvinar functioning also disrupts shifts of attention (Petersen, Robinson, & Morris, 1985). Moreover, people with damage to this thalamic region are likely to have attentional difficulties involving the ability to filter stimuli, attending to one input and ignoring others, and in the ability to "latch on" to new stimuli. The pulvinar receives an important input from the superior colliculi, and it is thought that the ability of incidental but salient visual stimuli to adjust the attentional spotlight alluded to earlier depends critically on this axis.

The cingulate gyrus

The cingulate gyrus (or just cingulate) is another cortical "node" in the brain's attentional network. It appears to be involved in several separate attentional processes: For instance, the cingulate as a whole provides an interface in which sensory inputs are linked to "emotional tone" (was the movement in the periphery of your visual field a tree bending in the wind or a mugger?). Additionally, the anterior regions of this structure are critically involved in response selection (ignore the wind-blown tree, but run away from the mugger!). The anterior cingulate (AC) becomes active in circumstances in which appropriate "correct" responses have to be selected in a deliberate (even effortful) manner. PET studies of participants undertaking the Stroop test reinforce this role for the AC. In one variant of this test, respondents are presented with a list of words spelling different colours. Some of the words are printed in the same colour that they spell, but others are printed in a different colour. On some trials participants have to name the word irrespective of the colour it is printed in, and on other trials they must name the ink colour irrespective of the word. The AC is much more active during colour naming than word naming (Pardo et al., 1990) because the former leads to a greater "interference" effect. This is caused by the tendency to read the word even though this is not required (referred to as a pre-potent response).

Hopfinger, Buonocore, and Mangun (2000) undertook an fMRI study of covert attention, employing a variant of Posner's classic paradigm (see Figure 9.4 above). They were able to look separately at "cue" (a directional arrow) and "target" processing effects (does a chequerboard display have grey/white squares?) because of an 8-second time-lag between cue and target. Cue presentation activated medial and dorsolateral frontal regions, inferior parietal and superior temporal regions, and the posterior cingulate gyrus (all bilaterally). Target processing, as expected, activated various sensory and motor regions, the ventrolateral frontal cortex and, critically, the anterior cingulate (see Figure 9.7). This study shows that the posterior and anterior cingulate can be dissociated into preparatory and response selection components respectively.

The parietal lobes

These are specialised for processing spatial relations and their role in attention is inferred from two independent research findings. First, parietal damage (on either side but especially the right) is associated with hemineglect, an attentional disorder in which half of the visual field is, effectively, ignored. (See later in this chapter.) Second, the P300 wave that we mentioned earlier is most marked in parietal regions. There is still debate about what exactly the P300 signifies, but one idea is that it reflects "attentional resource" allocated to a particular task. In other words,

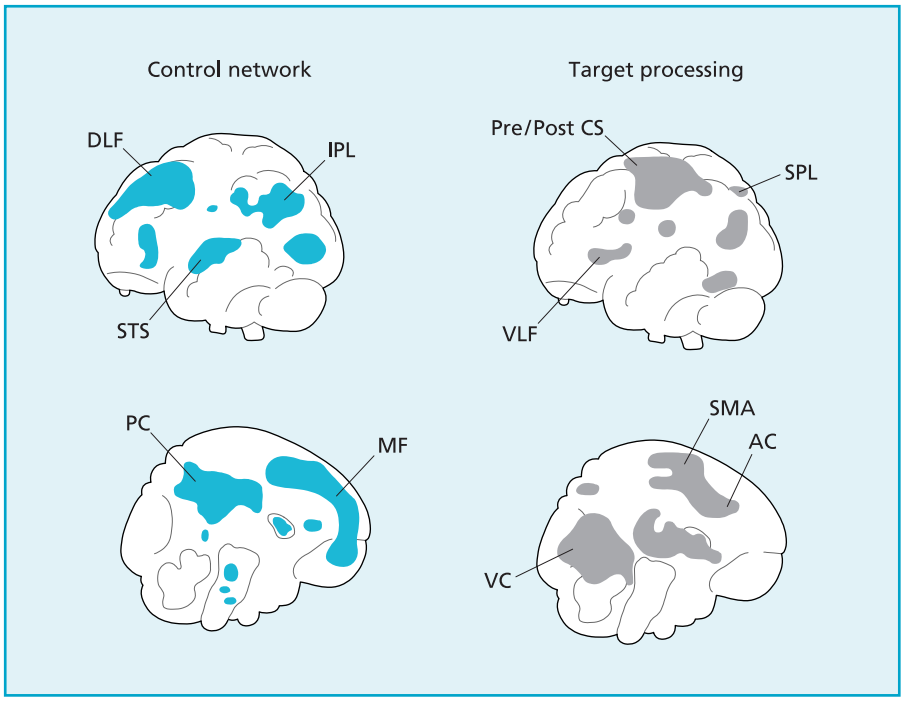


FIG. 9.7 Hopfinger's study of controlled spatial attention (Hopfinger et al., 2000). The left-hand upper and lower images indicate brain regions in a control network activated by cue presentation: medial and dorsolateral frontal regions, inferior parietal and superior temporal regions, and the posterior cingulate gyrus. Target processing, as expected, activated various sensory and motor regions, the ventrolateral frontal cortex and, critically, the anterior cingulate, indicated in the upper and lower images on the right. Posterior and anterior cingulate activations dissociated into preparatory and response selection components respectively. Note: all activations were bilateral, although only left hemisphere is shown. Source: Adapted by permission from Macmillan Publishers Ltd: *Nature Neuroscience* (Hopfinger, Buonocore, & Mangun, 2000), © 2000.

the more attention a person pays to particular stimuli, the larger the resultant P300. It is also noteworthy that individuals with damage to parietotemporal regions no longer generate P300s.

The frontal lobes

We have just seen that at least two regions of prefrontal cortex are implicated in attention control (Hopfinger et al., 2000). Top-down executive influences of this sort are inextricably linked to central executive working memory function, which we introduced in Chapter 7. Executive functions (in general) are also reviewed in Chapter 11, and the linkage between all three (executive functions, working memory, and attention) is explored separately below. However, other frontal regions not linked to executive functioning also appear to be important in influencing motoric aspects of attention. A form of neglect is seen in some individuals with premotor frontal damage, although this is somewhat different from the classic hemineglect syndrome to be discussed later. In the frontal form, individuals seem uninterested in making movements towards the neglected side—a motor as opposed to a sensory neglect (Buxbaum, 2006).

The frontal eye fields (FEFs)

Located laterally in the frontal lobes (BA 8), these are also important attentional nodes. These regions control voluntary gaze. This is important because we have already seen that the superior colliculi direct gaze in an involuntary manner towards unexpected stimuli. Clearly some mechanism is required to override this system, otherwise we would constantly be distracted by new stimuli. This job is performed by the frontal eye fields. As you might expect, damage to this region brings about a form of distractibility in which an individual's visual attention is constantly drawn to irrelevant visual stimuli. LaBerge has offered a neuroanatomical model of attentional control which includes many of the structures identified above. We summarise this model in Box 9.1.

Box 9.1 LaBerge's triangular model of attention

According to LaBerge (1995, 2000), attention comprises three elements: simple selection, preparation, and maintenance. Simple selection is typically brief, the goal usually being the identification of the selected item itself. Preparatory and maintenance functions are required to sustain attention in a more deliberate way over a short (preparatory) or longer (maintenance) period of time. Posner's spatial cues would be a means of evoking preparatory attention. Completing the Stroop test would be an example of maintained attention. LaBerge envisages attention as enhanced (excitatory) activity in discrete cortical association areas, which can be brought about by either top-down or bottom-up influences. Bottom-up control operates in two main ways: triggering shifts in attention, and directing attention to new locations. In each case, the processes are rapid and, effectively, involuntary. Attentional capture (the term used for this bottom-up process) encompasses those occasions when our attention is "grabbed" by some salient but peripheral event or stimulus. For LaBerge, it also accounts for the so-called pre-attentive visual search findings of Treisman and Gelade (1980) in which respondents report that non-conjunctive targets "pop-out" from the array (see Figure 9.3b). Once detected, the target then directs attention to itself, whereupon top-down influences (from the frontal lobes) "decide" whether or not to maintain attention to that item.

In LaBerge's "triangular" model of attention (see Figure 9.8), the three core components are the parietal lobe, the frontal lobe, and the pulvinar of the thalamus, although the model also implicates the visual cortex and the superior colliculi. An abrupt visual stimulus induces brief parietal activity, either directly or via the superior colliculi and thalamus. This is likened to a pre-attentive or orienting activation. The parietal lobe, which is assumed to be the anatomical location of spatial representations, has reciprocal (informational) connections with the frontal lobe. If the latter "chooses" to sustain (or even initiate) activity in the parietal lobe, it does so via the pulvinar, which can potentiate activity in particular cortical regions and inhibit it in others (LaBerge & Buchsbaum, 1990). The pathway from frontal to parietal lobe via the pulvinar is unidirectional, and is the means by which top-down "deliberate" control of attention can be effected.

LaBerge has subsequently modified his triangular model, making it more neuroanatomically (and less neuropsychologically) rooted (LaBerge 2002, 2006) by linking it with short- and long-term functional changes within cortical

columns. However, some features of LaBerge's (2000) model resonate with Corbetta and Shulman's (2002) model of attention, which we review later in this chapter.

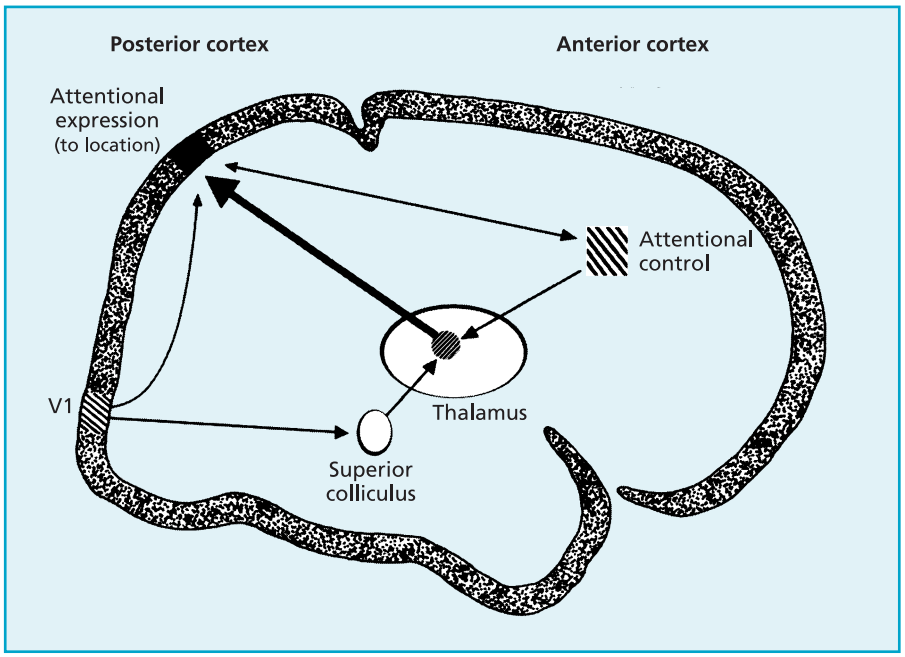


FIG. 9.8 LaBerge's triangular circuit of attention. Following preliminary processing in area V1 of the occipital cortex, a new visual stimulus may induce some "pre-attentive" registration in the parietal lobe, either by means of a direct input or via the superior colliculus and pulvinar of the thalamus. Sustained attention engages regions of the frontal lobe. Continued attentional control can be achieved by frontal output to the parietal lobe via the thalamus. (Adapted from LaBerge, 2000.)

ATTENTION, WORKING MEMORY, AND EXECUTIVE CONTROL

At present, there is no absolute agreement about which brain regions are critically implicated in either attention or working memory, but there *is* broad agreement that top-down attentional control involves the frontal lobes, and some frontal structures—the dorsolateral prefrontal cortex (DLPFC) and the anterior cingulate in particular—are involved in working memory and executive control (Chelazzi & Corbetta, 2000). A moment's thought suggests that working memory *must* be involved in (at least) top-down attention when a participant seeks to keep "in mind" information over a period of time that will guide his/her subsequent actions, as in the classic Posner et al. paradigm.

To underline the "common ground" between attentional mechanisms and working memory, PET and fMRI studies by Jonides et al. (1993), Smith et al. (1996), and Courtney et al. (1997) have all demonstrated a significant degree of overlap in both right parietal and frontal regions of activation during tasks of spatial attention and spatial working memory. Additionally, it has been known for some time that sustained effortful attention over longer periods (as required in

the Stroop test) engages medial frontal structures including the anterior cingulate and the frontal eye fields (Posner & DiGirolamo, 1998) in addition to DLPFC regions associated with the central executive control of working memory.

More recently, three independent lines of evidence have reinforced the view that working memory, attention, and executive control share a good deal of common ground. For example, Kane et al. (2001) reported a study of visually presented letter identification that included an "**anti-saccade**" condition: shortly before each target letter was presented, an attention-attracting cue appeared on the side opposite to where the letter would subsequently appear. For optimal performance, respondents had to resist the temptation to shift attention (and move their eyes) towards the cue. The researchers found that respondents with the smallest working memory capacities were most likely to make persistent attentional errors; suggesting that a common attention-executive (top-down) system underpins the relationship between distractibility and poor working memory.

The imaging studies cited earlier produced impressive results but have been criticised on methodological grounds including, in at least one instance, the conflation of spatial memory and spatial attention tasks, leading to difficulties in interpreting the "apparent" convergence of their anatomical representations (in other words, the tasks were so similar that functional overlap was almost inevitable). In an effort to overcome this problem, LaBar et al. (1999) conducted an fMRI investigation in which the same respondents undertook a working memory task (with no spatial attentional component) and a spatial attention task in which any working memory component was controlled for. Although some brain regions were only activated in one or other of the tasks, several, including the frontal eye fields and supplementary motor regions of the frontal lobes, the intraparietal sulcus, and the thalamus, were equally activated by both: a finding that LaBar and colleagues interpreted as supporting the view that working memory and spatial attention are represented by partially overlapping neural networks. (See Figure 9.9 for an illustration of the method and findings of this study.)

Third, in an ERP study by Awh, Anllo-Vento, and Hillyard (2000), participants were required to undertake both a spatial working memory and a spatial attention task using (virtually) identical stimulus displays. In the former, they had to "remember" the position of three dots presented briefly to the left or right of a fixation point. Irrelevant chequerboard-patterned probes were briefly presented on the same or opposite side during the retention period, and ERPs were recorded to these. After about 8 seconds, another dot appeared on screen and participants had to say whether or not it occupied a location of one of the original three dots. This completed the trial although performance on this was of no interest to the researchers. In the spatial attention condition, the stimulus sequence was almost identical, but the instruction was to pay attention to the "side" in which the dots appeared (rather than their precise locations) and to press a button whenever a faint/dim dot (not shown in the memory condition) appeared on the same side. Once again irrelevant chequerboard probes appeared during the 8-second delay period and ERPs to these were recorded. The key questions were: (a) whether the task manipulations would induce enhanced ERPs to chequerboard stimuli on the "cued" side, and (b) whether these would be similar or different in the spatial working memory and spatial attention conditions. As expected, ERP enhancement was observed on the cued side, but of greater interest was the considerable

Key Term
Anti-saccade: Inhibition of a reflexive eye movement towards a light target.

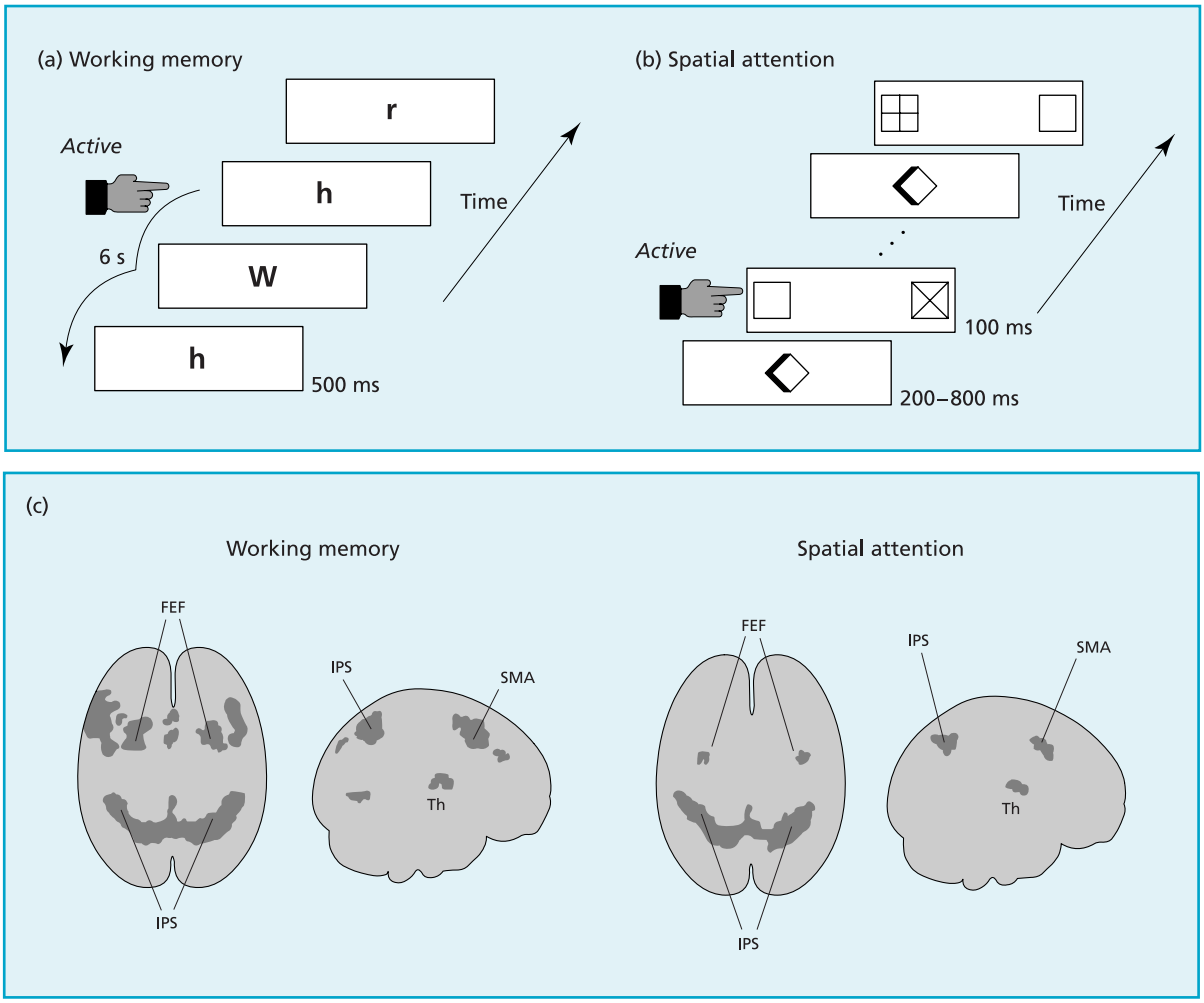


FIG. 9.9 LaBar et al.'s fMRI investigation of working memory and attention. (a) In the working memory task, respondents viewed a series of letters and had to press a button if the current letter was the same as the one shown two letters previously (called the 2-back paradigm; control condition not shown). (b) In the attention task the diamond figure with one side emboldened was the cue to signal a subsequent target: an X in a box. The cue signalled the correct direction on about 80% of trials (control condition not shown). (c) Although some brain regions (not shown) were only activated in one or other of the tasks, several, including the frontal eye fields and supplementary motor regions of the frontal lobes, the intraparietal sulcus, and the thalamus, were equally activated by both, suggesting that working memory and spatial attention are represented by partially overlapping neural networks. Source of (a) & (b): LaBar, K. S., Gitelman, D. R., Parrish, T. B., and Mesulam, M. M. (1999). Neuroanatomical overlap of working memory and spatial attention networks: a functional MRI comparison with subjects. *NeuroImage, 10*, 695–704. Reproduced with permission, © Elsevier, 1999.

overlap, both in terms of ERP amplitudes and location of maximum activation, in the two task conditions: a finding that the authors interpreted as providing strong support for a marked functional overlap in the mechanisms of spatial working memory and spatial attention.

Thus, evidence from studies employing three different methodologies (cognitive psychology, fMRI, and ERP) converges to illustrate the likely commonality between spatial attention, working memory, and executive control. To this we might add a reminder that placing "load" on working memory reduces available

resource for focused attention, and increases the likelihood of being distracted by irrelevant stimuli or events (Lavie, 2005).

INTERIM COMMENT

Both ERP and functional imaging studies indicate that augmented processing of attended stimuli can be observed relatively soon after stimulus presentation (within 50–70 ms). Attended channels continue to receive preferential attentional treatment at later stages of processing up to and including the P300 wave, usually associated with responses to stimuli with "semantic significance". None of these studies supports the idea of active inhibition of unattended channels.

Attempts to identify cortical and subcortical structures involved in mediating attention have been quite informative, and LaBerge's triangular model attempts to integrate some of these structures into a network that accounts for both "bottom-up" and "top-down" control of attention. The available evidence suggests that "top-down" attentional control overlaps significantly with executive components of working memory, and although some of the earlier functional imaging studies have been criticised for failing to distinguish adequately between attentional and working memory tasks, converging evidence from more recent studies, employing a range of procedures, has reinforced the view that both working memory and attention involve partially overlapping neural networks distributed in frontal and parietal regions. However, progress in this area is hampered by continuing uncertainties about the structure of working memory and the parameters and categories of attention.

NEUROLOGICAL ATTENTIONAL DISORDERS

HEMINEGLECT

Hemineglect (also known as unilateral or spatial neglect) is a collection of related (but not identical) disorders usually associated with inferior parietal or medial temporal lobe damage (but see later). An individual with this condition effectively ignores (or fails to pay attention to) one side of space with respect to the midline of the head or body. This is sometimes called **egocentric neglect**, and appears to be associated with hypofunction (or damage) in the angular gyrus (Hillis et al., 2005). The angular gyrus is sometimes identified as a key part of the temporal-parietal junction [TPJ] area, which we consider below. Much less commonly, a patient may appear to consistently neglect the left or right side of objects regardless of where they appear in the visual field. This is sometimes called **allocentric neglect**, and it is associated with underactivity (or damage) in the superior temporal gyrus (Hillis et al., 2005). Moreover, it should be noted that, in rare instances, neglect may involve different spatial referents such as left/right foreground and distance, or even left/right upper and lower space (Behrmann, 2000). In fact, a very small number of neglect patients may even evince a dissociation in the form of left-sided neglect for near space and right-sided neglect for far space, or vice versa. To

KEY TERMS
Egocentric neglect: Consistent errors to one side of the viewer (right or left).
Allocentric neglect: Consistent processing errors on one side of individual stimuli (either right or left) regardless of location with respect to the viewer.

complete the picture, neglect in the auditory or even somatosensory modality may be apparent. However, visual hemineglect is far and away the most common form of disorder, and this is what we will focus on.

Hemineglect occurs in between 25–30% of stroke-affected individuals according to Appelros (2002). Nine out of ten have a right-sided injury and left-sided neglect. The regions most frequently implicated are the angular (and supramarginal) gyrus, superior temporal and inferior frontal lobes, and associated subcortical structures (Vallar, 1998). About 10% of neglect cases have left-sided damage and right hemineglect although, for reasons that are not entirely clear, this is usually less severe. Taken together, these observations lead to the conclusion that although left- and right-sided damage may lead to contralateral neglect, right-sided structures are somehow more critically involved. One long-standing explanation for this finding was that whereas the left parietal lobe is only responsible for attention on the right side of space, the right parietal lobe has an "executive" control for spatial attention on both sides. Thus, following right-sided damage, the left parietal lobe can still mediate attention to the right visual field, but attentional control of the left side is lost. Therefore, left-sided damage is typically less disabling because the intact right side can continue to exert some control over both sides (Weintraub & Mesulam, 1987). An alternative explanation has invoked the different processing styles of the left and right hemispheres (see Chapter 3). According to Robertson and Rafal (2000), the left parietal lobe is chiefly responsible for local shifts in attention whereas the right parietal lobe is involved in more global shifts. Thus, following right hemisphere damage, the patient is limited to the local attentional shifts of the left hemisphere, leading to the fixation with local detail and the loss of effective disengagement. Neither of these accounts is, in fact, entirely satisfactory, but the model proposed by Corbetta and Shulman (2002) (to be reviewed later) overcomes some of these intrinsic problems and provides the most complete explanation for these apparent asymmetries.

The extent of hemineglect is variable, and may range from a general apparent indifference towards objects on the left side, to denial of the very existence of that side of the body (Buxbaum, 2006). One of Sacks' patients had **anosognosia** (Sacks, 1985) and famously called a nurse in the middle of the night to ask her to help him throw his own left leg out of bed, thinking that "the alien leg" had been put there as a cruel joke by fellow patients! Less severely affected patients may simply ignore items in their left visual field. Moreover, there is usually some recovery in the months following injury/damage and so, typically, the neglect is most marked early on, becoming less pronounced, though not usually disappearing completely, as recovery ensues. The late German artist Anton Raederscheidt suffered a right-sided stroke but continued to paint even though he had an initially severe form of hemineglect (Butter, 2004; Wurtz, Goldberg, & Robinson, 1982). In a famous series of self-portraits it is possible to see the effects of his hemineglect and how this diminished over a period of months as he partially recovered after his stroke. In an interview his wife described how, in the early recovery period, she had to keep guiding him to the left side of the canvas, and it is clear from the paintings themselves that Raederscheidt's gradual reconstruction of the left side of his visual space was a deliberate "non-fluent" process.[1] The case of Anton Raederscheidt highlights an important subjective feature of hemineglect. The individual is not so much desperate to re-find the missing half of their visual field, as utterly uninterested in it. It just doesn't exist as far as they are concerned,

Key Term
Anosognosia: A condition in which a person who suffers impairment following brain damage seems unaware of or denies the existence of their handicap, even if the handicap is severe (blindness or paralysis).

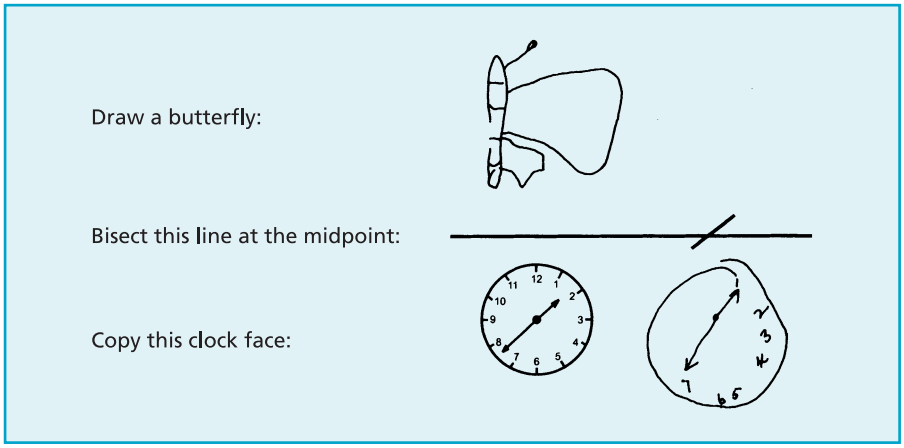


FIG. 9.10 Typical responses of hemineglect patients in drawing tasks.

and in Raederscheidt's case it had to be deliberately (and somewhat artificially) reconstructed.

What are the tell-tale signs of neglect in the visual modality, and why should it be classified as an attentional rather than perceptual disorder? Detecting neglect is quite straightforward: Ask the patient to copy some simple line drawings and the results will be similar to those shown in Figure 9.10. When probed about whether the drawing might be lacking certain details, the patient will usually deny this, saying that it is complete. On a simple line-bisection task (in which the respondent is required to indicate the midpoint of a series of uncalibrated horizontal lines of different lengths), the neglect patient typically places the bisecting line to the right of true centre (Marshall & Halligan, 1990). (This is the exact opposite of healthy controls who typically show a small left-oriented bias; sometimes called pseudo-neglect.) Finally, when asked to cross out every vowel shown on a sheet of random letters comprising both vowels and consonants, the neglect patient will "chalk up" many more hits on the right side of the array than on the left.

None of the previous observations entirely rules out the possibility that hemineglect may relate to sensory/perceptual rather than attentional deficits. However, three further lines of evidence strongly support the idea that it is an attentional disorder. For example, when identical objects are presented to both visual fields simultaneously, the "neglect" patient usually fails to report the object in the left visual field (a phenomenon known as "extinction"). However, if different objects are presented one at a time to each side, there will be normal or near-normal recognition even on the "neglected" side. Second, Mesulam (1985) reported that attention to objects on the neglected side can be improved by offering rewards for target detection there. And finally it has become clear that some processing of materials presented to the "neglect" side occurs even if the patient denies knowledge of that material. In one famous illustration by Marshall and Halligan (1988) a neglect patient was simultaneously shown two images of a house, identical except that the house presented on the left had flames coming out of some of its windows. The patient could not describe any differences between the images but, when asked to choose, expressed a clear preference to live in the house on the right!

The idea that hemineglect results from a lack of awareness of the existence of one side of visual space seems alien to those of us with intact attentional mechanisms, but it was further demonstrated in the reports by Bisiach and Luzzatti (1978) of two hemineglect cases. The researchers asked their patients to imagine that they were standing in a famous Milanese square opposite the entrance to the cathedral, and to report the various buildings and other landmarks that came to mind. (Both knew this location well, having lived in the city for many years before their illnesses.) Later, the same respondents were asked to imagine themselves standing on the cathedral steps looking back to their initial vantage point, and now to report buildings and landmarks (again in their mind's eye) that they could see from this new vantage point. The results of this study are represented in Figure 9.11. When the two patients imagined themselves standing opposite the cathedral, most of the identified landmarks were to the right. When they imagined themselves standing on the steps of the cathedral looking back, most of the identified landmarks were, once again, to the right. This study reveals some important features of "imaginal"

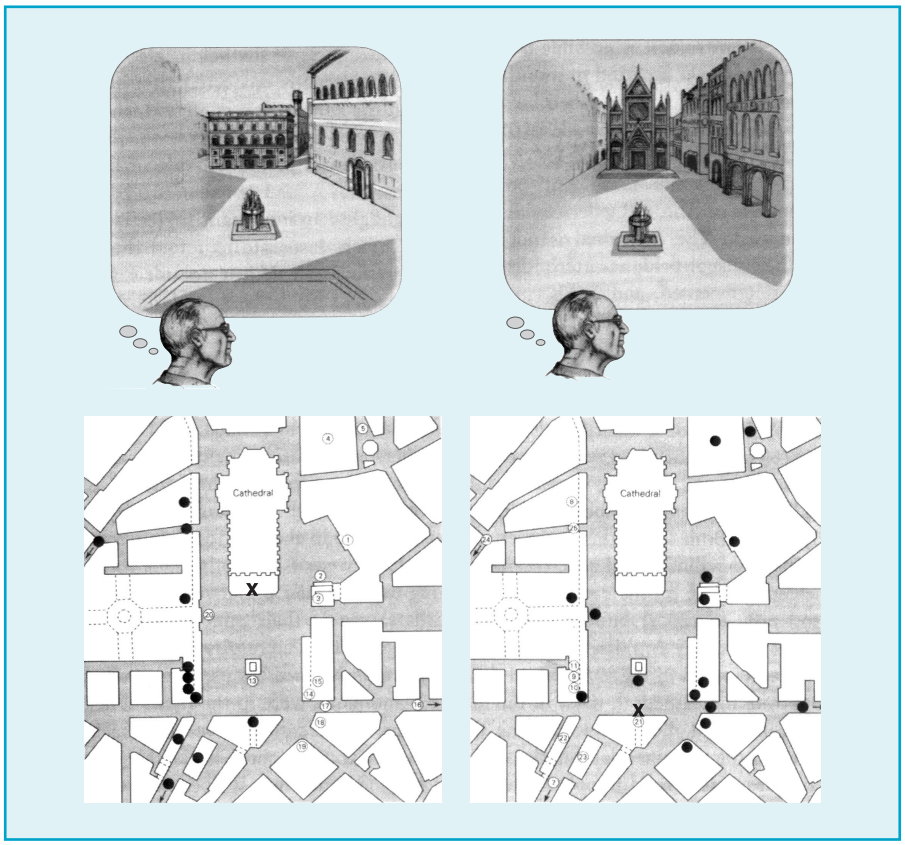


FIG. 9.11 Hemineglect and imaginal spatial attention. When asked to imagine the view from the steps of the cathedral (marked "x" on the left-hand map), both patients identified more landmarks and buildings to the right. When asked to imagine the view from the opposite end of the square (marked "x" on the right-hand map), both patients once again identified many more landmarks and buildings to the right. Source: Bisiach, E., & Luzzatti, C. (1978). Unilateral neglect of representational space. *Cortex*, *14*, 129–133. As redrawn in *Cognitive neuroscience: The biology of the mind* (Figure 6.38) by M. S. Gazzaniga, R. Ivry, and G. R. Mangun: Copyright © 1998 by W. W. Norton & Company, Inc. Used by permission of W. W. Norton & Company, Inc.

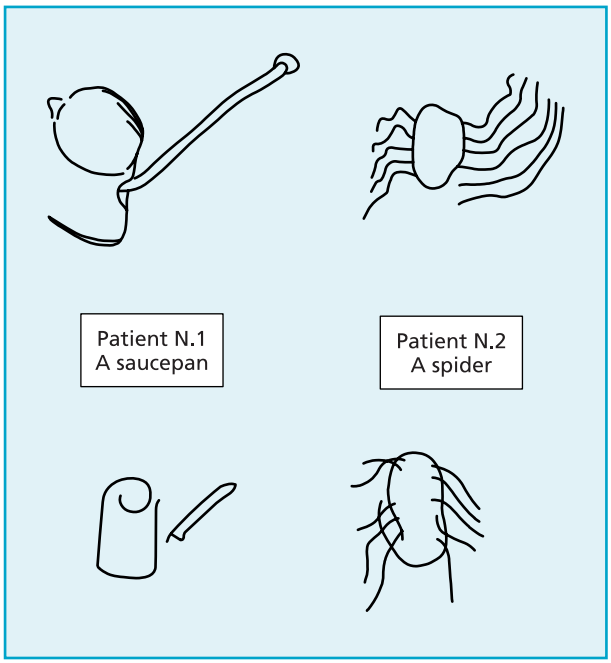


FIG. 9.12 Chokron et al.'s (2004) study of imaginal hemineglect. Respondents were invited to draw images of a saucepan and a spider from memory, either with their eyes open (upper figures) or closed (lower figures). In these illustrations, there is more evidence of symmetry/completion in the lower than upper figures. Source: Chokron, S., Colliot, P., and Bartolomeo, P. (2004). The role of vision in spatial representation. *Cortex, 40*, 281–290. Reproduced with permission.

hemineglect. First, it cannot be related to memory impairment because the total number of recalled landmarks was similar to the number generated by normal controls. Second, the attentional disturbance could not be caused by external cues because the entire test relied on imagery. The most parsimonious explanation of these findings is that the patients behaved as if they were missing the concept of one side of space—the left—even when they effectively rotated themselves through 180 degrees.

However, since this landmark case study, questions have been raised about the generalisability of its findings. For example, according to Gainotti, D'Erme, and Bartolomeo (1991), about two-thirds of neglect patients do not in fact have "neglect" for imaginal tasks like that of Bisiach and Luzzatti. Moreover, there have been no recorded cases of individuals with imaginal neglect but no conventional visual neglect as well. In a clever test to establish the importance of vision on imaginal spatial representation, Chokron, Colliot, and Bartolomeo (2004) asked six right-hemisphere-damaged neglect patients to draw a series of objects from memory with their eyes either open or closed. Some of the drawings are shown in Figure 9.12. In most, there is more evidence of neglect in the former than the latter condition. The authors suggested that this finding "highlighted" the importance of vision in capturing attentional control and holding it (inappropriately for these neglect patients) to the right side of space. At the very least this implies that the two forms of neglect (imaginal and conventional) may be dissociable (partly distinct) and that conventional visual neglect is the more problematic.

Corbetta et al. (2005) have shown that recovery from hemineglect maps onto measureable functional changes in the cortex. This group followed-up 11 stroke-induced neglect cases for 39 weeks. Reduced neglect was strongly associated with the reappearance of normalised activity levels on the right side. Interestingly, changes in activation were not restricted to the specific location of stroke, reminding us that damage in one location can influence (in this case, suppress) activity in anatomically distant but functionally linked locations. In other words, neglect (or its absence) is mediated by a network of structures rather than one specific/critical location. Recovery of function can, incidentally, be significantly enhanced through engagement with effective physiotherapies, which may soon be supplemented by computer-based virtual reality technologies (Kim et al., 2004). However, and perhaps somewhat counterintuitively, Chokron et al. (see above) raised the possibility of *suppressing* visual control (for example, by means of light deprivation) as a means of aiding recovery from unilateral neglect. This has yet to be tested but it would be the exact opposite of conventional therapies, in which a strong emphasis is placed on re-training visual awareness.

BALINT'S SYNDROME

This is a rare but very disabling condition in which the individual manifests one or more of a trio of symptoms that could easily be mistaken for blindness for all but a very restricted area of the visual field. Balint's cases may be unable to point or reach towards a visual target (called optic ataxia; see an earlier reference to this condition above), they seem unable to shift gaze voluntarily to a new target (called **ocular apraxia**), and they may be unable to easily identify different objects in the same region of visual field presented together (known as **simultanagnosia**). When, for example, a crossed spoon and fork were held out in front of a Balint's patient, he reported only the presence of the spoon, and then later after a repeat presentation, the fork, yet the objects overlapped. However, such individuals are not blind, and can actually "see" objects anywhere in the visual field *if* they can direct attention to that location—and therein lies the problem. The ocular apraxia means that Balint's patients cannot redirect their gaze to areas adjacent to their present focus of attention (although a redirection may occur involuntarily). It is this lack of voluntary control that defines Balint's syndrome as a profound spatial attentional disorder (Damasio, 1985).

KEY TERMS
Ocular apraxia: The inability to move the eyes voluntarily to objects of interest despite unrestricted eye movements and normal visual fields.
Simultanagnosia: Inability to recognise multiple elements in a simultaneously displayed visual presentation.

Farah (1990) further illustrated the attentional deficit seen in Balint's individuals. When shown a complex meaningful picture similar to that in Figure 9.13 the patient could identify different elements of the picture as his attention switched *involuntarily* around the scene, but he could never grasp the full meaning of the picture because it was visually scanned in such a piecemeal way. So the attentional disorder in Balint's compromises the appreciation of spatial relationships, which will influence the understanding and interpretation of visual displays (Robertson & Rafal, 2000).

However, many Balint's patients also display impaired object recognition, especially when more than one object is presented, even if they overlap (see above). In fact, the problem may be in deciding what actually constitutes "an object" (essentially a "binding" problem). Consider the findings of Humphreys and Riddoch (1992) working with their Balint's patient GK. He viewed arrays comprising randomly positioned all-green or all-red dots, or a mixture of the two. In each case, GK usually only reported seeing one colour of dot. However, if the array was changed to show pairs of dots (one red and one green), the same distance apart as in the initial arrays but joined by a line to look a bit like a series of dumbbells, GK now usually reported seeing both colours of dot. In other words, the connecting line created a new "object" (dumbbell) which GK was able to attend to in its entirety.

Balint's is almost always associated with damage to dorsal occipital-parietal regions, although more recently collected anatomic data suggest, as was the case with hemineglect, that different features of the syndrome may be dissociable, and

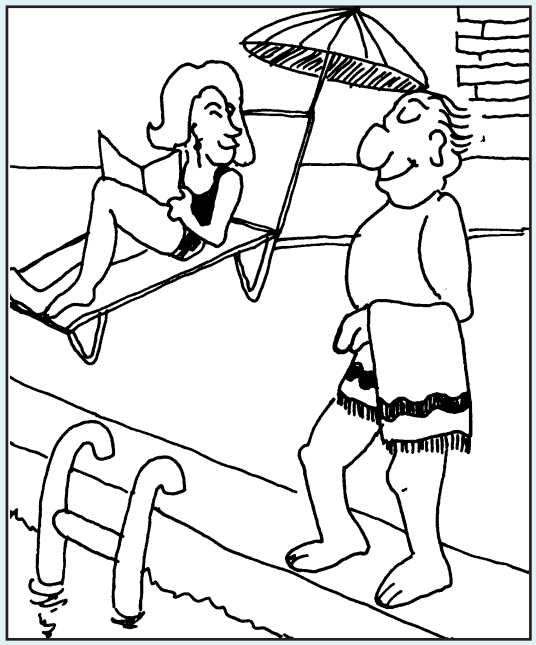


FIG. 9.13 A picture/story stimulus similar to those used by Farah. When Balint's patients view figures similar to the one shown here, their inability to voluntarily scan the entire figure and appreciate the "story" that it depicts is apparent.

linked to distinct cortical regions (and white matter pathways that connect them; Rizzo & Vecera, 2002). Bilateral damage to the superior parietal lobule (a key area in the "where–how" stream described in Chapter 8) is frequently seen, which explains why Balint's syndrome is also known as dorsal simultanagnosia.

INTERIM COMMENT

Balint's syndrome and hemineglect demonstrate that our ability to construct a complete model of our visual world depends on being able to attend to different elements of it, to switch attention to new objects or new regions of space very quickly, and to use this specific information to build a relational map of the "big picture". In hemineglect, parietal damage means that this skill is lost (usually) for the contralateral visual field. As a result, attention appears to be focused on the remaining intact half. The person is not blind to the other half of the visual field, and can, under certain circumstances, see objects in it. But their attention is somehow "drawn" to one half of the visual field, and they do not even seem to "miss" the other half.

Balint's syndrome is a rarer and more disabling condition in which attentional control, even to half the visual field, is lost. Instead, we see a sort of single object-based attentional system operating without voluntary control. Although Balint's syndrome is not in any way related to tunnel vision, the experience of the disorder must be a little like only seeing visual stimuli from the end of a long tube, which roams around the visual field unpredictably. Balint's has been likened to having hemineglect on both sides, although this is an oversimplification of the links between the two disorders. Compared to hemineglect, there is usually much more widespread damage in Balint's, which is most likely to involve more dorsal regions, bilaterally.

A final point to note is that damage to the "where–how" stream affects not only spatial attention but also object recognition, reminding us that the dorsal route undoubtedly interacts with, and contributes to the functions of, the ventral stream in this process.

TOWARDS AN INTEGRATED MODEL OF ATTENTION

Posner and colleagues (Posner et al., 1987) proposed a model of visual attention that emphasised change and selection. They argued that the redirection of attention must involve at least three processes: disengagement (from the present focus), redirection (to the new stimulus), and engagement (with the new stimulus). The three elements, they suggested, depend on the sequential interaction of different brain structures: "*the disengage*" process depends on intact parietal functioning, "*the redirect*" on the superior colliculi, and "*the engage*" on the thalamus.

The evidence in support of this hypothesis merits consideration: as we have seen, patients with parietal damage find it difficult to disengage from an attended stimulus, and this problem is not related to "engage" deficits, which, under appropriate circumstances, can be shown to be normal. (See our discussion of hemineglect and Balint's syndrome.) We also noted earlier that patients with

collicular damage, as seen in supranuclear palsy, have difficulties redirecting gaze, and that individuals with pulvinar thalamic damage struggle to "latch on" to new targets. A network comprising some of these structures was designated the posterior attentional system by Posner. Subsequently, Posner (1992) proposed a second attention network that becomes active during intentional (endogenous) processing, such as listening out for "salient" target words, or covertly awaiting the presentation of a visual target having been "cued" to attend to a particular location. Posner thought that this so-called anterior network comprised parts of the cingulate, medial, and dorsolateral frontal regions, and that it clearly overlapped considerably with the component structures that contribute to the executive functions of the frontal lobes (to be discussed in Chapter 11). Endogenous control of attention was achieved by its modulation of parietal regions.

Corbetta and Shulman (2002) have developed what has quickly become an influential model of attention. Like Posner, these researchers acknowledged the importance of both anterior and posterior influences on attention, but they have argued that both combine to mediate attention in real-world settings. Their approach is commendable for three reasons: First, they have relied on meta-analysis of (mainly) functional imaging studies. Thus, their conclusions are based on findings from several independent studies, each of which has employed somewhat different experimental methods, making consensus findings all the more noteworthy. Second, by pooling data, the resultant sample size is much more "respectable" than would be the case with single studies. Third, their model offers a plausible explanation for the laterality effects seen in hemineglect (Corbetta et al., 2005).

Corbetta and Shulman envisage two interacting "arms" in their attention network. One primarily operates as a top-down control system involved in preparing, applying, and controlling attention to stimuli and, if necessary, organising appropriate responses. This system also responds to the detection of stimuli, particularly if they are pre-cued. The second is viewed as a bottom-up network, specialised for the detection of behaviourally relevant, salient, but unexpected stimuli. Conceptually, the top-down arm is analogous to Posner's anterior system and the bottom-up arm analogous to his posterior system, although anatomically, quite different regions have been identified in the two models.

If we take a closer look at the top-down "arm", a meta-analysis of fMRI studies indicates a network of cortical regions that become activated when a respondent anticipates a stimulus (i.e., following a cue) and that remain activated during the preparatory period for up to about 10 seconds: this network includes the dorsal regions of the parietal lobe and posterior frontal lobe. If we extend the analysis to include studies where attention to actual stimulus attributes (colour, movement, shape, etc.) is required, similar areas of activation are seen in parietal regions, plus marked activation in BA 8 (the frontal eye fields; see above). Although these activations are generally bilateral, there is some evidence that where a change in motor response is dictated by a particular stimulus, increased activation is more marked in left posterior parietal regions, an observation that jibes well with our review of apraxia in Chapter 5. The main components of the top-down attention arm, referred to by Corbetta et al. as a dorsal system, are illustrated in Figure 9.14a.

Turning now to the bottom-up (or stimulus-driven) arm, Corbetta and Shulman conceptualise this system as a "circuit-breaker", capable of interrupting and even re-orienting attention in response to a salient or unexpected stimulus

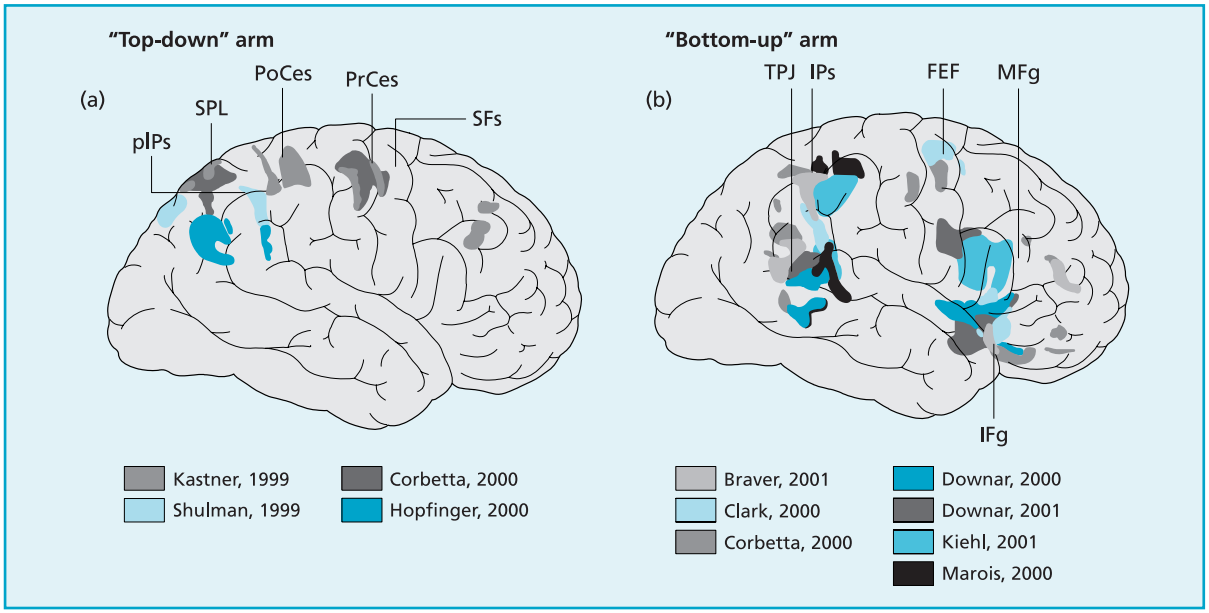


FIG. 9.14 Corbetta and Shulman's model of attention. (a) The bilateral top-down arm: results of a four-study meta-analysis indicate regions activated by cues preceding target stimuli. Areas of maximal activation included pIPs (posterior intraparietal sulcus), SPL (superior parietal lobule), PoCes and PrCes (post- and precentral sulcus), and SFs (superior central sulcus). Comparable left hemisphere activations were also found (not shown). (b) The right hemisphere bottom-up arm: results of a seven-study meta-analysis indicate regions in a ventral fronto-parietal network that are activated to unexpected stimuli. Areas of maximum activation included the TPJ (temporo-parietal junction), IPs (intraparietal sulcus), FEF (frontal eye field), and the MFg and IFg (medial and inferior frontal gyrus). Activation in the left hemisphere is much less pronounced (not shown). Source: Adapted by permission from Macmillan Publishers Ltd: *Nature Reviews Neuroscience* (Corbetta & Shulman, 2002), © 2002.

(such as a fire alarm or a flash of lightning). This arm involves a quite different set of cortical locations and is strongly (though not completely) lateralised to the right hemisphere. Parietal and frontal regions are implicated but these are more ventral (hence Corbetta et al.'s reference to this as the ventral system) than the regions in the mainly dorsal top-down arm (see Figure 9.14b). However, this "stimulus-driven" arm can exert powerful effects on the top-down arm: For example, low-frequency task-relevant stimuli such as rare distractors that are the same colour as attended stimuli will activate it, but will also activate the top-down circuit, presumably so that they can be evaluated and if necessary "deliberately" responded to. Task-irrelevant distractors on the other hand will only have this effect if they are very salient (e.g., the fire alarm). Key nodes in this arm are the right temporo-parietal junction (TPJ) and the right medial and inferior frontal gyri. Finally, there is some evidence that activity in this ventral system is partly mediated by a noradrenergic (NA) input from the locus coeruleus (part of the ascending reticular activating system; see above). There is, for example, a more dense NA innervation of the right than left thalamus. This observation is significant because NA release is thought to increase **signal to noise ratio** in threatening situations where effective attentional control may mean the difference between life and death.

KEY TERM
Signal to noise ratio: Degree to which relevant information can be perceived against a background of irrelevant information.

In their 2002 paper, Corbetta and Shulman speculated that damage to the strongly right-lateralised stimulus-driven system was likely to be implicated in hemineglect (see our earlier discussion of this disorder). If this ventral system was

compromised, an individual might be indifferent to the left side because stimuli there would not exert their "circuit-breaker" effects. However, there is something wrong with this argument because it seems that the right temporo-parietal junction (TPJ) area actually responds equally well to unexpected stimuli on both sides, so damage here might be expected to cause bilateral deficits. Moreover, TPJ activation does not correlate with motor preparation, whereas most neglect cases show contralateral impairments in movement preparation and initiation. The authors were aware of these problems, and they suggested that hemineglect probably resulted from a more dynamic dysfunction (i.e., at least not localised only to the TPJ), although the anatomy of this network was not defined.

However, Corbetta et al. (2005) *were* able to describe in more detail the *network of dysfunction* implicated in the neglect syndrome. This study, which we introduced earlier, followed up a group of hemineglect patients during their recovery (for a period of 39 weeks), recording fMRI signals early on post-stroke, and again several months later. We summarised their research as suggesting that recovery was associated with "normalisation" of balanced cortical activity bilaterally. However, re-examination of their findings, especially relating to changes in activation over time, merits closer scrutiny. For example, dorsal parietal activation (part of the top-down attention system, you might recall) was markedly reduced on the right side and paradoxically *increased* on the left side shortly after stroke although neither site was itself damaged. This strongly suggests that the ventral arm ordinarily interacts with the dorsal arm to redirect attention, but following right-sided stroke, ipsilateral (same-sided) ventral–dorsal interaction is reduced, giving rise to a functional imbalance in which the left dorsal parietal lobe is relatively hyperactive. The right TPJ is crucial in this because damage to it (or to the ventral system of which it is part) will prevent it from sending the "circuit-breaker" signal to the dorsal arm (on the same side). So left-sided neglect results from two additive dysfunctional processes: First, stimuli on the left will be less likely to invoke "capture" because the right TPJ is compromised, and second, reduced activity here will bring about reduced activation in the dorsal system on the right, giving free rein to left posterior dorsal areas to influence top-down attention to the right side, and hence induce a marked rightward bias. A schematic (simplified) version of this model is shown in Figures 9.15a and b.

INTERIM COMMENT

Corbetta and colleagues have offered a neuropsychological model of attention that, in certain respects, builds on ideas first suggested by Posner and Mesulam. However, although their model has two "arms" (a top-down and a bottom-up component), these interact continuously in real-world settings to mediate directing attention (the dorsal arm), circuit breaking (the ventral arm), and re-orienting attention (ventral influence on the dorsal arm). In fact, it is, essentially, a unitary model with specialised component systems in it rather than two attentional control networks. In comparison with LaBerge's model it is less neuroanatomically rooted, and more concerned with cortical functions/dysfunctions. However, like LaBerge's model it envisages attention as being "controlled" by a continuous interaction between top-down and bottom-up influences (particularly the effects of the latter on the former). It additionally offers a compelling explanation of many of the features of hemineglect.

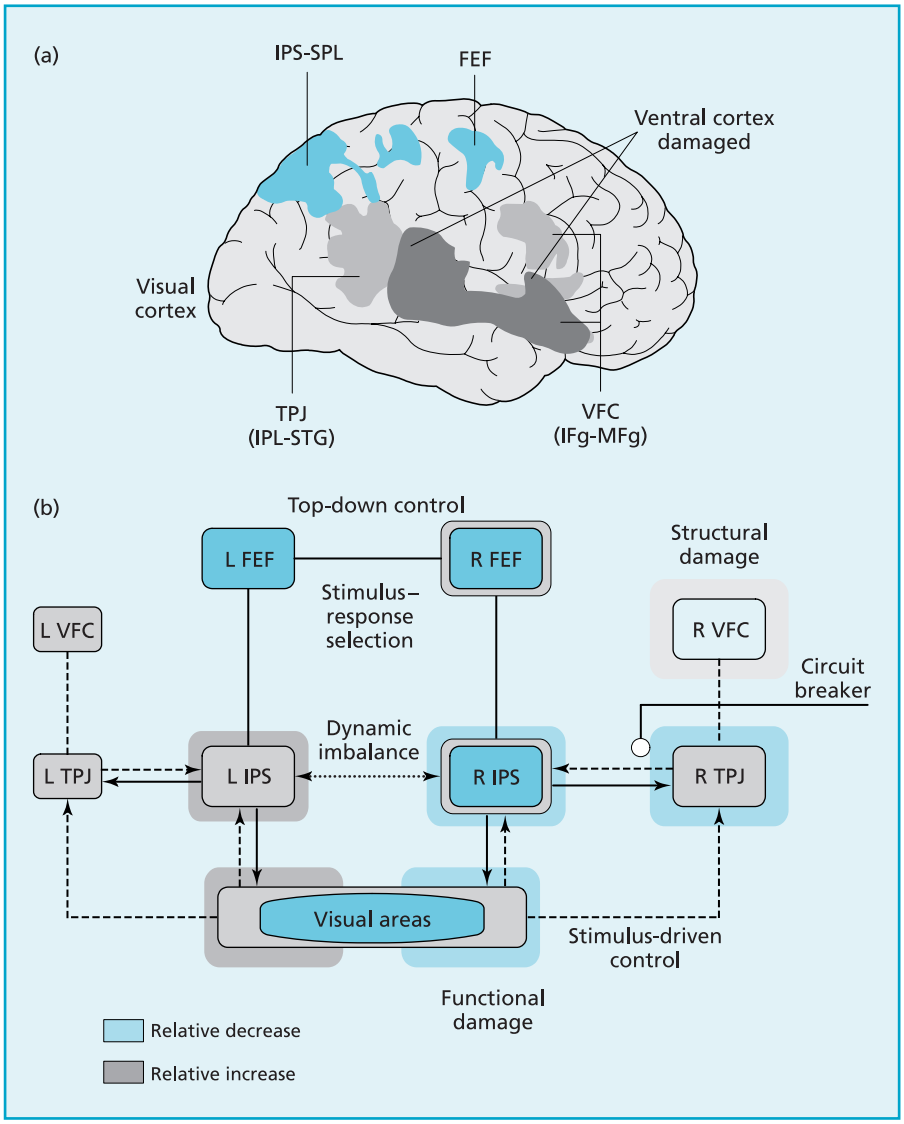


FIG. 9.15 Corbetta et al.'s (2005) explanation of hemineglect. (a) Major components of the dorsal (top-down) and ventral (bottom-up) attention arms (as depicted in 9.14a and b). The dark area represents location of lesions in the right hemisphere associated with hemineglect, encompassing an area extending from the TPJ (temporo-parietal junction) into VFC (ventrofrontal cortex). (b) Ventral damage in the right hemisphere exerts dual effects, depicted in this schematic diagram. Stimuli in the left visual field are unable to invoke "capture" because the right TPJ is compromised. Additionally, reduced right ventral activity leads to reduced activation in the dorsal system on the right, giving free rein to left posterior dorsal areas to influence top-down attention to the right side, and hence induce a marked rightward bias. Source: Adapted by permission from Macmillan Publishers Ltd: *Nature Neuroscience* (Corbetta, Kincade, Lewis, Snyder, & Sapir, 2005), © 2005.

On the other hand, it is a new model and needs to be tested empirically. Moreover, some puzzling features need to be clarified. For example, dorsolateral and cingulate regions do not feature at all in the 2002 model (and only the former features in the 2005 model), yet both regions have been implicated in executive control. The frontal eye fields, on the other hand, feature extensively in the general model, yet their primary function is thought to be related to the control of head and eye movements (Joseph, 2000) rather than executive control. One question for future research will be about the involvement of the frontal eye fields in non-visual attentional tasks. Additionally, a complete account of the attentional dysfunctions in hemineglect will need to consider (a) the different disturbances giving rise to egocentric and allocentric forms, and (b) how information in the neglected side still seems to undergo considerable "covert" processing.

CONSCIOUSNESS

Despite an upsurge in recent interest, a consensus definition of consciousness still eludes us. Nevertheless, we humans do at least know what it is like to *be* conscious—it seems to be restricted to when we are awake, and it involves "experience" of external stimuli (so-called "phenomenal awareness"); awareness of internal states and mental operations such as thoughts, feelings, and emotions and by extension a sense of self as "cognate"; and, arguably, awareness of other people's mental states too. Research in the area has recently been intense, indicating that consciousness is now a legitimate, and indeed urgent, domain of psychological enquiry. There are clearly important links between consciousness and neuropsychology, and we have included our discussion of it here because of the apparent intimate relationship between consciousness and attention (Maia & Cleeremans, 2005). However, as we mentioned in the introduction to this chapter, consciousness, at least as recently conceptualised (Blackmore, 2003), encompasses rather more than "focused attention": Pinker (1997) suggested three aspects meriting independent consideration:

- *Sentience or basic phenomenal awareness*: the private subjective experience of something.
- *Access to information*: being able to report on the contents of one's mental experiences.
- *Self-knowledge*: awareness of one's own mental state moment by moment, sometimes referred to as metacognition (thinking about one's thinking).

As you can see, even a consideration of the parameters of consciousness is complicated. Fortunately, many excellent articles and texts about various aspects of it have recently been published, and the reader keen to delve deeper is urged to refer to Dennett (1991), Chalmers (1995), Pinker (1997), Edelman and Tononi (2000), and Blackmore (2003) for highly accessible sources on consciousness in all its manifestations.

Perhaps we should also say at this point that we are taking it as axiomatic that consciousness, like all other aspects of cognition, is ultimately dependent on

physical processes in our brain. In this sense, we are declaring our allegiance to what philosophers would call (some form of) "materialism", and simultaneously eschewing "dualism", the doctrine associated with René Descartes, who argued that the mind was a separate non-physical entity that interacted with the physical nervous system in the brain's pineal gland. These days, dualism has few supporters in the scientific fraternity (the neurophysiologist Sir John Eccles, who died in 1997, was a notable exception), although we also feel obliged to acknowledge that dualist ideas seem to be widely entrenched in the minds (or should that be brains?) of members of the lay public, given continued popular interest in religion, astrology, spiritualism, and so on.

Three disparate lines of enquiry have obliged us to broach the subject of consciousness: First it should be apparent from dipping into the various chapters in this book that changes in neuropsychological functioning are often accompanied by subjective (or even objective) changes to consciousness. Second, several additional lines of psychological and neuropsychological research (not already mentioned) have nevertheless begun to shed light on the nature of human consciousness: we review some of these below. And third, researchers have started to think about the structure of consciousness from a neuroscientific perspective—this quickly divides into two separate issues: From a practical point of view, what parts of the brain seem to be involved in consciousness? And from a conceptual point of view, what sort of neuronal architecture—network(s) of neurons—would be necessary for a "consciousness system" to operate?

Wilhelm Wundt's Leipzig facility, set up in 1879 to examine the contents of consciousness through introspection, is often regarded as the first "experimental psychology laboratory". Other 19th-century academics, notably Hughlings-Jackson, Helmhotz, Huxley, James, and even Freud, wrote extensively about consciousness, and in Freud's case about the "subconscious" mind too. However, the advent of behaviourism at the beginning of the 20th century, which we touched on in Chapter 1, heralded an era of psychological enquiry in which consciousnesss was not only frowned upon, but effectively put quite beyond the pale as an area of experimental investigation. Even the "father" of modern-day cognitive neuroscience, George Miller, warned in his classic text *Psychology: The science of mental life* (1962) that consciousness was a poorly defined and slippery concept that psychologists would do well to avoid if possible. Despite these warnings, many cognitive psychologists and neuropsychologists working in the latter parts of the 20th century felt that their work touched on aspects of consciousness: Baddeley, for example, thought of his working memory central executive as a "conscious" control system (Baddeley, 2001), and Sperry and colleagues were aware that data from their investigations of people who had undergone the split-brain surgical procedure (see Chapter 3) might also inform ideas about the nature of consciousness.

In fact, it is unclear quite when or how consciousness became, once again, an acceptable area of study for researchers, although the change certainly occurred within the working life of the first author. Some have argued that the widespread availability of in-vivo imaging techniques, permitting correlation between subjective experiences and objective brain activations, was a tipping point (e.g., Frith et al., 1991). In our view, another contributing factor has been the realisation (probably felt by most researchers at some stage in their careers) that the methods of conventional experimental neuropsychology mean that it can, for the most part, only address certain (arguably rather superficial) types of question. Whatever

the reason or reasons, having languished on the sidelines of scientific psychology for more than a century, consciousness has quite suddenly become a respectable and even pressing domain of neuropsychological and neuroscientific inquiry.

However, we should also sound a note of caution because despite its newfound legitimacy, many researchers have argued that some aspects of consciousness will *always* remain beyond the parameters of psychological investigation. Indeed, returning for a moment to Pinker's tripartite conceptualisation of it, other authors, notably Chalmers (1995), have argued that the question of how physical processes in the brain give rise to conscious subjective experiences—sometimes called "qualia" (this would be "sentience" in Pinker's terms)—and whether such qualia are ever truly accessible to anyone other than the person having the experience, remains a moot point. One might ask, for example: Is my impression of the colour blue the same as yours? In Chalmers' terms, this is the "hard—others such as Searle (1992) might say intractable—problem" of consciousness, in comparison with access awareness and self-awareness, domains that lend themselves slightly more readily to experimental enquiry.

CONSCIOUSNESS AND NEUROPSYCHOLOGY

In this section we briefly review some of the material described elsewhere in this book that we consider to inform (or be relevant to) ideas about consciousness. To avoid unnecessary duplication, we simply list these to enable readers to refer back to such "points of interest" as they wish:

- In Chapter 1 we described some recent research on a region of medial parietal lobe known as the precuneus. One (of several) feature of this region is that it is more active when the respondent is awake but not actively engaged with an overt cognitive task: during meditation for example. It also becomes more active when there is a task requirement to manipulate imagery from a personal viewpoint or perspective. We suggested that a prudent interpretation of the functional significance of the precuneus may be that it is involved both in supporting self-referential mental representations and more generally in the modulation of consciousness, or even as an element in a wider consciousness network.
- In Chapter 3 we discussed some of the consequences of undergoing the split-brain procedure. One of the more intriguing findings to emerge from this work was that after surgery, the right and left hemispheres sometimes appeared to function as separate conscious entities. An early illustration of this was provided by Sperry (1968) who reported the anecdotal experience of a split-brain patient perplexed to be reaching into her cupboard with her right hand for a pink dress, only to find her left hand then reaching in for a blue one. In another example, a patient could not explain why he was drawing a picture of a car with his left hand; the actual reason was that an image of a vehicle had just been briefly presented to his (non-speaking) right hemisphere. Such observations initially prompted both Sperry and Gazzaniga to suggest that split-brain patients had dual consciousness; although Gazzaniga et al. (2002) later revised his views by suggesting that in fact only the left hemisphere is able to engage in "high-level" consciousness, roughly equivalent to Pinker's "self-knowledge"—an idea that we briefly return to towards the end of this chapter.
- In Chapter 4 we described the phantom limb phenomenon, and we suggested

a number of mechanisms that might explain how it arises. Clearly people with "phantom" experiences would normally claim to have unimpaired consciousness, but their experiences are relevant to this discussion because such individuals develop a conscious (sentient) awareness for something that is, in fact, absent: a limb, breast, or genitals for example. Moreover, "dissociative-like" experiences can quickly be induced in intact individuals (as described in Box 4.2). These two examples illustrate that conscious awareness is not inextricably linked to sensory or even perceptual processing, but is in fact some way removed from both.

- In Chapter 7 the issue of consciousness cropped up several times in our review of memory and amnesia. First (as we noted earlier), the central executive component of working memory in Baddeley's model is widely regarded as an attentional control mechanism, and there has been an implicit assumption that the system as a whole plays a role in consciousness (Baddeley, 2001). Second, review of cases like HM suggests that amnesia may, in some instances, be restricted to remembering that depends on conscious retrieval of material, with "procedural memory" being preserved. And third, this debate has been broadened into consideration of other distinctions between declarative and non-declarative memory. Three experimental procedures—priming, classical conditioning, and implicit learning—have been used to explore effective memory (which does not appear to require conscious awareness) in healthy individuals.
- In this chapter we have reported several instances of abnormal or dysfunctional consciousness in the context of attention; hemineglect and Balint's syndrome are just two examples. In crude terms these disorders represent impaired conscious awareness (here we see the intimate link between consciousness and attention) for half, or all, of the visual field. Note also that in hemineglect at least, closer observation of the nature of the deficit again raises questions about the extent to which information on the neglected side is, in fact, being processed semantically despite not registering consciously.
- In Chapters 10 and 11 we will encounter further examples of neuropsychological cases or phenomena that inform particular aspects of consciousness, especially in Pinker's third domain of "self-knowledge". Damage to specific regions of the frontal lobes (medial orbital regions in particular) can impair appropriate social functioning (as in the case of Phineas Gage). Dorsolateral damage can affect access to information and thus "self-knowledge". And more widespread frontal damage (probably including damage to the anterior cingulate) can impair executive control more generally. The point of these examples is that deficits are apparent without the individuals being consciously aware of them. In the case of impaired social functioning this can, of course, have serious if unintended consequences, leading to confrontations with the police or worse.

INTERIM COMMENT

We have identified the above areas of interest to underline our earlier point that many of the things that neuropsychologists are interested in *say something* about the nature of (impaired) human consciousness. In the following section we

consider some additional examples of psychological research (not reviewed elsewhere in this book) which also inform current thinking about consciousness. We hope we can convince you that no matter how difficult it may be to do research on consciousness, to continue to ignore it on the grounds that it is beyond investigation altogether would be misleading, if not negligent. On the contrary, the examples in both the previous section and the one that follows show that researchers are now beginning to chip away at the "consciousness edifice", and make real progress in the process.

However, two general points should be made before the next section. First, despite our intuitive sense of the importance of consciousness, we need to be aware that a vast amount of psychological processing occurs without conscious awareness. Having learned to drive a car, for example, you do not re-run the conscious agonies of coordinating your interaction with the clutch, brakes, and steering every time you get into a vehicle in the way you did when you were learning to drive. In fact the process of acquiring skills is marked by the gradual replacement of conscious (deliberate) control with more automatic control (Shiffrin & Schneider, 1977) which can be plotted and observed using functional imaging techniques (Petersen et al., 1998). If we go back to the driving analogy, you may well have experienced arriving safely in your car at your destination without very much (or even any?) recollection of the journey there (see Norman and Shallice's ideas on supervisory attention in Chapter 11). Second, we are also generally oblivious to (i.e., not consciously aware of) the intermediate component stages in most psychological processes in which we routinely engage. For example, we are not aware of the process of feature binding that takes place in the course of object recognition (Humphreys & Riddoch, 2001). Our sentience (to use Pinker's term again) is of the complete object (an antique spoon that someone is showing us for example), which, perversely, we may then begin to analyse consciously in a deconstructive way in terms of its individual features: how shiny it is, its feel, size, value, and aesthetic appeal, and so on. Similarly, the act of "reading" tends only to engage consciousness at the final stage of semantic processing of whole words or even sentences, not, for example, during feature detection of individual letters, although reading clearly involves letter identification.

An excellent example of how conscious awareness is about the complete "percept" rather than any intermediate processes leading to it is provided by the famous Rubin vase/silhouettes illusion (see Figure 9.16). No matter how many times you have seen it (and therefore know the trick), your brain does not allow you to see intermediate or mixed-up percepts; you either see the vase or the two faces. (See Windmann et al., 2006, for a review of attentional control over this and other bi-stable visual stimuli.)

PSYCHOLOGICAL OBSERVATIONS RELEVANT TO CONSCIOUSNESS

We now turn to consider briefly three paradigms from experimental psychology of relevance in our consideration of the nature of consciousness. These are *the readiness potential*, *attentional blink*, and *inattentional/change blindness*, which we describe below, and we comment on their importance for consciousness in the interim comment section that follows.

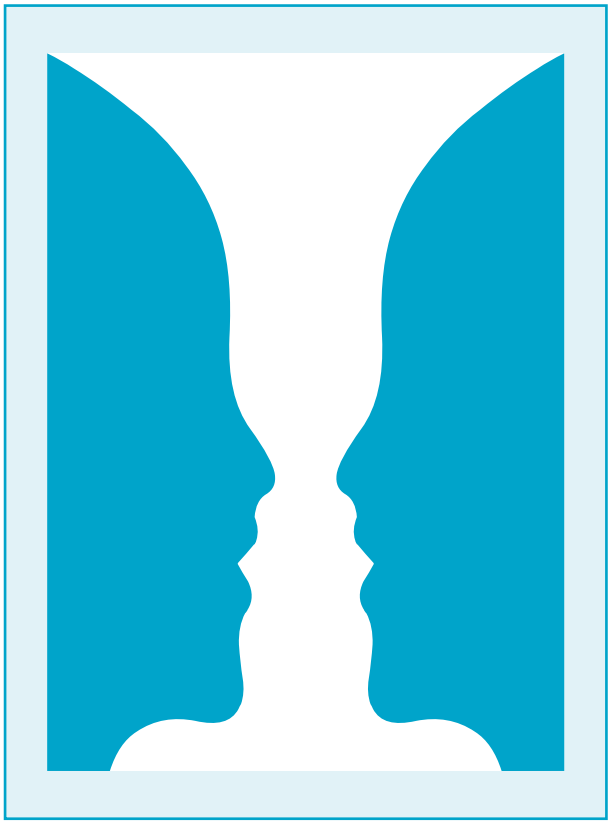


FIG. 9.16 The Rubin faces/vase illusion, one of several bi-stable illusions. At any one time, viewers report seeing either the faces or the vase, never an intermediate or ambiguous image.

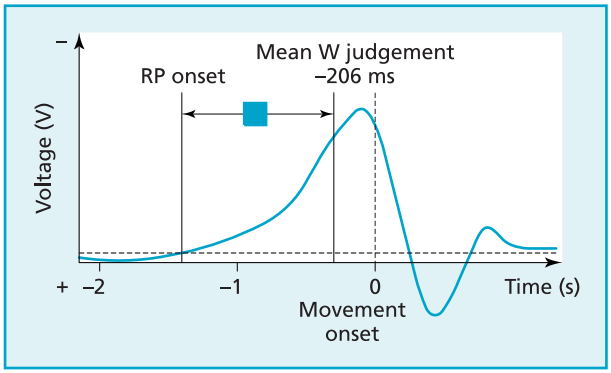


FIG. 9.17 Pooled results of Libet et al.'s study of the readiness potential (RP). The RP can be detected up to 1.5 seconds before movement onset, and up to 1 second before reported conscious awareness of intention to move (W judgement).

The readiness potential (bereitschaftspotential)

It is possible to record a negative ERP (usually from the SMA area of the frontal lobes) that builds up over a period of 1 or 2 seconds prior to an intended movement. Libet et al. (1983) adapted this paradigm by inviting respondents to make periodic key presses "whenever they felt the urge to", and additionally to indicate, by noting the position of a hand on a slow-moving clock face (which eliminated movement reaction time), the point at which they became "aware" of their "intention" to make a movement. Typical results for this experiment are shown in Figure 9.17. They indicated that conscious awareness of the intended movement typically occurred about 200 ms before the movement itself. A rather more surprising finding was that the readiness potential was detectable (as a negative-going voltage change) some 350 ms or more before this. In other words, conscious awareness of the intention to make a movement occurred at least a third of a second *after* electrical changes anticipating the movement were clearly measureable in the SMA. Sirigu and colleagues (2004) have recently confirmed Libet et al.'s original findings. Haggard and Eimer (1999) repeated this experiment with a further modification in which respondents could also choose which hand to make the movement with. Separate potentials were, additionally, recorded for each hand/hemisphere. Haggard and Eimer confirmed the occurrence of a readiness potential several hundred milliseconds before awareness of the intention to move, although "awareness" corresponded more closely to the lateralised potentials relating specifically to the particular hand about to make the movement. Conscious awareness thus seems to be more closely time-linked to selection of a specific movement than the general imperative to move, although it still came after it.

Attentional blink

In the simplest version of this paradigm, a respondent views pairs of visual stimuli such as short words or four-digit numbers. Each presentation appears only briefly (for about one-tenth of a second or less) and is immediately followed by an irrelevant mask (to eliminate visual after-traces

called iconic images) before the second image is shown. If the gap between successive stimuli is less than 500 ms and the respondent has to "attend" to the first of the two images, there is a good chance that the second image will not be reported at all. For obvious reasons, this phenomenon has been dubbed "attentional blink". A recent study by Sergent et al. (2005) employed this paradigm and additionally recorded separate ERPs to both the first and second images. The researchers found that when the interstimulus interval (ISI: the gap between the first and second image) was about 250 ms, detection of the second image was severely compromised compared to another condition in which the ISI was about two-thirds of a second. Poor detection was related to ongoing processing of the first image, as reflected by the continuing ERP to it, and the absence of a separate fully developed ERP to the second image. In other words, respondents failed to detect the second image because they were still "consciously" processing the first. This effectively occupied their attention, causing them to neglect the second image. A schematic diagram illustrating Sergent et al.'s stimulus sequence is shown in Figure 9.18.

Inattentional/change blindness

Inattentional blindness may occur when a participant is paying attention to one particular task (say, a visual search task) but other non-task-relevant stimuli are periodically presented. When later quizzed as to whether anything else (other than the visual search stimuli) had appeared on screen, a significant proportion of participants will say no. Simons and Chabris (1999) described a dramatic and

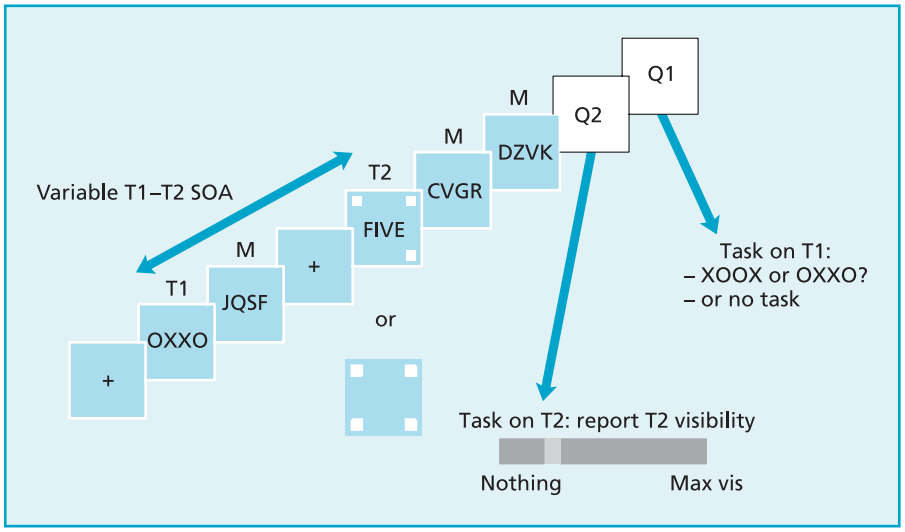


FIG. 9.18 Sergent et al.'s stimulus train (2005). Each trial involved the same sequence of stimuli. The critical ones are those presented at T1 (either OXXO or XOOX) and T2 (a number [FIVE in this example] or BLANK). Both are followed by a mask (M). The sequence is completed by two question cards: Q2 asks whether anything was seen at T2, and Q1 asks what was seen at T1. In this study the time gap between T1 and T2 was either 258 ms or 688 ms. Source: Reproduced by permission from Macmillan Publishers Ltd: *Nature Neuroscience* (Sergent, Baillet, & Dehaene, 2005), © 2005.

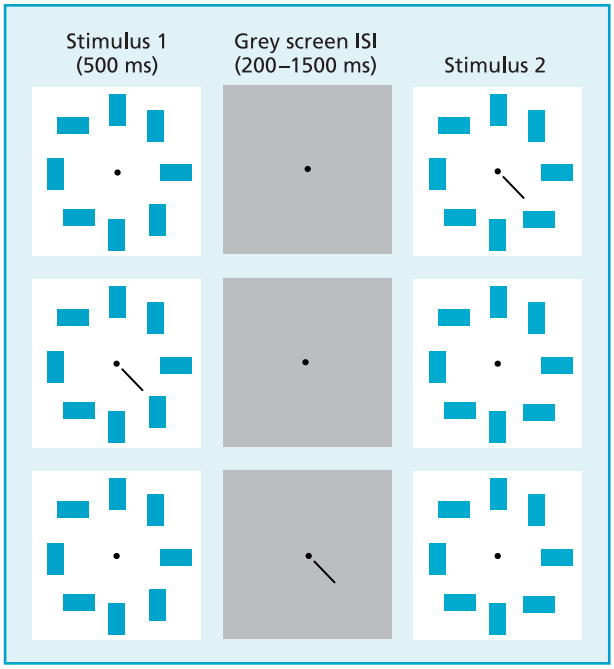


FIG. 9.19 The stimuli used in Simons' (2000) study of change blindness. Top row: when the cue is indicated by the pointer with the second image, change blindness is often apparent. Bottom row: when the cue is indicated as soon as the first image has been replaced with the grey screen, there is a marked reduction in change blindness. (For completeness the middle row shows Simons' control condition when attention was directed with the initial stimulus and little or no change blindness resulted.) Source: Simons, D. J. (2000). Current approaches to change blindness. *Visual Cognition*, *7*, 1–15. Reproduced with permission.

humorous example of this phenomenon. Their respondents had to watch a short film of two teams of people playing "catch" with a ball: they were told to pay particular attention to just one of the teams. At one point, a person in a gorilla suit walked "into shot", beat their chest in authentic gorilla style, and walked off again. Despite this intrusion, about half the observers failed to spot anything untoward!

Change blindness is a closely related phenomenon that has recently been examined by Simons (2000) and reviewed by Rensink (2002). A respondent may be required to view a stimulus array similar to that shown in Figure 9.19 (top left-hand image) for 500 ms. This is followed by a grey screen mask which lasts for up to 1.5 seconds, to be followed by a second array that is either identical to, or subtly different from, the initial array (see Figure 9.19 right-hand image). Even when directed to the part of the array that might have been changed, about 50% of respondents failed to notice any difference. This "change blindness" should be compared with the situation in which the respondent is cued (with an arrow) to focus on part of the array when the grey mask appears (the first array has, of course, disappeared at this point). Now respondents nearly always correctly identify a change (see bottom row of Figure 9.19). "Spot-the-difference" games of the sort that sometimes appear in popular magazines essentially tap the same phenomenon.

INTERIM COMMENT

At first glance, these three examples may seem to be of little interest for students of consciousness. However, each actually says something rather important: Libet et al.'s observations indicate that changes in the brain related to an intended action precede conscious awareness of the intention to act. This has important consequences for people who believe in **free will** because it strongly suggests that the "intention" is already being processed before awareness kicks in. It also undermines a long-standing theory of how the brain works, attributable to Spinoza (1632–1677), and known as dual-aspect theory. This argues that the mental state of consciousness and physical brain activity form two sides of the same coin, so the temporal delay seen in Libet's paradigm would not be predicted by it (there should be no delay). However, we see that conscious awareness still has a potential benefit in this situation because it occurs in time to allow the respondent to stop (or modify) an action before it actually occurs.

Attentional blink shows us that conscious awareness of a stimulus (access awareness in Pinker's scheme) involves effort and uses up resources, which may curtail or even preclude attention to succeeding stimuli. Remember that

KEY TERM
Free will: A philosophical term for the capacity of rational agents to choose a course of action from among various alternatives.

attentional blink *only* operates if the person has to process (attend to) the first image. The phenomena of inattentional and change blindness have been interpreted as showing that, contrary to our intrinsic sense of having a complete image of *the world before us*, we actually have a somewhat partial view which, according to Lamme (2003), is nevertheless given privileged status by attention. If that status is achieved, other stimuli may go unnoticed. Thus once again we see the intimate relationship between conscious awareness and attention, and we return to this issue below.

CONSCIOUSNESS AND THE BRAIN

Two methods lend themselves to establishing the areas of the brain that subserve consciousness. First, we can simply compare activations in the brains of individuals with impaired, disordered, or altered consciousness to those recorded from normally conscious people. Second, we can compare, within individuals, levels of activation when they are performing a task (usually something fairly demanding) presumed to involve consciousness with levels of activation when they are resting. Although neither method is foolproof, reassuringly similar findings emerge from each line of research. Baars and colleagues (Baars, Ramsoy, & Laureys, 2003) employed the first, admittedly somewhat crude, method in measuring functional changes (reduced PET activation compared to conscious control participants) in four types of unconsciousness: coma, persistent vegetative state, general anaesthesia, and sleep. Their findings are illustrated in Figure 9.20. In the three clinical states, fairly widespread bilateral hypo-metabolism was seen in a distributed network comprising dorsal and medial frontal and parietal regions. Similar, though less pronounced, reduced metabolic activity was observed in healthy individuals during slow-wave sleep.

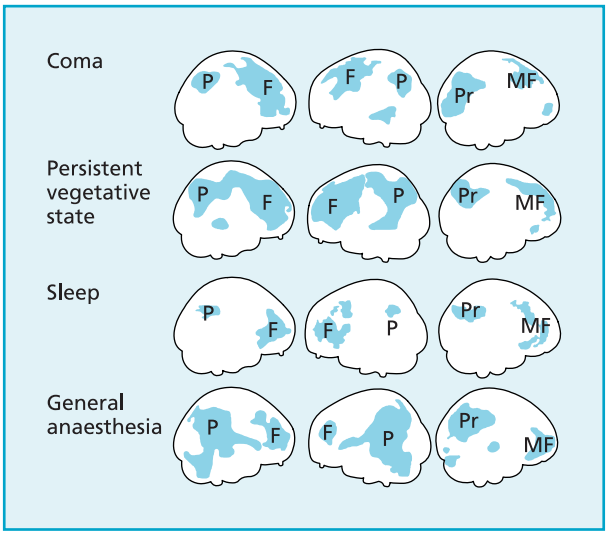


FIG. 9.20 Regions of hypofunction in different types of non-consciousness (Baars et al., 2003). Reduced PET activations (compared to conscious control participants) in four types of unconsciousness: coma, persistent vegetative state, general anaesthesia, and sleep. There is widespread bilateral hypo-metabolism in each clinical state in a distributed network comprising dorsal and medial frontal and parietal regions. Similar, though less pronounced, hypofunction was seen in healthy individuals during slow-wave sleep. Source: Baars, B. J., Ramsoy, T. Z., and Laureys, S. (2003). Brain, conscious experience and the observing self. *Trends in Neurosciences*, *26*, 671–675. Adapted with permission, © Elsevier, 2003.

Petersen et al.'s (1998) study, mentioned earlier, employed the second method. They compared PET activations in verbal (word generation) and spatial (maze-learning) tasks when respondents were naïve to each task, thus necessitating plenty of conscious effort, with activations once the tasks were learned. Their findings are illustrated in Figure 9.21. Although different regions were activated in the two tasks, frontal and parietal activation, common to both tasks during skill acquisition, clearly diminished with practice, implicating their involvement in conscious effort but not well-rehearsed tasks.

Obviously, Petersen et al.'s study is not specifically about consciousness; we are inferring that different levels of conscious effort would be required at different stages of skill acquisition, and participants were, of course, conscious throughout.

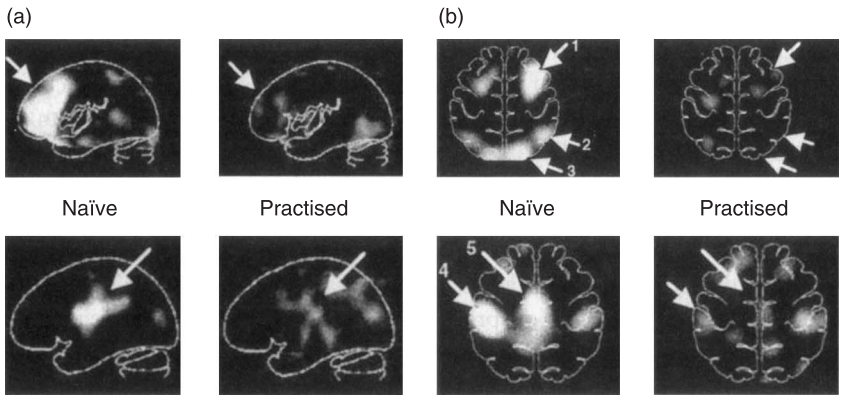


FIG. 9.21 Petersen et al.'s (1998) study of brain activation at the beginning of a task and once it has been learned. PET activations in (a) a verbal task and (b) a spatial task when respondents were naïve to each task (first and third columns) and when they had learned them (second and fourth columns). Frontal and parietal activation, common to both tasks during skill acquisition, clearly diminished in relation to reduced need for "conscious effort" once the skill was acquired. Source: Petersen, S. E., Van Meir, H., Fiez, J. A., and Raichle, M. E. (1998). The effects of practice on the functional anatomy of task performance. *Proceedings of the National Academy of Sciences*, *95*, 853–860. Reproduced with permission.

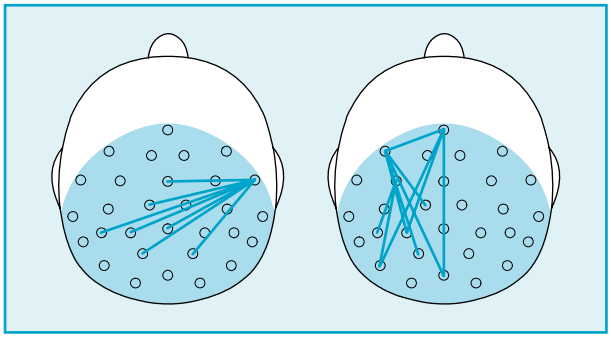


FIG. 9.22 Rodruguez et al.'s (1999) study of EEG phase synchrony to face and non-face stimuli. A schematic diagram depicting EEG desynchrony (in the 180–360-ms latency period) in the left figure in response to the random doodle, and greater EEG synchrony in the right-hand figure during the same latency period to the image of a face. Source: Reprinted by permission from Macmillan Publishers Ltd: *Nature* (Rodriguez et al., 1999), © 1999.

Indeed, differentiating the effects of consciousness from other psychological processes such as familiarity, learning, attention, and so on is a particular problem for this sort of research. To try to circumvent this problem, McIntosh, Rajah, and Lobaugh (1999) devised a PET study involving a simple visual discrimination task in which participants learned to respond to one stimulus and ignore a second. There were, however, two tones, although respondents were not explicitly briefed about these: one signalled the imminent presentation of a visual stimulus and the other the absence of a stimulus. There were three blocks of trials to enable the researchers to plot any associative learning between auditory and visual stimuli; participants were subsequently divided into those who noticed the association and those who did not. The most pronounced differential level of activity to tones between the "aware" and "unaware" groups was recorded in the left prefrontal cortex (BA 9), suggesting that this region was related to conscious awareness of the significance of the tones. However, this formed part of a more extensive circuit which included the right prefrontal cortex, and superior temporal lobes, cerebellum, and occipital cortex (all bilaterally).

For a more detailed analysis of the temporal effects of conscious processing researchers employ EEG (or ERP) methods. For example, Rodriguez et al. (1999) used a 30-electrode EEG procedure to measure the degree of neuronal synchrony (coincidental firing of neurons at different cortical locations) to images that resembled faces when seen "the right way up" but appeared to be meaningless "doodles" when inverted. Their findings are illustrated schematically in Figure 9.22. Marked EEG synchrony was only seen for the faces. This was detectable for

about 350 ms after the image had been shown and ranged over extensive regions of occipital, parietal, and frontotemporal cortex, especially on the left side. We should, however, sound a note of caution at this point because, whereas at one time long-range synchronous firing was thought to be *the* neuronal signature of consciousness (Crick & Koch, 1990), it is now regarded as a necessary *but not sufficient* feature of it, possibly related to "feature binding" (Enger & Singer, 2001), as happens when a viewer puts together facial features to perceive an entire face.

Other researchers have emphasised one additional feature of neuronal activation that distinguishes between conscious and unconscious experience—that it must be "recurrent" (i.e., bidirectional, also sometimes called "re-entrant"). Imagine a visual input exciting neurons further and further forward in the ventral processing stream (see Chapter 8): researchers think that conscious recognition of the stimulus will nevertheless only occur when recurrent excitation (back in the direction from which it came) occurs. This can be illustrated very easily with reference to backward masking. A mask presented about 40 ms after a target stimulus will prevent the target from being consciously perceived if its (the mask's) forward progress along the ventral pathway is sufficiently forceful to inhibit any recurrent processing of the target (Dehaene et al., 2001). Astonishingly, this can happen even if the mask itself is presented so briefly as to be invisible (Lamme, Zipser, & Spekreijse, 2002).

In summary, brain studies of consciousness prompt the following tentative conclusions: Consciousness seems to be associated with widespread increases in activation, sometimes likened to "amplification", in various cortical regions (and subcortical structures, particularly the thalamus, have also been implicated: e.g., Tononi & Edelman, 1998). The extent of this activation/amplification will vary depending on the nature of the task, although conscious effort invariably recruits frontal (and anterior cingulate) regions in addition to other temporal and parietal regions. At the neuronal level, long-range synchronous processing seems to be a necessary, but not sufficient, condition for consciousness. Extensive recurrent processing, on the other hand, may be both necessary and sufficient for it. A stimulus that fails to achieve such processing is unlikely to be consciously perceived.

GLOBAL WORKSPACE THEORY (GWT)

GWT emerged almost 20 years ago (Baars, 1988) as a conceptual model of high-level cognitive processing. Over the intervening period, as research into consciousness has gathered pace, both scientists and philosophers have realised that GWT may provide a heuristic account of the neural architecture of consciousness itself. Despite this, it is important to realise that GWT presently remains a conceptual rather than physiological model. Moreover, although we will describe the general features of GWT, many questions, some of which we also identify in Box 9.2, have yet to be satisfactorily answered. In other words, although there is considerable interest in GWT as a model of consciousness, there are several versions of it. We should also note that GWT is a "work in progress": accounts of it by the same authors have, in some instances, changed significantly over time (e.g., Dehaene, Kerszberg, & Changeux, 1998 vs Dehaene et al., 2006).

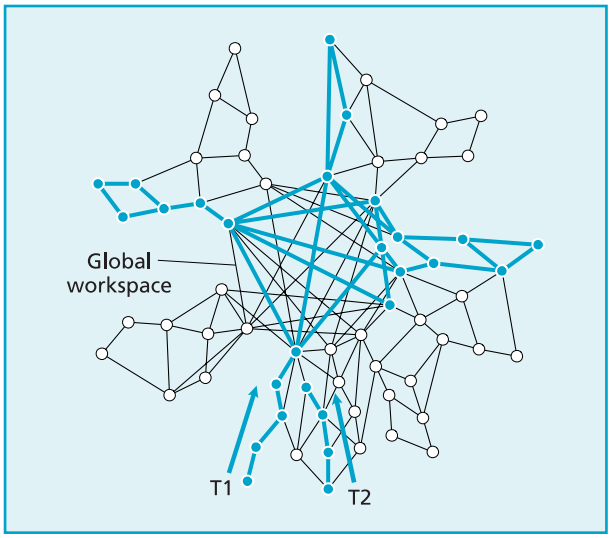


FIG. 9.23 Dehaene's (2003) schematic of a global workspace network. Two stimuli (T1 and T2) compete for entry into the global workspace (depicted by the interconnected network). T1 gains access and is broadcast throughout the network. T2 is consequently prevented from accessing the workspace. Adapted from Dehaene, S., Sergent, C., and Changeux, J.-P. (2003). A neuronal network model linking subjective reports and objective physiological data during conscious perception. *Proceedings of the National Academy of Sciences*, *100*, 8520–8525. Reproduced with permission.

A schematic diagram of a global workspace is shown in Figure 9.23. It is envisaged to be an extensive neuronal network probably involving prefrontal, anterior cingulate, and other thalamo–cortical interactions (as illustrated in Figure 9.24). The basic idea of GWT, as it applies to consciousness, is that at any given time we only have conscious access to a small proportion of all ongoing cognitive processing and there is a constant competition between (unconscious) cognitive processes for access to consciousness. These competing influences can, additionally, be biased by top-down (attentional) or bottom-up influences such as stimulus salience (a loud noise or a bright image). Cooney and Gazzaniga (2003, p. 162) have referred to the conscious awareness that results as:

> *. . . a fluctuating stream of transiently self-sustained, self-modifying workspace states, the characteristics of which are postulated to determine the contents of the subject experience of the individual . . .*

Access to the global workspace is not *just* competitive: it operates on a "winner-takes-all" basis. However, although conscious experiences may have fleetingly "won out" to reside here, their occupancy of the workspace is likely to be short-lived as other competing interests gain assent. Nevertheless, occupying the workspace does bestow two privileges: first because "winner-takes-all" operates, brief competing influences will, in effect, be prevented from gaining access unless they can "trump" the current "privileged" contents. This can be seen very clearly in the fate of the second stimulus in the "attentional blink" phenomenon, and is illustrated in Figure 9.23 by the failure of T2 (the second stimulus) to gain access to the workspace currently occupied by T1 (the first stimulus). Second, material currently in conscious awareness is "privileged" in the sense that it can be "broadcast" across the global workspace to be available to (and perhaps to influence) other modular processors such as those concerned with language output or attention.

Thus far our account of GWT would (we hope) be widely accepted by most consciousness researchers. The arguments begin (and quickly go way beyond the remit of this book) when we look more closely at the overlap between workspace occupancy and conscious awareness. To give just a flavour of the ongoing debates, consider the perspective of Baars and colleagues (Baars, 1998). They use the metaphor of "the theatre of the mind" to represent the sum of neuronal processing in the brain: Actors on the stage represent the potential contents of consciousness, and the "spotlight" of attention, falling on a few or even just one actor, represents full conscious awareness. In this scheme, attention is the means of bringing material into consciousness (the attentional spotlight). Baars later added the "active working memory elements" to his model (Baars, 2003), subsequently clarified by Baars and Franklin (2003) as encompassing "reportable" mental

rehearsal and visual imagery, and the conscious elements of the central executive. This view has been even more forcefully stated by Maia and Cleermans (2005) who have suggested that attention, working memory, cognitive control (the central executive again?), and consciousness depend on a single mechanism, conceptualised as a global workspace with strong top-down control from the prefrontal cortex.

Now consider an alternative perspective such as that shared by psychologist Lamme (2003) and philosopher Block (2005). They have argued that there is a need to distinguish between the core and fringes of consciousness—called, by Lamme, access awareness and phenomenal awareness respectively. Access awareness would be equivalent to Baars' spotlight, but phenomenal awareness is proposed to account for instances when it seems that information is briefly available to the individual but "forgotten" or "erased" before it can be reported. (In fact, this also resonates with Pinker's distinction between *access to information* and *sentience* or basic phenomenal awareness.) For example, in Simons' change blindness study reviewed earlier, a cue presented *after* the first array had been replaced with the grey screen effectively eliminated the effect (i.e., no change blindness). So remnants of the no-longer-displayed array must have been briefly "accessible" when the cue appeared. Lamme, in fact, likened phenomenal awareness to "iconic" memory, whereas access awareness was likened to working memory. A consequence of Lamme's ideas is that many inputs may reach the conscious state of phenomenal awareness, and attention selects from these the inputs that will be consciously reported.

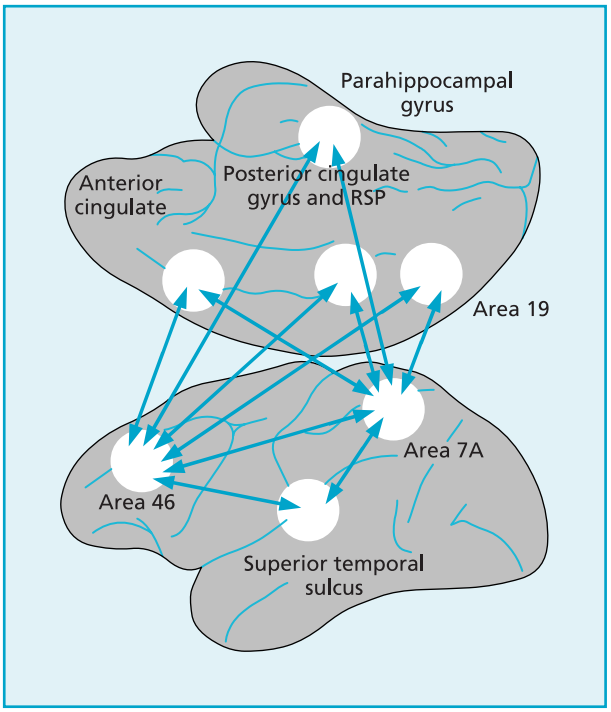


FIG. 9.24 Anatomical components in a global workspace. The global workspace is envisaged to extend bilaterally across much of the cerebral cortex. With permission, adapted from Goldman-Rakic (1988), the *Annual Review of Neuroscience*, *11*, © 1988 by Annual Reviews.

To bring the debate up to date, consider the conflicting views of Dehaene et al. (2006) and Koch and Tsuchiya (2007). Dehaene et al. have argued that only true consciousness permits "reportability". If a respondent cannot provide a report of an event or stimulus, it cannot be considered to have entered consciousness. On this basis, Lamme's "phenomenal" consciousness is not true consciousness, and Dehaene et al. prefer to use the term "preconscious" for this type of processing. Information in preconsciousness nevertheless may cause "recurrent" excitation in the ventral stream which may last for a short period (perhaps 1 or 2 seconds) after removal of the stimulus, and may thus be accessible to true consciousness if top-down influences (such as a relevant cue) provide the necessary attentional amplification. In other words, a "trace"—in effect, a fleeting iconic (visual) or echoic (auditory) memory—may remain, and be available and accessible to true consciousness if attention is directed towards it, which is exactly what happens in the Simons "change blindness" paradigm. Incidentally, in this model, even recurrent excitation would be necessary *but not sufficient* for conscious awareness, which also requires top-down directed attention. As in Baars' model, attention is a mechanism for permitting entry into the global workspace, and thus into full

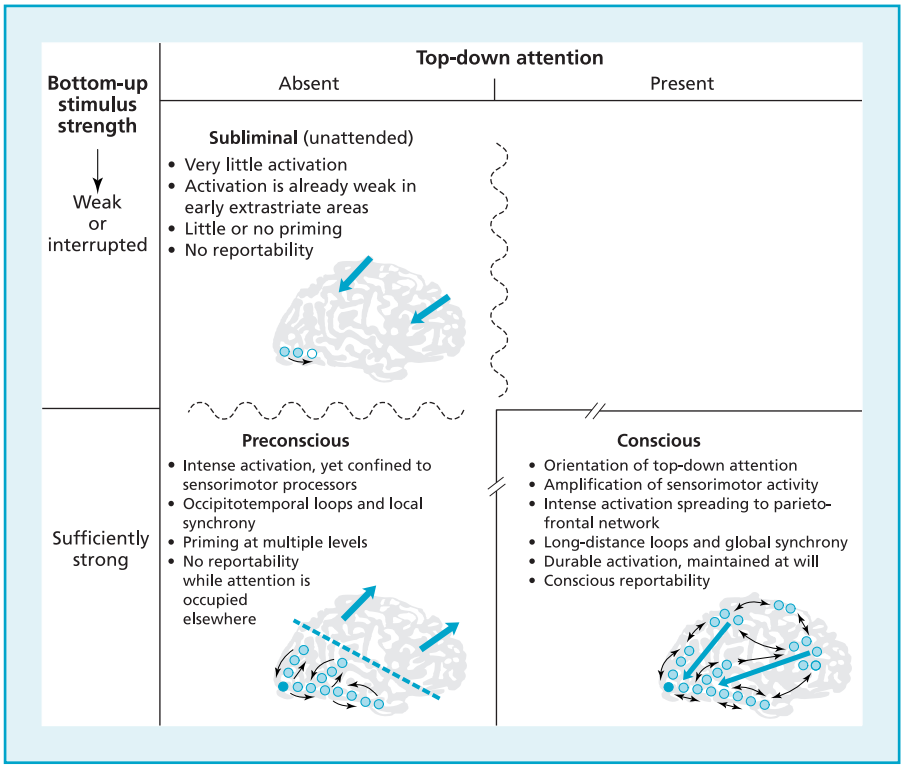


FIG. 9.25 Dehaene et al.'s (2006) tripartite model of consciousness and attention. Reportable conscious awareness is only possible if stimulus strength is sufficiently strong and top-down attention is directed to amplify it. If attention is directed elsewhere, strong stimulus strength alone will not be sufficient to bring about conscious awareness. However, this state of preconsciousness may lead to full conscious awareness if attention is redirected sufficiently quickly. Some stimuli never acquire sufficient strength to enter conscious awareness and are likely to remain subliminal and unattended. Source: Dehaene, S., Changeux, J. P., Naccache, L., Sackur, J., and Sergent, C. (2006). Conscious, preconscious and subliminal processing: A testable taxonomy. *Trends in Cognitive Sciences*, *10*, 204–211. Reproduced with permission, © Elsevier, 2006.

consciousness, and the boundary between preconsciousness and full consciousness is sharp. Dehaene et al.'s (2006) model, which, for completion, also includes an illustration of subliminal (non-conscious) processing, is represented in Figure 9.25.

Koch and Tsuchiya, on the other hand, take issue with the idea that consciousness should be defined by reportability, citing a number of instances when attentional processing is apparent without consciousness: Male and female nude images attract the viewer's attention even when the images are rendered invisible (and thus unreportable) by means of a masking procedure called (appropriately perhaps) flash suppression (Jiang et al., 2006). Similarly, a degree of conscious processing seems possible with minimal top-down attention: as, for example, in dual-task studies where a core task that is occupying attention does not necessarily preclude correct identification of a briefly presented image in the periphery (Braun & Julesz, 1998).

At this stage of the debate, it is difficult to know whether the preceding arguments are a case of "splitting hairs" or the delineation of a crucial distinction

with profound consequences for cognitive psychology and neuropsychology. After all, almost everyone agrees that the contents of our conscious experience are ordinarily constrained by what we pay attention to. However, one additional piece of evidence garnered by the oldest psychological research method of all, introspection, suggests to us that consciousness is not quite the black–white issue that Dehaene et al. have implied: When you scan a visual scene (panning round a room for instance) you remain aware of parts of the visual field beyond your focus of attention, although your ability to provide a verbal description of peripheral items might be impoverished compared with a description of your current focus of attention.

So the debate continues, and both "attention" and "consciousness" still resist clear and unequivocal definition. However, it is reassuring to note that psychologists, neuropsychologists, neuroscientists, and philosophers are collaborating in efforts to clarify these interconnected issues once and for all. We have identified some of the questions currently attracting attention in Box 9.2.

Box 9.2 Unresolved issues relating to GWT and consciousness

- What is the exact relationship between GWT and attention?
- What is the exact relationship between GWT and working memory?
- Are there different types/levels of consciousness within GWT?
- What, exactly, is the relationship between synchrony, recurrent excitation, and GWT?
- Must the global workspace itself always involve frontal activations to cause conscious awareness?

SELF-KNOWLEDGE/AWARENESS

Pinker's third component of consciousness is self-knowledge or awareness. This *should* be of interest to neuropsychology because as we have seen, for example in our review of hemineglect, brain damage may lead to a revision of the parameters of self-awareness by rendering patients "indifferent" to half their visual field or, in the case of anosognosia, one side of their own body. However, in the clinical setting, leaving aside the impoverished self-awareness seen in gross neurological disease (such as late-stage Alzheimer's), psychiatry has in fact arguably shown more interest in self-awareness. Impairments of this sort are apparent in cases of body-dysmorphic disorder (Albertini & Phillips, 1999), other delusional disorders (Blakemore & Frith, 2003), and, most intriguingly, in certain cases of schizophrenia (Spence et al., 1997; Stirling, Hellewell, & Ndlovu, 2001).

Earlier in this section, we mentioned that their observations of post-recovery split-brain patients initially led both Sperry and Gazzaniga to speculate about the possibility that such individuals experienced a form of dual consciousness. Because of concerns about the authenticity of the early findings, Gazzaniga has subsequently revised his views, developing an idea earlier mooted by Bever (1983) that the left hemisphere has an enhanced role in high-level self-awareness, as both an "interpreter" of why events (both external and internal) occur, and a selector

of appropriate responses (Gazzaniga et al., 2002). As Gazzaniga has argued, such a system would offer enormous adaptive benefit, enabling information about different events to be woven together into a causal chain to guide future behaviour.

Gazzaniga's evidence is somewhat anecdotal (mostly from split-brain patients), but worthy of review nonetheless. For example, in the small number of patients with both left and right hemisphere language skills, the left hemisphere is better at making associative links between pairs of stimuli. When asked to choose one of six possible words linking two tachistoscopically presented words ("bleed" would, for example, link "pin" and "finger"; "oven" would link "bread" and "roast"), left hemisphere performance was significantly better than right. In another tachistoscopic study, patients were briefly presented with images to the right and left of a fixation point: a snowy scene to the left (going to the right hemisphere) and a chicken's foot to the right (going to the left hemisphere) for example. Then they were asked to choose one cartoon from an array of pictures on the table in front of them to go with each of the tachistoscopically presented images. In this example, one patient chose a picture of a chicken with their right hand and that of a shovel with their left, both ostensibly correct. But when asked why they had made those choices, the patient confabulated (made up part of their answer) by saying the chicken went with the chicken foot (correct) and the shovel was needed to clear out the chicken shed (incorrect). In a final example, if certain commands were flashed to the right hemisphere (i.e., left of the fixation point), some patients could read the words and follow the command, to laugh or walk for example. But when asked why they were laughing to themselves or walking out of the room, they generated confabulated answers such as "I just wanted some fresh air". Confabulation was absent when commands were presented to the left hemisphere. In each of these examples it appears that the left hemisphere is interpreting actions initiated by the right, which itself is contributing little to the interpretive process.

Cooney and Gazzaniga (2003) have extended this logic to explain "anosognosia for hemiplegia" (unawareness of left-sided paralysis, usually associated with right hemisphere damage): If the area of the brain that normally signals a problem (i.e., right parietal lobe) has itself been damaged, there is, in the authors' words, "no system to file a complaint" (Cooney & Gazzaniga, 2003, p. 164). As the patient no longer registers the existence of "left limbs", the intact (left hemisphere) interpreter system concludes that everything must be OK!

INTERIM COMMENT

Intriguing though these ideas are, it is difficult to evaluate Gazzaniga's hypothesis for two related reasons: First, the proposal is primarily derived from observations of a very small number of split-brain patients (we encountered this problem in Chapter 3). Second, the findings themselves rely heavily (though not exclusively) on verbal report, which, for most split-brain patients, means output from the left hemisphere. So the hypothesis could be confounded given the functional isolation of the left from the right hemisphere in this syndrome. Extending the hypothesis to include neurological conditions like anosognosia does not provide a true test of it (although the findings are certainly consistent with it) because once again most forms of hemineglect are related to right-sided damage. Finally,

although some brain-damaged individuals are unaware of their own cognitive impairments and also prone to confabulation (Joseph, 2000), many with pronounced left hemisphere damage are both well aware of their impairments and "enjoy" full consciousness. An "interpreter" function for the left hemisphere therefore remains, for the time being, an interesting possibility rather than an established fact.

NOTE

1 Some of Raederscheidt's self-portraits can be viewed at www.physpharm.fmd.uwo.ca/undergrad/sensesweb/

CHAPTER SUMMARY

Attentional mechanisms allow us to make the most of the cognitive limitations of the brain, which has evolved to permit detailed processing of a relatively small proportion of all the potential incoming sensory (and self-generated) material to which it has access. As researchers have examined attentional processes it has become clear that "attention" is not a unitary phenomenon, and it probably needs to be partitioned into a series of related but distinct domains.

Researchers have made progress in examining the processes involved in selective attention, and an evolving view is that the diverse findings (relating to early/late and object/space based attention for example) can be best understood if attention is viewed as a resource with a finite capacity. There is continued interest in distinguishing between pre-attentive processes and voluntary orienting in different types of visual search.

Both ERP and functional imaging research confirm that "top-down" (attentional) influences can effect cortical processing within a very short period of time following stimulus onset, and this appears to be a facilitatory one for the selected material. However, both the cocktail party phenomenon and negative priming remind us that certain non-attended material can also influence high-level (semantic) processing.

Several cortical and subcortical structures appear to be involved in mediating attentional processes. Posner's and Mesulam's theories have been further refined by LaBerge (1995, 2000) into a model that distinguishes between bottom-up (automatic/incidental/pre-attentive) and top-down (deliberate/executive) control. There is a growing consensus that top-down attentional processes overlap significantly with the central executive function of working memory.

Recent research into the neurological disorders of hemineglect and Balint's syndrome is reviewed. Particular attention is paid to the underlying pathologies of these conditions in the context of established visual processing streams in the cortex. Corbetta and Shulman's model of attentional control in the brain is described and reviewed in some detail.

Recent developments in our understanding of how the brain might "mediate" consciousness are considered within Pinker's tripartite taxonomy. Material is drawn both from other parts of this book and from experimental work described elsewhere to illustrate that psychology and neuropsychology are making important

contributions to debates about the nature of consciousness. Global workspace theory is introduced as a conceptual model of consciousness, and we offer a flavour of ongoing debates about the parameters of such a system, and implicitly of consciousness itself, and its links to/overlap with attention and working memory.

Finally, we introduce Gazzaniga's ideas about the highest level of human conscious control (an interpreter/integrator function of diverse inputs/outputs) which, he has argued, depends on a left hemisphere located (or biased) region of the workspace.

CHAPTER 10

CONTENTS

10

Emotion and motivation

INTRODUCTION

Emotion is fundamental to human experience. Every action we take, every decision we make, has an emotional context and therefore all our cognitive functions are coloured by our emotional state. Similarly, motivation is crucial to real-life function. We do not perform cognitive operations aimlessly for no reason. We do things that will achieve outcomes that we need or want, or to avoid outcomes that would be harmful or unpleasant. The vast majority of our behaviour is aimed at either obtaining rewards (which can be tangible or more abstract—as we will see, social approval, inclusion in a group, altruism, and perceived status can all be extremely rewarding) or avoiding punishments (which can, again, be tangible or more abstract). Emotional responses are crucial to motivated behaviour; if something elicits positive emotions we will seek it out, while if something elicits negative emotions we will avoid it.

In the 17th century, the philosopher Descartes used the famous phrase "I think, therefore I am" to suggest that thought is what makes us who we are. Three and a half centuries later, in his influential book *Descartes' error*, Antonio Damasio (1994) argued that it is not only thought that defines us, but, more fundamentally, *feeling*. Logical thought does not make us human, rather it is the interaction between what we think and how we feel that is at the core of who we are and what motivates us to behave in the ways we do. Thus to understand human neuropsychology, we must explore the topics of emotion and motivation.

Given that many cognitive neuroscientists now accept the importance of emotion and motivation in the study of behaviour, it is surprising that, until recently, this topic did not have a place in most cognitive neuroscience or neuropsychology textbooks. Indeed, the first edition of this book did not cover the topic. The study of emotion and motivation has been a huge growth area in the last 5–10 years and this is reflected in the inclusion of chapters in the most up-to-date texts. So why have emotion and motivation been sidelined for so long? In his recent book, Ward (2006) argued that traditional cognitive psychology theories were derived from computer-based models of information processing. And computers, of course, do not compute emotions and are not motivated to behave.

This is a reasonable explanation; however other factors may also be important. Most significantly, the advent of brain-imaging techniques has allowed us to access emotional and motivational function in a way that was not previously possible.

Emotions are not easy to measure empirically. People can describe how they feel (or don't feel) and psychologists can observe behaviour and characterise it as normal or abnormal by reference to expected behaviour. However, there is no objective "right or wrong" when it comes to emotion. Patients can be given a memory test, or an attention test, and an objective score can be derived from the number of correct and incorrect responses. In the realm of emotions, quantification is far more difficult. Similarly, although psychologists can qualitatively assess the extent to which a patient is motivated, objectively measuring that motivation is considerably harder. Some attempts to quantify emotional and motivational function will be discussed below.

Functional neuroimaging has revolutionised the study of human emotion and motivation. We can put people in a scanner and measure directly their brain responses to emotional information or to motivational cues. This has allowed us to develop brain-based models of emotional and motivational processing. These models are proving particularly valuable in psychiatry, as most psychiatric disorders are characterised by emotional disturbances. It has also led to new areas of research opening up, in particular the field of "social neuroscience" which considers the basis of interactive and social behaviour, which is so fundamental to human experience. Although social neuroscience is largely beyond the scope of this book, we will briefly consider some of the basic ideas and approaches at the end of this chapter.

DEFINITIONS AND MEASUREMENT OF EMOTION AND MOTIVATION

DEFINING EMOTION

There is a wealth of language available for describing emotions. If you try listing words that describe subtly different emotional states, you will quickly discover just how rich our emotional vocabulary is. When did you last feel happy, sad, pleased, sorry, excited, disappointed, anxious, upset, elated, nervous, frightened, optimistic, disgusted, outraged, angry, embarrassed, smug, or apathetic? You can recognise and relate to all these (and many more) distinct emotional states. How do we distil this vast emotional experience into concepts that are experimentally useful?

One approach that has been used in psychology is to consider two dimensions of emotional experience. The first is pleasantness or unpleasantness; most emotions can be characterised as more or less pleasant. The second is intensity; an emotional experience can vary in the extent of its impact. For example, losing a favourite scarf or the death of a family member are both events that may make us sad. However the sadness is of a different order of magnitude in the two cases. Osgood, Suci, and Tannanbaum (1957) suggested that emotions can be classified according to these two dimensions of valence (pleasant vs unpleasant) and arousal (intensity). Factor-analytical studies in the last 50 years have failed to improve on this basic dimensional model.

An alternative approach has been to try to reduce the vast number of subtly distinct emotional states to a small group of universal basic emotions. This approach has its origins in the work of Charles Darwin who studied the emotional experience of people from widely different cultures around the world. He concluded that a core set of emotions with evolutionary significance cut across cultural divides and are universally experienced. These same basic emotions can also be identified in animals. In an attempt to operationally define these basic emotions, Ekman and Friesen (1971) focused on recognition of facial expressions. They concluded that regardless of culture, six basic emotional expressions could be recognised: happy, sad, fearful, angry, disgusted, and surprised. Although many psychologists are uncomfortable with reducing emotional experience to these six basic emotions, and it is clearly a simplistic categorisation, Ekman's faces have been widely used in the recent study of emotion, as we shall see.

DEFINING MOTIVATION

The concepts of emotion and motivation are closely related. Indeed, some emotion theorists (e.g., Davidson et al. 1990) have used motivation to define emotion, suggesting that emotions can be characterised as those that make us approach and those that make us withdraw. Emotions can thus be seen as reactions that dictate our motivated behaviour. The study of motivation is associated with very precise definitions and concepts based on an extensive animal literature. It is an interesting irony that motivation has been very little studied in humans until the last few years—but, by contrast, the animal literature has long been dominated by studies involving motivation. The complexities of animal learning theory, although applicable to humans, are beyond the scope of this book. However, certain definitions are important to establish.

Motivated behaviour is any behaviour or action performed to obtain rewards or avoid punishments. A **reward** is defined as anything an animal will work for, while a **punishment** is defined as anything an animal will work to avoid or escape. **Reinforcement** is the process whereby behaviour is modified by rewards and punishments and a **reinforcer** is any stimulus that elicits behavioural modification. A reinforcer can be primary (or unconditioned) or secondary (or conditioned). A primary reinforcer elicits motivated behaviour without any learning, while a secondary reinforcer only elicits the response after learning or conditioning has occurred. The classic example comes from "Pavlov's dogs". Pavlov observed that dogs automatically salivate on tasting appetising food. Food is a primary or unconditioned reinforcer. Presented with a novel food, dogs will not automatically salivate until they have tasted the food and learned that it is pleasant. Once this conditioning has occurred, dogs will salivate on seeing the food before any tasting has taken place. Taking this further, Pavlov realised that he could train dogs to salivate on presentation of a light or a tone, if this initially abstract stimulus reliably predicted food. The light or tone is referred to as a secondary or conditioned reinforcer. Pavlov's experiments are examples of classical conditioning, where learning occurs without any intervening action from the animals. Another type of learning is **instrumental learning** where animals learn to perform an action to obtain a reward or avoid a punishment. Thus a rat presented with a lever and a food dispenser can be taught to press the lever to obtain food.

KEY TERMS

Reward: In animal learning, anything that an animal will work to obtain.

Punishment: In animal learning, anything an animal will work to avoid.

Reinforcement: Typically some form of reward (positive reinforcement) or punishment (negative reinforcement) that affects the likelihood of a response being repeated.

Reinforcer: A stimulus that elicits a change in behaviour.

Instrumental learning: A type of learning where an animal learns to perform an action to obtain reinforcement.

As an example to illustrate these concepts, consider a situation where an animal hears a tone signalling that they will be given an electric shock a few seconds later. However, if they press a lever they can escape the shock. Here, the shock is a punishment, the unpleasant unconditioned stimulus that the animal will work to avoid. The tone is a conditioned, secondary reinforcer, something that the animal has learned to associate with shock, via classical conditioning, and responds to accordingly. Pressing the lever is an instrumental response, a motivated behaviour that the animal has learned will avert an unpleasant outcome. To illustrate the link between emotion and motivation, bear in mind that this process is driven by the basic emotion of fear. Electric shock causes instinctive fear and the tone comes to elicit fear after conditioning has occurred.

Salivating dogs and lever-pressing rats may seem a long way from complex human behaviours. However, the same basic principles govern almost everything we do. Over our lives we learn which cues signal positive and negative outcomes, and we learn how our actions and behaviours can increase the probability of positive outcomes and decrease the probability of negative ones. The complexity of modern human life raises some interesting theoretical questions. For example, is money a primary or secondary reinforcer? Humans will work for money and, to a certain extent, this is because money is a means to an end. We use money to buy things that are essential to life. However, perhaps money itself has become a primary reinforcer, given that we will continue to work for more money long after our basic needs have been met. Such questions are the province of social neuroscience, which we will consider briefly at the end of this chapter.

MEASURING EMOTION

As discussed in the introduction, empirical measurement of emotion is less straightforward than measuring memory function or object recognition. However, various techniques for accessing emotional function have been used. Self-report has always been an important tool for assessing mood state, with **Likert scales** relatively widely used. A Likert scale is a questionnaire response format where people are asked to choose a number corresponding to how they feel about a particular statement (e.g., 1 = strongly agree, 4 = neutral, 7 = strongly disagree). A similar approach is a visual analogue scale, a line 10 cm long marked with an extreme position at either end. Participants place a cross at the position on the line that best represents how they feel (see Figure 10.1 for an example). However, any type of self-report is, by definition, subjective and therefore experimenters have sought alternative approaches to measuring emotion.

KEY TERM
Likert scales: A simple measure of subjective experience. Participants must make a mark on a line that corresponds to how they feel.

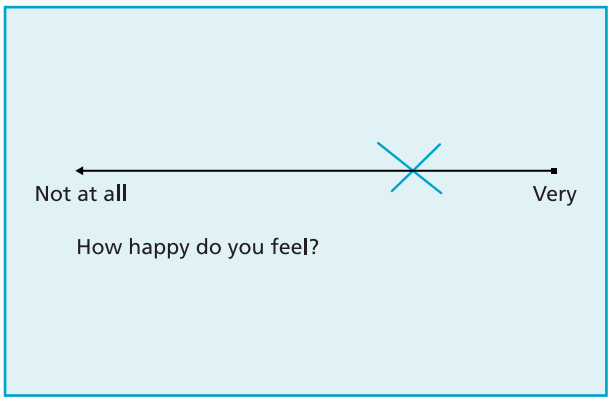


FIG. 10.1 An analogue scale for rating feelings.

One popular approach is to introduce an emotional element to a standard cognitive task and study how the emotional context affects cognition. An example of this is the van Restorff effect. If people are given a list of words to memorise, they will typically remember the first few and the last few words better than words in the middle of the list. However, if an emotionally salient word is included in the middle of the list (for example, a swear word), most people will recall this word

much more easily than an emotionally neutral word in a similar position. The emotional content of the word is thus facilitating cognition. We will return to the effect of emotional context on cognitive processing later in this chapter.

Face emotion processing

A measure of emotional processing that is emerging as a literature standard is recognition of face emotion. The stimuli used are often Ekman's emotional faces or variants on them (see Figure 10.2). These are black and white photographs of actors making the expressions that correspond to the six basic emotions discussed above. One assessment tool based on Ekman's faces uses images that have been morphed using computer technology to express emotions to a gradual increasing extent. For example, mixing 10% of a fearful face with 90% of the same face with a neutral expression generates a face that is just very slightly fearful; 20% fear with 80% neutral gives a slightly more fearful expression, and so on up to 100% fearful. Participants can then be tested to determine at what point they recognise the fearful emotion. Most will not recognise a 10% fearful face as showing fear, but as the intensity of the fear in the face increases, the emotion will be recognised. This paradigm (Young et al., 1997), and variants of it, can be used to assess abnormalities in emotional recognition. For example, Dolan and Fullam (2006) have found that patients with antisocial personality disorder have impaired recognition of sad faces.

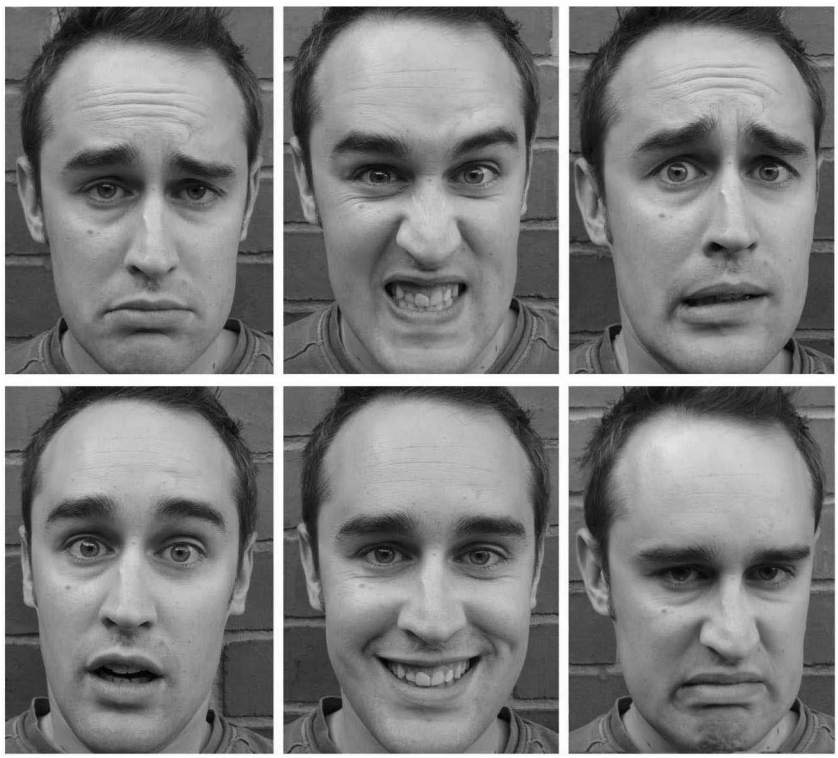


FIG. 10.2 The six universal expressions similar to those depicted in the Ekman face series (thanks to MTS).

FIG. 10.3 Examples of (a) positive and (b) negative emotional images. These photographs are typical of the emotionally arousing images found in the IAPS.

International Affective Picture System (IAPS)

It is possible to recognise emotional states in faces without experiencing an explicit emotional response. Thus it is possible to identify a face as sad or angry without feeling sadness or anger ourselves. Interestingly, fear may be something of an exception. From an evolutionary standpoint, fear in another human face is a cue telling us that a potentially threatening situation is present, which suggests that we too may have reason to be afraid. Think of those wildlife films where one animal in a herd spots a predator and makes a fearful response. The other animals in the herd instantly respond by showing fear, even if they haven't yet seen the predator themselves. However, in a laboratory context, the Ekman faces provide a test of how well participants recognise other people's emotions, rather than studying their own emotional responses. The IAPS pictures (Lang, Bradley, & Cuthbert, 1998) are a set of images designed to elicit an emotional response. Positive pictures include cute babies, kittens, etc. (things that make us instinctively think "aaah"). Negative pictures include scenes of decaying food, mutilated bodies, etc. (things that instinctively elicit a "yuck" response). These pictures have been extensively standardised using the dimensional measures of valence and arousal (see Figure 10.3).

Skin conductance

The IAPS pictures are designed to elicit emotional arousal. One way to measure this objectively, rather than relying on subjective report, is to use skin conductance response (SCR; also referred to as galvanic skin response or GSR). When we experience emotional arousal there is a slight change in the activity of the sweat glands which affects the electrical conductivity of the skin. This can be measured by placing sensitive electrodes on the tips of the fingers. Even subtle and transient arousal that is not apparent to an observer can be detected using this technique. For example, the IAPS pictures only elicit a fleeting emotional arousal effect, but this can be detected using SCR. A person whose emotional response is abnormal may not generate these SCR responses; for example, criminal psychopaths show some abnormalities in their responses to IAPS pictures (Levenston et al., 2000). You may recognise SCR as the technique underlying lie detector tests. The principle is exactly the same: Telling a lie causes a transient increase in emotional

arousal and even if this is not apparent to the most skilled observer, the change in SCR can often be detected.

Mood induction techniques

Emotional pictures produce a fleeting emotional arousal effect. To achieve a longer-lasting change in emotional state, mood induction techniques have been developed. The aim of these is to elicit a short-term change in mood state; most typically, they attempt to elicit transient sad mood (often in studies relating to clinical depression). There are various ways this can be achieved and often a combination of methods is used to maximise the effect. Participants can be asked to think about sad events in their lives, or they may be played clips from sad films or sad pieces of music. Such approaches can successfully generate temporary sadness which influences cognitive performance and has a significant effect on brain function as measured by imaging techniques.

MEASURING MOTIVATION

As discussed above, motivated behaviour is behaviour that is aimed to obtain rewards or avoid punishments, and the study of motivated behaviour typically looks at how rewards and punishments affect learning. There is a huge literature in animal research but this has not readily translated to human neuropsychology. There are a number of reasons for this. First, punishments in humans present ethical problems. Electric shock can be used in animal studies but is not ethically acceptable in human studies. Primary rewards also present problems. An animal can be deprived of food for a period of time before an experiment, ensuring that a food reward is extremely motivating. Again this poses ethical problems in humans. Second, humans learn associations far more quickly than animals; it is much harder to study the process of acquisition when it occurs almost instantly. There are also many layers of prior conditioning and socialisation to deal with. For example, even a hungry human subject may not want to receive chocolate as a reward if they are trying to lose weight: unlike a hungry animal, which will always want food. Human subjects are also motivated in subtle ways by the social context of the study; for example, they may be trying to avoid looking stupid or, in some legal situations, they may want to appear less able to complete a task than they actually are. In spite of these problems, various experimental measures of motivated behaviour have been developed. Two of these are described below, the second of which has become probably the most widely used paradigm for studying reinforcement-related behaviour in human neuropsychology.

Conditioned preference paradigms

This is a paradigm that has been adapted directly from the animal literature. Subjects develop a conditioned preference for initially neutral stimuli if they are reliably associated with rewards (Baeyens, Hermans, & Eelen, 1993; Johnsrude et al., 1999; Niedenthal, 1990; Todrank et al., 1995). In the Johnsrude paradigm, participants are presented with abstract patterns in the context of a working memory task and these patterns are paired with food reward on a

percentage of trials. In a second phase, participants are given a forced-choice preference test. Normal participants show a marked preference for the pattern paired most frequently with reward. Interestingly, because they believe they are performing a complex working memory test, their conscious attention is focused on this task and they are largely unaware of the reward-related contingencies. Thus although they reliably prefer the pattern most often paired with reward, if they are asked to explain their preference, they will say "I just like the shape of that one" or something similar. (You may notice similarities between this paradigm and "implicit learning" procedures described in Chapter 7.)

The Iowa gambling task

This is a more complex task developed by Damasio, Bechara, and colleagues that assesses how rewards and punishments influence decision making. Participants select cards from decks and receive rewards and punishments (in the form of play money) depending on their selections. The task is described in more detail in Box 10.1.

Box 10.1 The Iowa gambling task

Participants are shown four decks of cards. Unknown to them, two are high-risk decks and two are low-risk decks. The high-risk decks offer a prospect of immediate large rewards, but carry a cost of even larger long-term penalties. The low-risk decks offer smaller immediate rewards, but even smaller long-term penalties. Figure 10.4 shows a computerised version of this task. Over a series of trials, participants will gain most money by choosing cards from the low-risk rather than the high-risk decks. Participants repeatedly select cards from the four decks with the object of gaining as much money as possible. Initially the participant samples all four decks. They develop a short-lived preference for the high-risk decks based on the large rewards, but then as they experience the large punishments they start to prefer the safer low-risk decks.

This task was designed as a model for real-life decision-making situations where we must assess the risks associated with certain courses of action and weigh these against the potential benefits of those actions. Normal participants gradually learn the consequences of choosing from the different decks and then choose the low-risk decks on the majority of trials. Interestingly, they still occasionally opt for the high-risk decks, "gambling" on a favourable outcome. If SCR is measured while performing the task, these risky "gambles" are associated with elevated SCR indicating transient emotional arousal (Bechara et al., 1999). There is some debate about how soon people understand the contingencies of the task, with Maia and McClelland (2004) suggesting that understanding occurs earlier than Bechara et al. claim. Bechara et al. (2005) have suggested that this interpretation does not detract significantly from the theories they derive from using the task.

INTERIM COMMENT

Emotion and motivation are difficult to define and difficult to measure objectively. We can describe our emotional experiences in great and elaborate detail; however, obtaining an empirical measurement is extremely challenging. We have described various techniques for accessing emotional experience, but the reader will probably have realised that many of these approaches are rather oblique. We can produce a set of scores that provide a quantified description of a person's memory function, for example, but we cannot pin down their emotional function so easily. Although motivated behaviour has been widely studied in animals, it is less accessible to human research. There has been a dearth of paradigms for assessing motivated behaviour. The Iowa gambling task is emerging as a standard tool to study how rewards and punishments influence decision making; however this task only captures certain high-level aspects of motivated behaviour. As we shall see later, brain-imaging techniques provide an alternative approach for studying emotion and motivation, using paradigms that do not require an explicit behavioural measure. First, however, we will consider the classical neuropsychological literature on emotion and motivation.

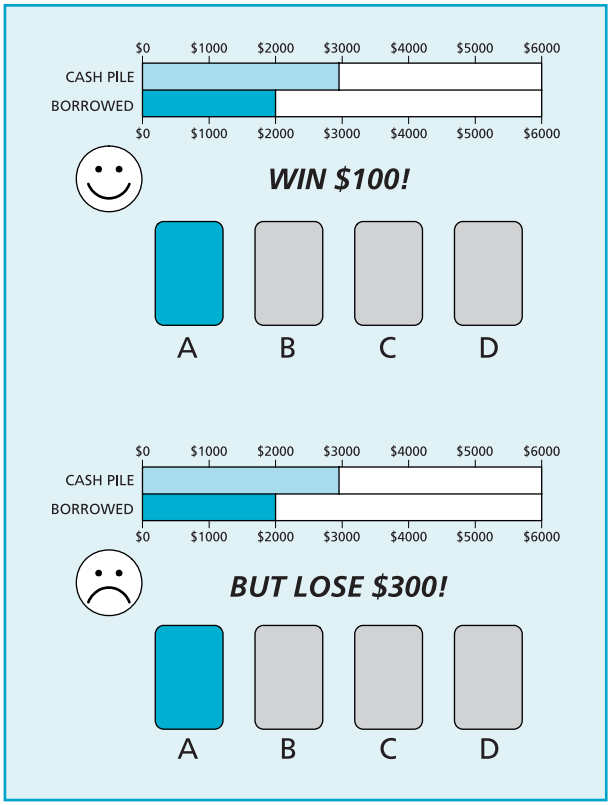


FIG. 10.4 The Iowa gambling task. Computerised version of the task showing a trial on which a participant receives a small reward but a large penalty after choosing one of the two high-risk decks. We are grateful to Professor Antoine Bechara of CALTECH for providing this figure.

EVIDENCE FROM NEUROLOGY AND NEUROPSYCHOLOGY

EFFECTS OF VENTRAL FRONTAL LESIONS ON BEHAVIOUR

One of the most famous cases in neurology is that of Phineas Gage. Details of Gage's case are given in Box 10.2. In brief, Gage was severely injured in an accident in 1848 which damaged his frontal lobes (see Figure 10.5). In spite of the dramatic nature of the accident, most of his mental faculties were well preserved afterwards. However, there were marked changes in his personality. This was the first case to suggest to neurologists that motivational and emotional functions could be impaired in isolation from marked cognitive impairments.

Gage's case has been revisited recently by Damasio (1994) who studied Gage's skull (stored at the Havard Medical School museum), and used imaging and computer techniques to reconstruct the brain lesion. The most extensive damage was to the ventromedial part of the anterior prefrontal cortex. Damasio (1994) also reported on the case of a "modern day Gage", a patient named Elliot who had

Box 10.2 Phineas Gage

Phineas Gage was a 25-year-old railroad worker in Vermont. In the summer of 1848 he was working on a railroad using explosives to blast a path through rock. The correct technique was to drill a hole, pack it with explosive, cover it in sand, "tamp" it down with an iron rod, light a fuse, and retreat to safety. Due to a momentary lapse in concentration the covering sand was not added to a particular hole and Gage tamped straight onto the explosive with the iron rod. There was an instant explosion which blew the iron rod up through Gage's cheek, his brain, and his skull before flying through the air and landing 100 yards away. Astonishingly, Gage was still conscious (though understandably rather stunned). He was able to talk while being transported to hospital and climbed out of the cart at the hospital by himself. He was patched up and treated for several subsequent infections, but within 2 months was pronounced cured. The vision in his left eye was affected, but otherwise his sensory processing, motor skills, language, and memory all seemed unimpaired. However, the accident had a dramatic effect on his personality. Although we are dependent on the rather moralistic accounts of the mid 19th century, it seems clear that Gage went from a pillar of the community to a rather feckless character who made very poor judgements and failed to function in society. The classic quote is "Gage was no longer Gage". The sad story of Phineas Gage ends in 1861 when he died of a series of intense seizures, doubtless a legacy of his accident.

surgery to remove a tumour from the orbital surface of the brain. After surgery his intellectual abilities were normal; however, he lost the social skills needed to function in the world. Furthermore, while he could describe the changes in his abilities, he appeared completely detached about them, describing them as if they were affecting someone else. Other patients with orbitofrontal lesions have also been described (Stuss et al., 1986) and social impairments are commonly reported. Patients have reduced social awareness and are less concerned about the societal rules governing behaviour. These are complex functions which we will return to later in the chapter. However, these neurological cases make it clear that normal emotional and motivational behaviour depends on the orbitofrontal cortex.

EFFECTS OF AMYGDALA LESIONS ON BEHAVIOUR

In animals, the effects of amygdala lesions have been extensively described. The term **Kluver-Bucy syndrome** (named after the scientists who first described it) is used to describe the multiple emotional and motivational deficits resulting from focal amygdala damage. In humans, however, focal damage to the amygdala is extremely rare. Although there are illnesses that do cause amygdala damage, the lesions are by no means confined to the amygdala but affect other structures as well. Neurosurgical procedures that selectively lesion the amygdala are occasionally used as a treatment for intractable epilepsy. Historically, psychosurgery has also used amygdalectomy to treat extreme aggression. Although it is important to remember that these cases are people whose brains were already

Key Term
Kluver-Bucy syndrome: A collection of emotional impairments resulting from amygdala damage in animals.

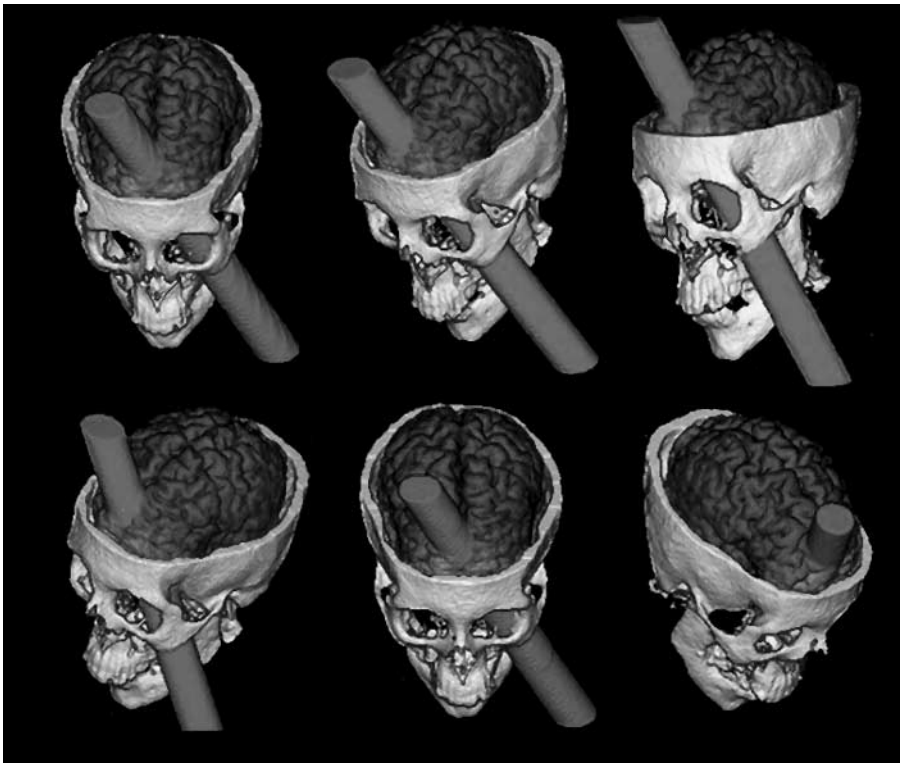


FIG. 10.5 Phineas Gage's accident. A computer-generated graphic depicting the path of the tamping rod (entering via the left cheek and exiting medially through the top of the skull). Source: Damasio, Grabowski, Frank, Galaburda, & Damasio (1994). Reprinted with permission from AAAS.

abnormal before the surgery, they do provide interesting information about the effects of amygdala damage. Sensory and cognitive functions are not typically affected to any significant extent. There is some evidence that amygdala lesions affect primary motivated behaviours, such as eating and sexual behaviour, at least temporarily. There is much stronger evidence that emotional behaviour is affected. Narabayashi et al. (1963) described 60 patients who had about one-third of their amygdala destroyed to treat aggression or hyperactivity. The majority of these patients showed decreased emotional excitability and "normalised" social function. They did not become emotionless but generally calmer and more cooperative. The effects of complete lesions of the amygdala have been somewhat mixed, but since these surgeries have only been performed on patients with extreme disturbances of emotional function prior to surgery, it is hard to interpret these findings. An interesting aside concerns the famous amnesic case HM (see Chapter 7) whose temporal lobes (including most of both hippocampi and amygdalae) were surgically removed. Although the neuropsychological focus has been on his memory deficits, a striking observation about his post-operative behaviour is that he was extremely placid and content at all times, even in circumstances where negative emotions might be expected (Corkin, 1984).

NEUROPSYCHOLOGICAL STUDIES OF EMOTION AND MOTIVATION

Amygdala damage and emotional faces

Patients with amygdala damage can recognise faces and can generate and communicate a normal range of facial expressions (Anderson & Phelps, 2000). However, they have selective impairments in their ability to recognise facial emotions. In studies of patients with bilateral amygdala damage, Adolphs et al. (1994, 1999) showed pictures of fearful faces and asked patients to rate how afraid the person was. Patients rated the degree of fear significantly lower than controls. This finding generalised to sadness (Adolphs & Tranel, 2004) and other negative emotions, but not to happiness. When patients with amygdala damage were asked to make more complex social judgements based on facial expression (how approachable or how trustworthy the person was) they also showed impairments (Adolphs, Tranel, & Damasio, 1998). Other expressions of social emotions (such as guilt and flirtatiousness) are also sensitive to amygdala damage (Adolphs, Baron-Cohen, & Tranel, 2002). More recently, Adolphs and colleagues have investigated these deficits in more detail and have suggested that patients with amygdala damage fail to process information conveyed in the eyes of faces. Eye information is particularly important in many emotions, including fear. In a single-case study they asked a patient with apparent fear recognition deficits to focus particularly on the eyes in the faces, and her deficit disappeared. However, the most recent study from this group adds another complicating factor (Gosselin et al., 2007). The same patient was found to be impaired at recognising scary music (and sad music to a lesser extent). Obviously eye information is irrelevant here and therefore the role of the amygdala in emotion recognition extends beyond evaluating information from eyes.

Amygdala damage and conditioned learning

Johnsrude et al. (2000) used the preference conditioning paradigm described earlier to assess performance in a group of patients with unilateral anterior temporal lobe resections. These patients all had some degree of amygdala damage, as well as damage to surrounding regions. A comparison group of patients with unilateral frontal lobe lesions were also assessed. Patients with frontal damage showed an impairment on the working memory task used to "mask" the conditioning procedure but established normal conditioned preferences for rewarded patterns. By contrast, the patients with amygdala lesions performed normally on the working memory task but showed severe impairments of preference conditioning. This clearly implicates the amygdala in human conditioned learning. The Johnsrude paradigm looks at conditioning with positive reinforcers. The amygdala has also been shown to be involved in negative conditioning in humans. Phelps et al. (1998) used a fear-conditioning paradigm in a patient with bilateral amygdala damage. A mild shock was paired with a visual stimulus on repeated trials. After the conditioning phase, the patient showed normal SCR response to the shock itself, but unlike control participants, she failed to show SCR response to the conditioned visual stimulus. The patient knew at a cognitive level that the stimulus predicted a shock, so this wasn't an inability to learn about relationships. However this knowledge failed to translate into an emotional response.

Orbitofrontal cortex and motivated decision making

The Iowa gambling task (described earlier) is probably the most widely used neuropsychological test of motivational function. Bechara et al. (1994) demonstrated significant impairments in patients with orbitofrontal lesions, with patients continuing to opt for high-risk decks. Strikingly, patients understood and could explain the contingencies. They had understanding of the task but did not use this to guide behaviour. Bechara et al. interpreted this as suggesting that orbitofrontal patients are insensitive to future consequences of behaviour, an explanation consistent with their observed everyday behaviour. This account has not been universally accepted; for example, Maia and McLelland (2004) have suggested that reversal learning impairments could explain Bechara's findings and this would be consistent with other reports of reversal learning deficits following orbitofrontal damage. However, in defence of their explanation, Bechara et al. (2005) cite the abnormal skin conductance responses (SCRs) observed in patients. Control participants showed elevated SCRs when they were about to make a high-risk choice. Patients with orbitofrontal lesions did not. Interestingly, they *did* show normal raised SCRs to receiving rewards and punishments.

Gambling impairments in orbitofrontal patients have also been reported by Rogers et al. (1999). Their participants were less able to make accurate judgements and more willing to take risks. Patients with bilateral amygdala lesions were also impaired on the Iowa task (Bechara et al., 1999) and failed to show anticipatory SCRs to risky choices. However, these patients also failed to show the normal elevation of SCRs in response to receiving rewards and punishments.

INTERIM COMMENT

The case study of Phineas Gage first showed that emotional and motivational behaviour could be affected broadly independently of cognitive function. Since then, further cases have confirmed that emotion and motivation constitute a dissociable domain of neuropsychological function. Two brain regions have emerged as particularly important: the amygdala and orbitofrontal cortex. The amygdala appears particularly important in controlling emotional recognition and conditioned learning, while the OFC controls decision making based on emotionally or motivationally salient information. As we shall see later, neuroimaging data have enabled us to observe the normal functioning of these two regions more closely. However, we will first consider how emotion interacts with other systems: first the somatic system and second the cognitive system.

THE INTERACTION BETWEEN SOMATIC AND EMOTIONAL SYSTEMS

The presence of elevated SCR responses to emotional stimuli makes it clear that emotional response can elicit changes in the physiological state of the body. SCR measures increased sweating, but increased heart rate and respiration rate are also

observed in response to arousing stimuli. The relationship between the brain's and the body's response to emotional information has underpinned several important theories.

JAMES-LANGE THEORY OF EMOTION

William James and Carl Lange, two 19th-century psychologists, independently proposed that the feeling of emotion arises directly from the experience of bodily changes. The theory proposes that experiences elicit bodily changes and when we notice these we feel an emotion. Increased heart rate, sweating, etc. are thus not the *consequences* of emotional responses but the *causes* of them; we are afraid because our heart rate goes up rather than our heart rate going up because we are afraid. Lange was particularly forthright in his expression of the theory, claiming that vasomotor responses *are* emotions. However, there were various problems with this theory. First, it was felt at the time that the temporal pattern of events does not fit. Visceral changes were thought (wrongly as we now know) to be quite slow, while the feeling of emotion is very quick. Second, cutting nerves carrying visceral information to the brain in animals did not abolish their emotional responses. Third, visceral changes are similar for different types of emotional stimuli and this theory therefore struggled to explain the range of emotions we are capable of feeling.

CANNON-BARD THEORY OF EMOTION

Criticisms of the James-Lange theory led Cannon and Bard in the 1920s to propose that the feeling of emotion and the bodily sensations are independent. However, evidence subsequently suggested that the somatic and cerebral experiences of emotions interact with one another. In a famous (or infamous) experiment, Schachter and Singer (1962) demonstrated this interdependence. They told participants they were studying a vitamin supplement called Suproxin, when in fact they were injected with either adrenaline or placebo. Adrenaline is released by our hormonal system whenever we face a stressful situation, and increases blood pressure, heart rate, and respiration—all are indices of physiological arousal and therefore markers of the somatic experience of emotion. Schachter and Singer manipulated participants' interpretations of their physical sensations. Some were told that side effects of Suproxin were common and told what they might experience; others were given no information. The expectation was that the people who had been told about the "side effects" would attribute their experiences to the drug, while the naïve participants would be more likely to interpret their arousal as an emotion. Schachter and Singer went a step further and attempted to manipulate the emotion that these people would feel. The participants were required to wait in a room with another person, actually an experimental stooge. The stooge either displayed angry behaviour or was extremely happy and cheerful, in both cases engaging the participant in an interaction. Schachter and Singer observed and coded the actions taken by each participant, and also asked them to describe their emotion state. The participants who had taken the adrenaline but hadn't been told about its effects responded with emotions that matched those of the stooge (happy when the stooge was happy, but angry when he was angry). Those who had been warned of side effects and those who had taken a placebo did

not display any pronounced emotion. This experiment shows that there is an interaction between physiological effects and situational cues in eliciting emotion, which is problematic for both the James-Lange and Cannon-Bard theories.

SCHACHTER-SINGER TWO-FACTOR THEORY

Based on their famous experiment, Schachter and Singer proposed a two-factor theory of emotion. This proposes that we don't automatically know when we are happy, angry, or afraid. What we feel is some generalised arousal, and to understand it we consider situational cues and use them to label what we are feeling. The two factors are therefore:

1 Some component of the situation must trigger non-specific arousal marked by increased heart rate, rapid breathing, etc.
2 The situation/environment is then analysed for cues telling us what has caused the emotion.

This theory provides a good explanation of the experimental finding; the adrenaline provides the arousal and the stooge situation provides the means of labelling that arousal as a defined emotion. Other experimental data also fit this theory. For example, in a bizarre experiment, Dutton and Aron (1974) had an attractive female experimenter interview male participants either on a normal floor or on a swaying rope bridge at a height. She gave her telephone number to the men. Of those interviewed on the bridge, over 60% called the woman, compared to fewer than 30% interviewed on solid ground. One of the stranger cognitive psychology experiments, this was interpreted as participants on the bridge experiencing fear but mis-attributing the arousal to attraction towards the woman.

Schachter and Singer's experiment and the resulting theory have been criticised for various reasons and it certainly seems clear that the theory is an over-simplification of emotional experience. A more modern attempt to link somatic states to emotional experience is Damasio's somatic marker hypothesis.

THE SOMATIC MARKER HYPOTHESIS

Damasio's theory (1994, 1996) revisits aspects of the James-Lange view in that it ascribes a critical role to bodily responses in generating emotional feelings. In brief, the argument is that an emotive stimulus in the environment elicits an associated physiological affective state. Experiences of these types of associations are stored as somatic markers. In future situations, somatic markers are automatically activated at a physiological level and bias cognitive processing and decision making. In some ways, Damasio's theory is a scientific formulation of the concept of a "gut instinct" based on prior experience. The biasing process may occur unconsciously or consciously, engaging higher cortical cognitive processing. Somatic markers are proposed to orientate us towards the most advantageous options, simplifying the decision process. At a neurobiological level, Damasio proposes that the amygdala and ventromedial prefrontal cortex are the core components of this hypothesised mechanism. The behaviour of patients with damage to the amygdala and, particularly, the OFC is consistent with the hypothesis. The poor decision making shown by OFC patients is hypothesised to reflect a failure of their somatic marker system to guide behaviour appropriately.

THE INTERACTION BETWEEN EMOTIONAL AND COGNITIVE SYSTEMS

Thus far, we have highlighted the dissociability of emotional and cognitive processing, for example, describing patients with intact cognitive function but impaired emotional decision making. However, it is clear that emotional and motivational factors influence cognition in a whole host of ways. Think about the days in your life that are most memorable and they are probably days when emotionally salient events occurred. Think how difficult it is to concentrate on a task when you are angry or sad. Or think how much more focused you may be on some cognitive activity if there is a tangible reward for good performance. These everyday examples highlight the fact that while cognition and emotion may be independent in many respects, they interact extensively in our day-to-day experience.

There is a considerable literature on emotional effects on cognition, which is beyond the scope of this chapter. However, we will consider a few illustrative examples of the interaction between emotion and memory. We know anecdotally that emotionally arousing events are more readily remembered. The effect of emotional arousal on memory has been studied experimentally by Cahill and McGaugh (among others). In one study (1995) they showed two groups of participants 12 images, each accompanied by a single sentence of narration. Many aspects of the stories were similar but there was a key difference in emotional content. One version of the story was uneventful, involving a boy and his mother visiting his father in the hospital where he worked. They see an emergency accident drill on the way and the boy ends up staying with his father at the hospital while his mother goes to run some errands. In the other version of the story, the boy is actually involved in a car accident and sustains serious injuries. He is admitted to the hospital and stays there when his mother goes home. In a memory test 2 weeks after being shown the stories, both groups were tested for their recall of specific details. The people who viewed the emotionally arousing story were able to recall more details and this was due to them having significantly stronger memories for the emotional parts of the story. In a follow-up study, Cahill and McGaugh gave a **beta blocker** to participants before presenting them with the emotional story. This drug blocks the effect of stress hormones on the brain and it effectively abolished the emotional enhancement of memory. Further, Cahill et al. (1995) showed that patients with amygdala damage do not show the normal facilitation of memory for the emotional version of the story, suggesting that the effect is normally mediated by the amygdala.

We have so far considered how emotion may enhance memory, however emotion can also have the oppposite effect. One example of this is "memory narrowing" whereby people remember less detail of an emotional scene or situation. Reisberg and Heuer (2004) have argued that emotional arousal leads to a narrowing of attention, such that peripheral information is less likely to be attended to and therefore more likely to be forgotten. A real-life example is what is termed "weapon focus" in crime investigation. Witnesses to a crime can often remember a weapon in great detail, because it is the most emotionally salient detail. However their recall of other aspects of the scene is far poorer than might be expected. Another way in which emotion can impair memory is emotion-induced forgetting, whereby emotionally arousing stimuli can lead to amnesia for

KEY TERM
Beta blocker: A drug that blocks the effects of adrenaline and noradrenaline.

either preceding events or subsequent events. If people are shown lists of words or pictures, they are significantly less likely to remember the stimuli appearing before or after arousing stimuli than other items in the list (e.g., Hurlemann et al., 2005).

Emotional effects on memory (and other aspects of cognition) have aroused interest in the study of depression (see Murphy, Sahakian, & O'Carroll, 1998, for review). In general, memory recall tends to be congruent with one's current mood, so depressed people are more likely to remember sad information. This has been shown empirically in a number of studies, with depressed patients routinely showing enhanced processing of negative information. It may also be of great clinical significance, effectively creating a vicious circle of negative cognition. Once someone is depressed, their memory and attentional systems are biased towards sad information and this focus on "the negative" serves to enhance and exacerbate the initial depression.

INTERIM COMMENT

We have discussed briefly some of the ways in which emotion and motivation interact with bodily states and with cognitive processing. While emotion can be viewed as an independent aspect of function, dependent on distinct neural systems (including the amygdala and ventromedial frontal cortex as key components), it is clear that the full complexity of human emotional experience depends on the interaction of this system with others. Damasio's somatic marker hypothesis is a currently influential account on the role our bodily representations play in our emotional life, and many modern researchers believe that physiological arousal, emotion, and cognition conspire to drive our more complex social behaviours. In Damasio's words, "The action of biological drives, body states and emotions may be an indispensable foundation for rationality" (1994, p. 200). Indirect evidence suggests that the amygdala and ventromedial frontal cortex are critical mediators of this interaction and neuroimaging techniques have allowed us to look directly at how these structures regulate motivation and emotion.

NEUROIMAGING OF EMOTION AND MOTIVATION

As we discussed in the introduction, emotion and motivation have been somewhat neglected realms of neuropsychology, perhaps reflecting the problem of studying these functions using classic neuropsychological approaches. Functional imaging has provided us with the means to study these processes without even needing objective measures. In a simple experiment, one could image a person observing emotional faces compared with neutral faces. We have no measure of what the person is doing, but the neuroimaging results will tell us whether areas of their brain are significantly more activated when the faces are emotional. This in turn tells us something about the neuropsychology of emotion. Thus functional imaging has led to an even greater explosion of data in this area than in the other domains of neuropsychology discussed in this book.

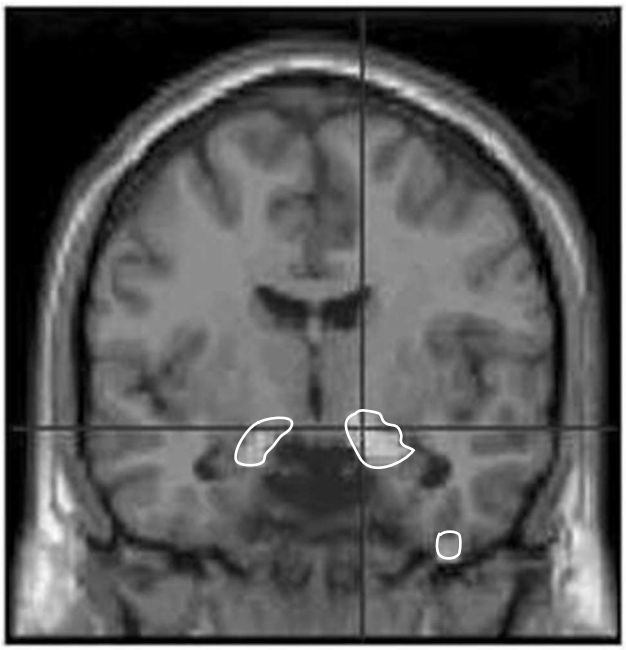


FIG. 10.6 Amygdala activation to emotional faces. Enhanced neural response in the amygdala associated with viewing aversive Ekman faces (sad, angry, fearful; see Figure 10.2) compared with neutral face expressions. Data obtained at the Neuroscience and Psychiatry Unit, Manchester.

NEUROIMAGING OF EMOTION

Imaging studies of face emotion

Imaging studies of emotion have predominantly looked at responses to emotional faces, often using the Ekman stimuli of the six basic emotions (see Figure 10.6). For fearful faces, amygdala response has been widely reported (Whalen et al., 2001), with increasing intensity of fearful expression resulting in increasing activity (Morris et al., 1996). In addition to the amygdala, fearful expressions have also been reported to activate the thalamus, anterior cingulate, and anterior insula (Morris et al., 1998). Facial expressions of anger activate regions of the temporal and prefrontal cortices, including anterior cingulate (Blair et al., 1999; Sprengelmeyer et al., 1998). Sadness, in contrast, activates right-sided temporal lobe regions and the amygdala (Blair et al., 1999). The processing of disgust has consistently been associated with insula response, increasing activity correlating with increasing intensity of disgust (Phillips et al., 1997). Disgust has also been shown to activate areas of the basal ganglia (Posamentier & Abdi, 2003). Happiness is the only positive emotion of the six and, interestingly, increasing happiness in stimuli has been associated with decreasing amygdala response (Morris et al., 1996).

Of the six basic emotions, surprise is the least investigated and has some distinct qualities. Specifically, surprise can be described as a "transitory emotion", in that it is briefly experienced and can change into other expressions depending on the nature of the surprise (Posamentier & Abdi, 2003). You may be surprised to see a long-lost friend and the surprise gives way to happiness. By contrast, you may be surprised to find your car windscreen smashed and the surprise gives way to anger. Kim and colleagues (2003) investigated brain responses to surprised facial expressions in relation to how they were rated (positive–negative) by participants. Negative ratings of surprised facial expressions elicited enhanced activation in the right amygdala, while positive ratings were associated with larger signal changes in ventral prefrontal regions.

Neuroimaging thus reveals a common network of regions involved in processing face emotion information, with some variation depending on the emotion involved. More recent studies have looked at face emotion processing in various patient groups as well as how social factors may influence normal face processing. One example of this is a study by Lieberman et al. (2005) who observed how race affects emotion processing. This study reported differential amygdala activity depending on the race of people depicted in the stimulus materials (photographs) and that of participants. Meanwhile Kaplan, Freedman, and Iacoboni (2007) have reported differences in responses to politicians' faces depending on the political affiliation of participants. These studies hint at the wide range of cultural and social factors that may influence how we process face emotion.

Imaging studies of other emotional stimuli

Face stimuli have been more widely used in imaging studies than other emotional stimuli. However there have been studies with emotional pictures and film clips. Lane et al. (1997) studied responses to emotional pictures using PET. Pleasant and unpleasant emotions were both associated with enhanced blood flow in regions including medial prefrontal cortex and thalamus. Unpleasant emotion additionally activated regions including parahippocampal gyrus, hippocampus, and amygdala. Pleasant emotion additionally activated part of the caudate. Similarly Paradiso et al. (1997) reported common activations for film clips eliciting different emotions, with some additional emotion-specific activations within the limbic system.

Emotional words have also been investigated. Whalen et al. (1998) found that the ventral anterior cingulate responded preferentially to emotionally toned words in a version of the Stroop paradigm. A similar finding has been observed in a study using an emotional go–no-go task with verbal stimuli (Elliott et al., 2000). In these studies, the valence of the words was incidental to the cognitive task. Direct evaluation of emotional valence of words (unpleasant and pleasant) has been shown to activate areas including ventral cingulate cortex, and left DLPFC. The evaluation of unpleasant words additionally activated subcortical regions, including the thalamus, caudate, and amygdala (Maddock, Garrett, & Buonocore, 2003). More recently, technical advances in stimulus delivery have allowed participants to listen to auditory input during noisy fMRI scanning. This has led to an interest in music as an emotional stimulus. For example, Koelsch et al. (2006) reported that unpleasant (permanently dissonant) music evoked response in amygdala, hippocampus, parahippocampal gyrus, and temporal poles. By contrast, pleasant music evoked responses in regions including inferior frontal gyrus and ventral striatum.

Imaging emotion generation

The studies described above have considered how the brain responds to external emotional stimuli, whether faces, pictures, words, or music. In general these studies have shown that both positive and negative emotional stimuli are mediated by neural responses in temporal and prefrontal cortices and limbic structures. Negative emotions tend to be more associated with amygdala responses while positive emotions may elicit differential prefrontal and striatal responses. Some of the stimuli used in these experiments may also have affected the emotional state of participants. Emotional film clips and music, in particular, can be used as part of mood-induction procedures as they can evoke a transient state of emotional experience. Happy music can lift our mood for example, while a frightening film clip may cause us to feel genuine fear. Neuroimaging studies have also looked more explicitly at the experience of emotion. Reiman et al. (1997) used either film clips or recall of personal experiences to generate emotional states in participants and found that the internal and external generation of emotion depended on subtly different brain regions. In a more direct attempt to separate perception of emotional content from subjective experience of emotion it was found that amygdala response was specific to perceiving emotion, while hippocampal and prefrontal responses were associated with subjective feelings of emotion (Garrett & Maddock, 2006). These studies are beginning to

explore the subtleties of emotional experience in a way that is inaccessible to classic neuropsychology. As we shall see in the last section of this chapter, understanding how emotion is perceived and generated has enormous implications for psychiatry.

NEUROIMAGING OF MOTIVATION

Imaging primary reinforcers: Taste and smell

In much of the animal electrophysiological literature studying reward processing, the rewards used are either appetising food or drink. Imaging studies of people eating or drinking are problematic because they involve large amounts of head movements, and an important prerequisite of good imaging data is that participants keep their heads still! So, rather than studying people actually eating, an alternative approach has been to use tastes and smells strongly associated with food. An fMRI study of taste and smell stimuli (Francis et al., 1999) demonstrated neuronal responses in the medial OFC in response to the taste of glucose and to the smell of vanilla. The OFC is known to contain taste and smell receptors and it is possible that this is simply an effect of sensory stimulation. However, evidence that OFC also mediates motivational aspects of taste and smell comes from a follow-up fMRI study by O'Doherty et al. (2000). Even if you do not recognise the term, you will be familiar with an effect known as "sensory-specific satiety". If you have just eaten a large amount of a particular food, the reward value of that food rapidly diminishes; after one chocolate biscuit you may be very keen to have another but after five or six, your desire to eat more is substantially reduced. O'Doherty et al. scanned participants before and after eating a large meal and then presented smells of foods that were part of the meal and foods that were not. The OFC response was significantly reduced for foods that were part of the meal. This is evidence that the OFC codes motivational as well as sensory properties. Small et al. (2001) studied a similar phenomenon in people eating chocolate during PET scanning. Participants were fed large amounts of chocolate and asked to rate how pleasant it was at regular intervals. As expected, it became steadily less pleasant and, as the ratings decreased, activation in medial OFC diminished. Recently a study of five food flavours (O'Doherty et al., 2006) demonstrated differential responses in human ventral striatum that directly reflected subjective preferences for the flavours.

Imaging studies of financial reward and loss

In the neuroimaging context, most studies of reinforcement have used financial rewards. As we discussed earlier, money is not a primary reinforcer in the classic sense; it has no intrinsic physiological value, but it does have enormous social value, and is a strong behavioural motivator in most modern societies. From an empirical viewpoint, money is a very useful reinforcer, as various parameters (size of reward, probability of reward, etc.) can be systematically and objectively varied. One of the first studies of financial reward was a PET study (Thut et al., 1997) in which participants performed a simple cognitive task under the two conditions. In one they were simply told "OK" while in the other they received money for accurate performance. Financial reward was associated with activation

in regions of an extended reward system, including midbrain, thalamus, dorsolateral PFC, and OFC.

In a more sophisticated study, Delgado et al. (2000) examined neuronal responses to receiving financial rewards and punishments. Participants were presented with a series of computerised cards on which they knew a number from 1 to 9 would appear, and had to guess whether the number would be greater or less than 5. They won money for correct guesses and lost money for incorrect guesses. Increased responses were seen in the dorsal and ventral striatum after a reward, while decreased responses were seen after a punishment. A similar study (Elliott, Friston, & Dolan, 2000) also assessed responses to winning and losing money and reported striatal responses to winning.

Imaging has also been used to look at important variables that affect motivation. One such variable is anticipation of financial reward. For example, Breiter et al. (2001) compared anticipation and outcome on a rewarded task and found that neural responses in regions including the extended amygdala, ventral striatum, and OFC were seen for anticipation as well as outcome. Another variable in reward studies is reward value, and O'Doherty et al. (2001) showed that medial OFC response correlated with amount of abstract ("play") money won on a task. We have also demonstrated a relationship between medial OFC response and reward value (Elliott et al., 2003). (See Figure 10.7.)

The most recent imaging studies of financial reward have used increasingly complex mathematical modelling to look at reward prediction (Knutson & Cooper, 2005; O'Doherty et al., 2006). These studies are predicated on the fact that reinforcement is critically dependent on the extent to which outcomes match expectations. If you fully expect to receive a reward, your response to it may be more muted than if it was at least partly unexpected. In fact if you do not receive an expected reward, the experience feels more like a punishment. Similarly, if you don't receive an expected punishment, you may feel almost as though you had received a reward (the positive experience of "getting away with it"). Thus reward and punishment responses in the brain are extensively modulated by expectations, and new modelling and analysis techniques in functional imaging are allowing these relationships to be explored.

Imaging gambling tasks

Neuropsychologically, the Iowa gambling task has been an important tool for studying how people translate knowledge of reinforcement contingencies into appropriate behavioural choices. Remember that patients with OFC damage understood the contingencies of the task, but failed to translate this knowledge into advantageous decision making. The Iowa task is extremely complicated and hard to use in an imaging context because there are so many variables to control. However, other gambling tasks have been used. Ernst et al. (2004) devised a "wheel of fortune" task where participants were presented with a circular spinner with blue and red segments of varying sizes. The size of the segments reflected the probability of winning on that colour and boxes below the spinner showed how large a win would be associated with each colour. Three types of condition were used:

1 High risk/high reward (e.g., a 10% chance of winning $7 vs a 90% chance of winning $1).

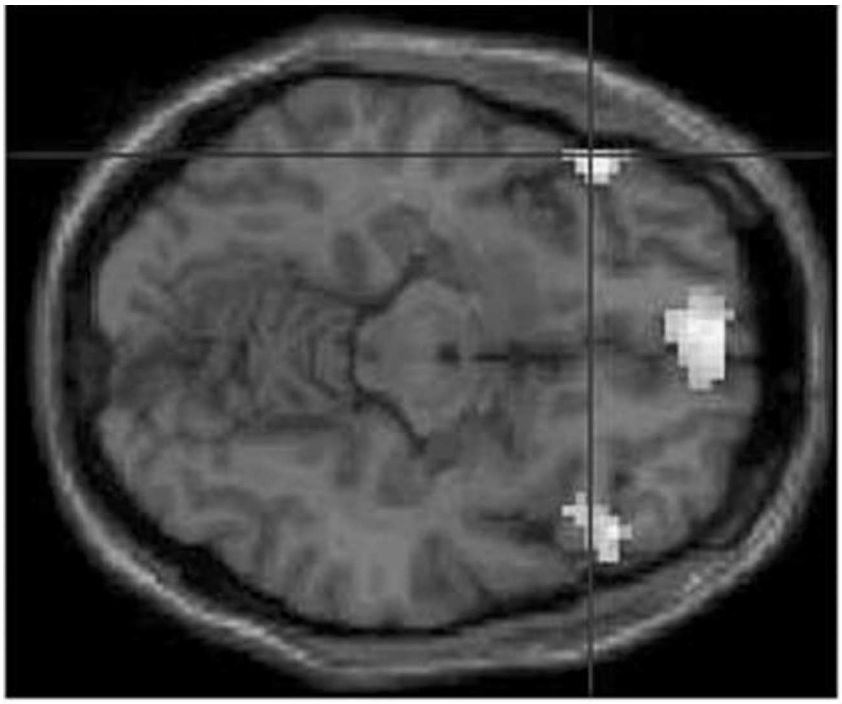


FIG. 10.7 Orbitofrontal activations to financial reward. Neural responses in the orbitofrontal cortex associated with varying the value of financial reward in a cognitive task. Data obtained at the Neuroscience and Psychiatry Unit, Manchester.

2 Moderate risk/moderate reward (e.g., a 30% chance of winning $2 vs a 70% chance of winning $1).
3 Equal risk/equal reward (a 50% chance of winning $1 on blue vs a 50% chance of winning $1 on red).

Participants chose the colour representing their preferred option. Ernst et al., found that the OFC was significantly responsive when participants were making their decision and that this response was particularly enhanced for high-risk choices. Rogers et al. (2004) also showed that the OFC was involved in making decisions on a gambling task.

These results essentially confirm the findings of studies in lesion patients. However fMRI allows us to explore the role of the OFC in more depth. Given the temporal resolution of fMRI it is possible to separate out some of the component processes of gambling tasks to determine exactly what the OFC is doing. In the Ernst et al. (2004) study, the OFC activity specifically related to the decision-making stage of the task. By contrast, once the decision had been made, anticipation of reinforcement was associated with activity in the ventral striatum. Studies have also allowed differences in individual behaviour on gambling tasks to be studied. Among normal people there is considerable variation in how willing someone is to take a risk. Some people are characterised as "loss averse" which means that they are less likely to make risky choices that could lead to a substantial loss. Tom et al. (2007) found that individual differences in loss aversion on a gambling task were predicted by neural responses in ventral striatum and prefrontal cortex. Studies like this hint at how fMRI can potentially be used to

characterise normal variation in emotional and motivational behaviour, which is an extremely interesting area not accessible to classical neuropsychology.

INTERIM COMMENT

Functional neuroimaging has revolutionised the study of emotion and motivation in humans. In studies of emotion, imaging has confirmed the importance of the amygdala and ventromedial prefrontal cortex, highlighting a particular role for the amygdala in the recognition and experience of negative emotions. However, imaging has also identified a wider network of mostly temporal and frontal regions involved in emotion and has been able to characterise dissociable roles for these regions depending on the exact emotional context. For example, distinct regions have been associated with the perception compared to the experience of different emotions. In studies of motivation, the OFC has again emerged as a critical region, but imaging has also clearly demonstrated the importance of striatal structures. With increasingly sophisticated modelling and analysis techniques, it is becoming possible to identify the neural correlates of different components of human reward systems and thus gain a deeper understanding of motivated behaviour.

SOCIAL NEUROSCIENCE

Historically, neuropsychology has focused principally on how humans function in isolation; how we attend our environment, how we recognise things, how we remember things, and so on. Perhaps the one exception has been the study of language where almost any attempt to analyse communication necessarily involves considering the participant interacting with someone else. However, much of our real-life behaviour involves a highly sophisticated level of social interaction. This may be explicit, as when we are interacting with a group of other people in an overtly social situation. But it may also be implicit. Imagine sitting on your own thinking about your current concerns: maybe you're trying to make a decision about whether to apply for a particular job; maybe you're trying to remember a conversation you had last week; maybe you're trying to decide what to do at the weekend. All these things require you to think about social interactions. All involve you thinking within parameters imposed by your social and cultural experiences and values. We are intensely social animals and the social context affects most of what we do. In considering the social context of our behaviour, emotion and motivation are critical concepts. Social interactions involve emotional responses and social factors are important motivators of behaviour. For most of us, social acceptance and approval are very important and, consciously or not, play an important role in guiding our decisions and behaviour. The recent boom in emotional and motivational neuroscience has therefore led to the emergence of a new cognitive discipline. Over the last 2 or 3 years, the term "social neuroscience" has started to be widely used. Specifically, social neuroscience is the study of the brain basis of social behaviour. There are many fascinating issues and topics within this new discipline and we only consider a few illustrative examples here.

THEORY OF MIND AND EMPATHY

Theory of mind is the ability to represent the mental states of other people, to appreciate their beliefs about the world, which may be distinct from our own. Imagine you are out with a friend and while they are at the bar you move their bag out of someone else's way. When your friend comes back and reaches for their bag, you will realise that they don't know it is somewhere different and will point them to it. This seems trivial but is a vital skill. The bag was at position A. It is now at position B. You know that because you moved it there. But you also know that your friend wasn't there when the bag was moved to B, so you realise that they still think it is at A. You are seeing the world from your friend's perspective. Very young children don't have this ability. Imagine the same situation with two 3-year-olds (transposing the action to a playgroup rather than a bar of course!). When the owner of the bag returns, the child who has moved it will not think to tell them. That child knows that the bag is now at position B and in their mind that is just a fact about the world that *everyone* should know.

Normal children develop theory of mind and it represents an important developmental milestone. Children with autism may not develop normal theory of mind. Influential theories of autism (see work by Frith and Baron-Cohen or example) suggest that a core deficit is impaired theory of mind. One paradigm that has been used with children is the "Sally-Anne task" (Baron-Cohen, Leslie, & Frith, 1985). Children are introduced to two characters (Sally and Anne). Sally puts a marble in a basket while Anne is watching. Anne then leaves the room and Sally moves the marble from the basket to a box. Anne then comes back. The child being tested is then asked "Where will Anne look for the marble?" Over the age of 4, normal children will reply "In the basket". Autistic children typically reply "In the box". When questioned they show that they can remember that the marble was in the basket initially, but they fail to grasp that Anne's belief about the marble is different from the reality of where it now is. This finding has been reproduced in a number of studies. The autistic child or adult finds it very difficult to represent the mental states of others and appreciate that they may be different from their own. It should be noted that there may be other deficits associated with autism, and also that the theory of mind difficulties can be overcome in individuals, but it does appear to be significant in most autistic people.

Theory of mind has been studied using neuroimaging. A meta-analysis of imaging studies by Frith and Frith (2003) identified three crucial brain regions—the temporal poles, medial prefrontal cortex, and temporo-parietal junction—which play distinct but interconnected roles in normal theory of mind. These areas can be activated by various different paradigms involving theory of mind. For example, one study by Gallagher et al. (2000) looked at responses to cartoons. Certain cartoons involve theory of mind in order to get the joke, while others do not. Cartoons involving theory of mind resulted in greater activation of medial prefrontal cortex. Similar results were seen for story comprehension, where some stories involved a theory of mind component and others did not.

The concept of empathy is somewhat related to theory of mind. It also involves seeing the world from another person's point of view but is more concerned with feeling what they feel. If you see another person in distress, you will probably experience some fellow feeling. If the distressed person is someone you

are close to, this may be particularly strong. In extreme cases, some people report feeling actual physical pain corresponding to the physical pain being experienced by a loved one. See Figure 10.8 for an example of a simple task probing empathy and theory of mind. Empathy has also been investigated using functional imaging and has been shown to depend on brain regions implicated in emotion: medial and ventral prefrontal cortex, temporal poles, and amygdala (Farrow et al., 2001; Lamm, Batson, & Decety, 2007; Vollm et al., 2006). See Figure 10.9 for

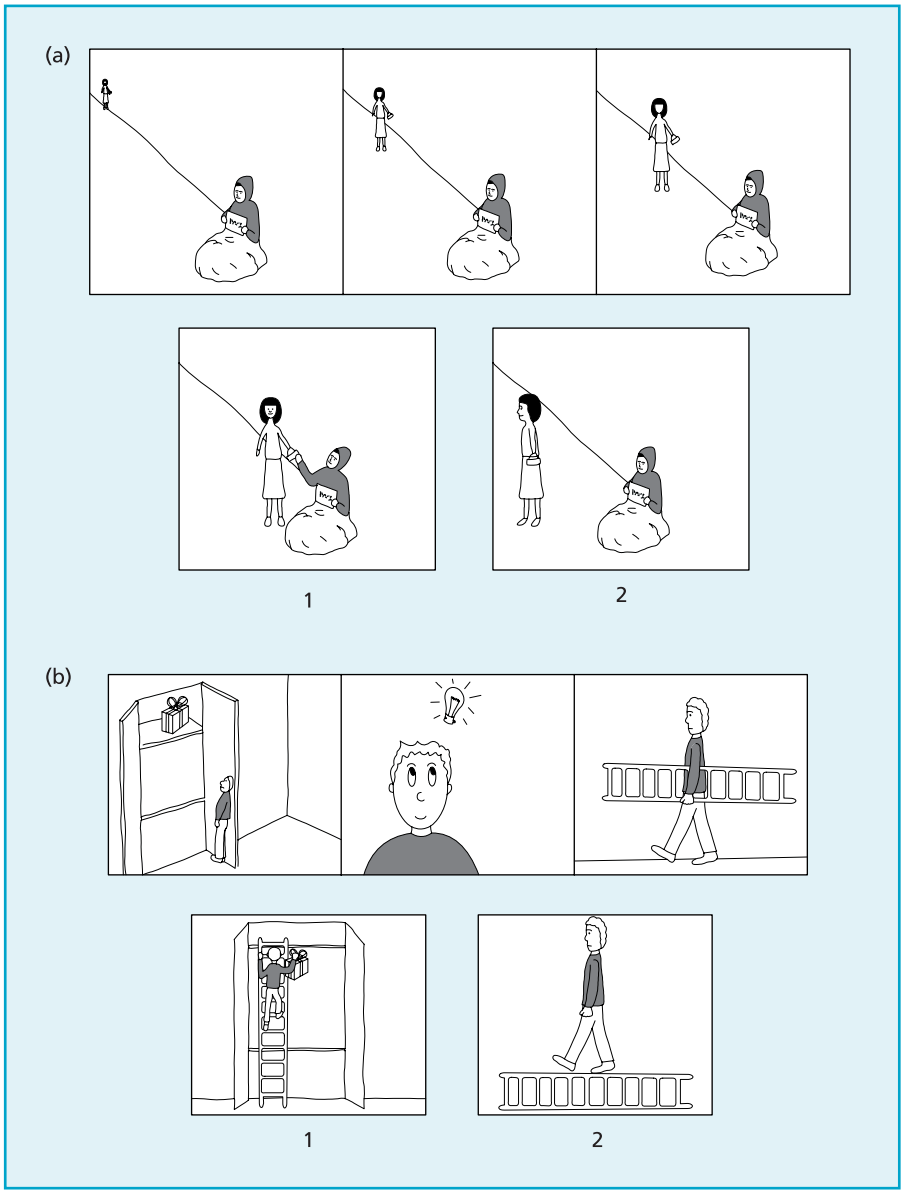


FIG. 10.8 Empathy and theory of mind cartoons. Stimuli used to assess (a) empathy and (b) theory of mind. Participants are asked to choose the frame (1 or 2) that best completes the cartoon. For the empathy cartoon, this involves choosing the picture that makes the person feel better, while for the theory of mind cartoon, it involves appreciating the intentions of the person. We are grateful to Dr Birgit Vollm, , for providing this figure.

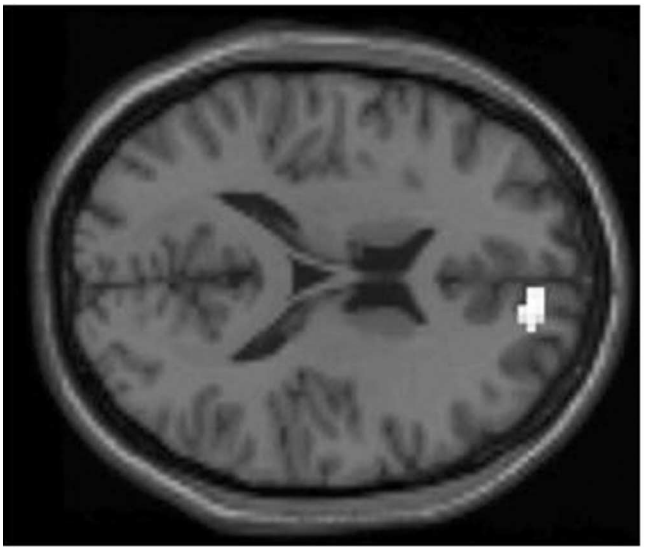


FIG. 10.9 Neural responses to empathy and theory of mind cartoons. Neural responses in medial prefrontal cortex to cartoons requiring an empathetic response. We are grateful to Dr Birgit Vollm, , for providing this figure.

medial prefrontal activation associated with empathy.

MIRROR NEURONS

In Chapter 5 we introduced the idea of mirror neurons, a type of brain cell that responds similarly when we perform an action or when we witness someone else perform the same action (see Box 5.5). Mirror neurons were first discovered in monkeys in the early 1990s. An Italian research team found individual neurons in the brains of macaques that fired both when the monkeys grabbed an object and when they watched another monkey grab the same object. Rizzolatti and colleagues, who made this initial discovery, believe that mirror neurons can explain how and why theory of mind and empathy may occur. If watching an action and performing that action can evoke the same response at a single neuron level, it is entirely plausible that watching an action and performing an action could also elicit the same *feelings* in people. From there it is a short conceptual step to understanding how observing an emotion can cause us to *feel* the emotion. Wicker et al. (2003) performed an imaging study of participants while they inhaled an unpleasant odour (butyric acid, which smells like rotten butter) and while they viewed a film of an actor pulling a disgusted face. The anterior insula was activated in both situations. Similarly, Keyser and colleagues have found that the same area of the somatosensory cortex was active both when participants were lightly touched on the leg with a soft stimulus, and when they viewed pictures of someone else being touched in the same spot. Also of interest is whether mirror neurons respond not only to other people's actions or emotions, but also to the *intent* behind those actions. Iacoboni et al. (2005) used fMRI to examine participants as they watched videos of a hand picking up a teacup. In one video, the teacup appeared on a table amid a pot of tea and plate of biscuits, suggesting that the hand was grasping the cup to take a sip as part of afternoon tea. In the other video, the table was messy and scattered with crumbs suggesting that tea-break was over and the hand was clearing the table. In a third video the cup was alone, with no context. Mirror neurons in the premotor cortex and other brain areas reacted more strongly to the same action when it occurred in a meaningful context, suggesting that the neurons are important for understanding intentions as well as actions. While this research is still preliminary, it is looking increasingly likely that mirror neurons will provide a crucial line of evidence for understanding social neuroscience.

SOCIAL COOPERATION

Another issue that has been studied in social neuroscience is how brain networks mediate social cooperation. Much of what we do is in collaboration with other people and therefore cooperation is an important social function. One tool that

has been used to study cooperation in the neuroscience context is the Prisoner's Dilemma game. This is a paradigm borrowed from economics and has many variants. In the classic game there are two players, each of whom must imagine they have been imprisoned for a crime committed in conjunction with someone else. Both participants must choose whether to come clean or deny everything. The choices made by both influence their prison terms. For neuroscience purposes, a version of the game is generally used where the prison aspect is replaced by winning and losing money. Players can cooperate or defect. If both defect, both win a small amount of money. If both cooperate, both win an intermediate amount. If one cooperates and one defects, the cooperator wins nothing and the defector wins the largest amount. On a single trial it pays to defect. However if players complete a series of trials, the best strategy to maximise gain is mutual cooperation. If players establish mutual trust and cooperate each time, they always win the intermediate amount. When two normal participants play the game, mutual cooperation is generally the strategy that develops over a series of trials. However, the paradigm can be experimentally manipulated by making one of the participants an experimental stooge who may adopt a more or less aggressive strategy. The response of the true participant to different strategies can then be observed. In a functional imaging version of the paradigm, mutual cooperation has been associated with reward areas (medial OFC and striatum), suggesting that social cooperation is intrinsically rewarding (Rilling et al., 2002). Playing against a more aggressive player results in different activation patterns (Rilling et al., 2007), which also depend on personality variables. Interestingly, playing against a computer, rather than a human player, results in less extensive neural responses. The game is logically the same with a computer, but the social context is different. These results therefore highlight the importance of social context in determining patterns of neural response.

UNDERSTANDING SOCIAL NORMS

Our final example concerns various studies of social norms. These are studies that look at how our brain responses have been socialised by the implicit rules of socially acceptable behaviour. In a study by Berthoz et al. (2002), participants were presented with stories that involved the violation of a conventional social norm (for example, someone spitting food across the table at a dinner party because they didn't like the taste). These norm violations were associated with activation of lateral orbitofrontal regions. An interesting recent direction in social norm studies is "altruistic punishment". The premise of these studies is that in situations where someone else has broken a social or moral rule, we feel that punishment is appropriate and perhaps even desirable. DeQuervain et al. (2004) found that reward regions of the striatum were activated when participants administered an altruistic punishment, suggesting that punishing transgression is positively reinforcing. Singer et al. (2006) performed a two-stage study. In the first stage, participants played interactive games with other people, some of whom played fairly while others did not. Participants were then imaged while watching those other people apparently experiencing electric shock. When people perceived as fair were "shocked", empathy-related activations were observed; these were considerably reduced when people perceived as unfair were "shocked". Studies like this are beginning to tell us a great deal about how our social behaviour is mediated at a neuronal level.

IMPAIRMENTS OF EMOTION, MOTIVATION, AND SOCIAL FUNCTION

PSYCHIATRIC DISORDERS

Elsewhere in this book we have referred to the neuropsychological problems experienced by patients with psychiatric disorders. Cognitive dysfunction is a symptom of many psychiatric problems. However, almost by definition, psychiatric disorders are primarily emotional and a whole book (or several books) could be devoted to the emotional and motivational problems experienced by patients. People who are depressed have emotionally biased memory systems, as we have discussed. They also have profound problems with motivation; depressed patients may say that they simply cannot be bothered to engage in daily activities. Figure 10.10 shows attenuated brain responses in medial prefrontal regions associated with a motivational task in depressed patients. Bipolar depression (or "manic depression") is a distinct subtype of depressive disorder, characterised by both depressive episodes and episodes of mania. In the manic phase of the disorder, patients may be inappropriately euphoric and highly aroused, suggesting a complex imbalance in emotional systems. Mania has not been widely studied using imaging techniques, as this patient population is very difficult to obtain reliable images from.

Meanwhile, patients with anxiety disorders show disproportionate fear in certain situations. This is most obvious in patients with specific phobias who can be incapacitated by irrational fears about particular stimuli. Patients with

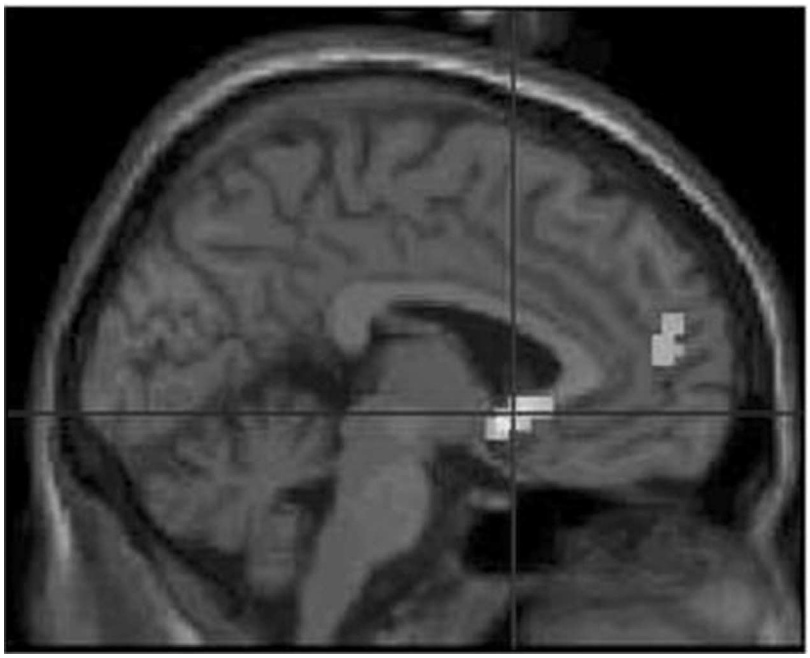


FIG. 10.10 Reduced medial prefrontal activations in depression. Attenuated neural responses in medial prefrontal regions in a depressed patient performing a financially rewarded task compared to a task with no rewards. Data obtained at the Neuroscience and Psychiatry Unit, Manchester.

addictions, whether to drugs, gambling, or sex, have a biased motivational system, such that they look to a particular stimulus for rewards to an extent that is detrimental to their social function. Eating disorders can also be characterised in terms of dysfunctional motivational states, such that the desire to achieve a perceived social ideal of slimness disrupts the basic physiological drive to eat.

If we consider the wider field of social neuroscience, more examples emerge. As we have seen, people with autism or Asperger's syndrome typically have problems with theory of mind. They find it extremely difficult to view the world from someone else's perspective. Meanwhile, people with antisocial personality disorder are thought to have deficits in empathy. They may be able to interpret the world from another rational point of view, but they do not have any sense of fellow-feeling. Finally, schizophrenic individuals who are paranoid or delusional can be thought of as interpreting social situations and interactions according to a completely skewed version of reality.

CHAPTER SUMMARY

Emotion and motivation are rapidly growing areas of study in cognitive neuroscience. Traditionally emotion and motivation have been difficult to study in a laboratory setting because they are such subjective concepts that are extremely difficult to quantify. In spite of these difficulties, some techniques have emerged allowing neuropsychologists to characterise emotional and motivational function in patients with circumscribed brain damage. From the classic case of Phineas Gage through to the modern series of studies by Damasio, Bechara, and colleagues, it is clear that two critical brain regions are the amygdala and ventromedial prefrontal cortex. Patients with damage to these regions typically have relatively spared cognitive function but pronounced impairments in emotion, motivation, and social function. Although these neuropsychological cases suggest a degree of independence between cognition and emotion, it is clear that the full range of emotional experience depends on interactions between cognition and emotion, as well as somatic responses. Emotion is associated with bodily responses as well as feelings, and both of these can colour how we perceive, interpret, and remember the world around us. Thus theories of emotion have attempted to explain the interactions with somatic states and with cognitive function.

Neuroimaging has led to huge advances in our understanding of emotion and motivation. These techniques essentially provide a human analogue of the electrophysiological techniques that have been a pillar of emotion and motivation research in animals. We can now look directly at what happens in people's brains as they experience different emotions or motivational contexts, without needing empirical measures of performance. Imaging studies of emotion have confirmed the importance of the amygdala and ventral frontal regions, as well as other limbic and frontal areas, but have also allowed more detailed exploration of how responses within this network depend on which emotion is involved, whether it is just perceived or actually experienced, and how it is generated. Ventral frontal regions and the amygdala also form part of the motivation circuitry, as well as striatal structures and other prefrontal areas. Researchers are now exploring how this human reward network responds under different conditions and how the different regions interact in different aspects of reward processing.

The explosion of interest in emotion and motivation has led to the emergence of a new discipline of social neuroscience. Our social interactions are dependent on emotional and motivational factors and neuroscientists are now starting to explore this wider context. For many, this is an extremely exciting new direction as it takes neuropsychology out of a sterile laboratory or clinical context and explores how our real-life behaviours are mediated by brain function. Social functions, as well as the basic component processes of emotion and motivation, are abnormal in many psychiatric disorders and therefore understanding these processes also has important implications for psychiatric research.

CHAPTER 11

CONTENTS

11

Executive functions

INTRODUCTION

The development of sophisticated neuropsychological testing techniques and the advent of in-vivo imaging have led to increased interest in the role of cortical regions, particularly the frontal lobes, in what neuropsychologists call "executive function(s)". However, it is important at the outset to be clear about the term itself, and the relationship between executive functions and the frontal lobes. Executive functions refer to a set of psychological attributes that are supervisory, controlling, and organisational. Although these skills are all critical for normal everyday behaviour, their somewhat abstract nature means that routine psychological assessments such as IQ tests or measures of sensory perception may fail to detect any executive dysfunctions. Executive functions include the ability to plan, initiate, and terminate actions, to think in abstract or conceptual terms, to adapt to changing circumstances, and to respond in socially appropriate ways. Individuals with impaired executive function show deficits in higher-level cognitive operations that require planning, flexible thought, and coordination of different subprocesses. Baddeley (1986) has used the term "dysexecutive syndrome" to identify these impairments.

At one time, psychologists used the terms "executive" and "frontal" in an almost interchangeable way because they believed that frontal lobe damage alone led to executive dysfunction. While this is often the case, we now need to qualify this relationship in two important though related ways. First, we should remember that the frontal lobes receive information from, and send information to, most other cortical regions and many subcortical systems (such as the basal ganglia, the limbic system, and the cerebellum) as well. Second, and consistent with the idea of distributed control, we find that damage to regions other than the frontal lobes can sometimes lead to executive dysfunction, although it remains the case that frontal damage is most frequently associated with it. For example, disorders characterised by basal ganglia pathology (Parkinson's disease being the most studied example) are often associated with deficits in executive function. The basal ganglia and frontal cortex are extensively interconnected and it seems that executive function depends on the functional integrity of this circuitry, rather than of the frontal lobes per se.

A further point should be made before consideration of the nature and causes of executive dysfunction. That is, executive function is less completely defined and understood than, for example, memory or attention. As yet, there is no clear

agreement on the underlying causes of some of the executive deficits we will review, and therefore explanatory models of executive dysfunction (some of which we consider later in this chapter) may seem circular, overlapping, or of limited general application. Nevertheless, any comprehensive model of executive function must give due consideration to the range of psychological skills the frontal lobes and their connections subserve.

DOMAINS OF EXECUTIVE DYSFUNCTION

There remains considerable disagreement among researchers as to how to partition executive function (see, for example, Roberts, Robbins, & Weiskrantz, 1998). Historically, a sort of "mass-action" approach to frontal lobe function has been favoured, with the region assumed to act as a unit in the coordination of executive functions. More recently though, neuropsychologists have used dissociations to tease apart apparently independent components of executive function. Even so, it remains a matter of debate as to how many such components we need to consider. One way of looking at different aspects of executive dysfunction is to partition them into three domains, and we will consider:

1 impairments in the initiation, maintenance, and cessation of actions (action control);
2 impairments in abstract and conceptual thinking;
3 impairments in the ability to organise behaviour towards a goal.

However, readers should note that these "functional" domains do not map particularly well onto distinct "structural" frontal regions, so further revision of the fractionation of executive functions is likely in the future (see further discussion later in the chapter).

IMPAIRMENTS IN ACTION CONTROL

People with frontal damage often display what neuropsychologists call "psychological inertia" (Lezak, 1983). Although this can take a variety of forms, there are two basic components. First, appropriate actions may simply not be initiated: an individual may, for example, neglect personal hygiene, or there may be a marked reduction in self-initiated speech, even with repeated prompting. The individual seems indifferent to, and uninterested in, the world around them, and often (though not always) oblivious to their own indifference.

The second component of psychological inertia is characterised by difficulty in terminating or amending behaviour once started. It can be observed in the laboratory as well as social settings. The drawings in Figure 11.1a illustrate the attempts of one "frontal" patient to complete the "memory for designs test" (Graham & Kendall, 1960) in which a set of simple geometric shapes are shown one at a time for a few seconds, and the respondent then has to draw each one as soon as the design is covered up. Although the actual designs vary considerably in their complexity and format, the drawings by the frontal patient all look very similar (in comparison with the drawings in Figure 11.1b by a control participant), which is indicative of **perseverative** responding: repeating the same behaviour, or type of behaviour, again and again.

KEY TERM
Perseverative: A response may be perseverative in the sense of being an unnecessary or inappropriate regurgitation of an earlier response.

Both inertia and perseveration can also be seen in the pattern of responding of some individuals in tests of verbal fluency. When asked to name as many items as quickly as possible beginning with the letter "F", a patient with executive impairments may first generate words comparatively slowly, and then get "stuck in a rut" by generating only words that are interrelated; such as "*finger . . ., fingernail . . ., fingers . . .*" and so on. Sometimes erroneous (but semantically related) intrusions such as "*ring-finger*" may slip in.

Another behavioural manifestation of executive dysfunction (which overlaps in some ways with the next category of disorder) has been described by L'hermitte (1983) and L'hermitte, Pillon, and Serdaru (1986). The "environmental dependency syndrome" (as it has come to be known) describes a pattern of behaviour in which environmental cues trigger responses irrespective of their appropriateness at the time. For example, when shown into a room in which there was a table with a hammer, nails, and some pictures, one of L'hermitte's patients started hanging the pictures; another patient left to her own devices in a kitchen began washing the dirty dishes. This pattern of behaviour is sometimes referred to as "stimulus-driven" or "utilisation" behaviour, because the apparent impulsivity of such patients is influenced by immediate circumstances rather than the broader social context. Parents will recognise this as a common feature of child behaviour (perhaps not the washing up), and it is interesting to note that, in neurodevelopmental terms, the frontal lobes are one of the last cortical regions to mature (in late adolescence). However, "utilisation" can lead to embarrassingly inappropriate social behaviour in adults with frontal lobe damage, as happened when L'hermitte showed one of his patients a disposable cardboard bedpan, only for the patient to commence using it!

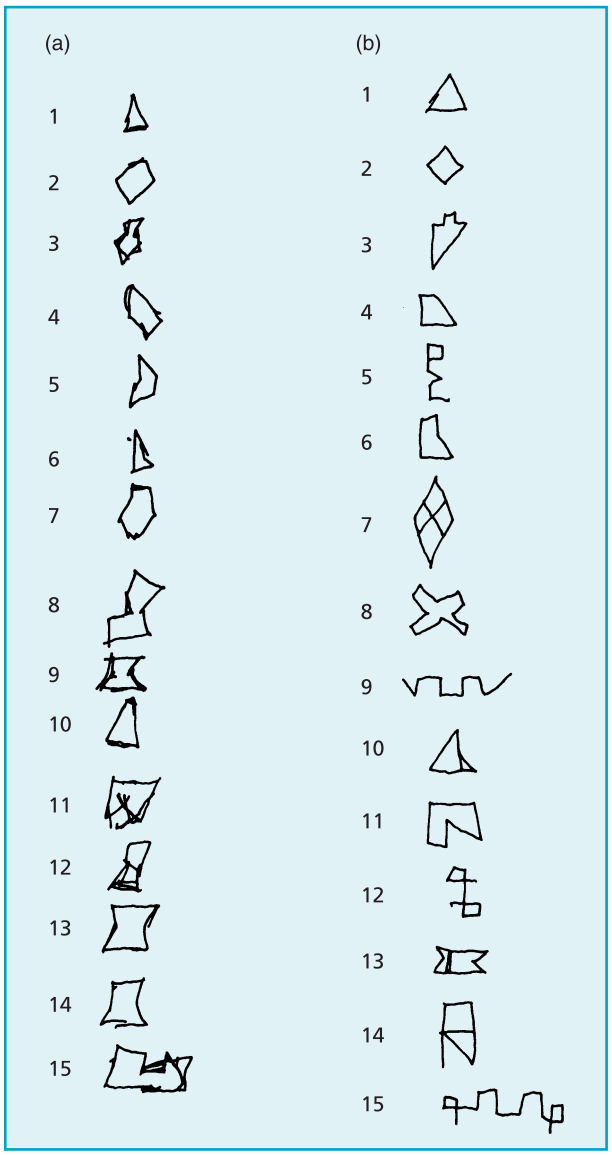


FIG. 11.1 The memory for designs test. The respondent views a series of abstract figures one at a time for a few seconds each. Immediately after each presentation, they try to draw the design. A control participant's drawings are shown in the right column (b). Although they are not perfect, this person scored zero errors. The drawings of the same figures by a patient with frontal lobe damage are shown in the left column (a). The patient's drawings provide an indication of perseverative responding: each drawing looks similar to the previous one. The patient's error score was > 20, which is indicative of marked damage.

IMPAIRMENTS IN ABSTRACT AND CONCEPTUAL THINKING

A similar pattern of fixated or inflexible thinking is also seen in other manifestations of executive dysfunction. The Wisconsin card sort test (WCST) (see Chapter 2) was developed to examine concept formation and the ability of participants to overcome the tendency to perseverate. In this test the respondent must sort a pack of cards one card

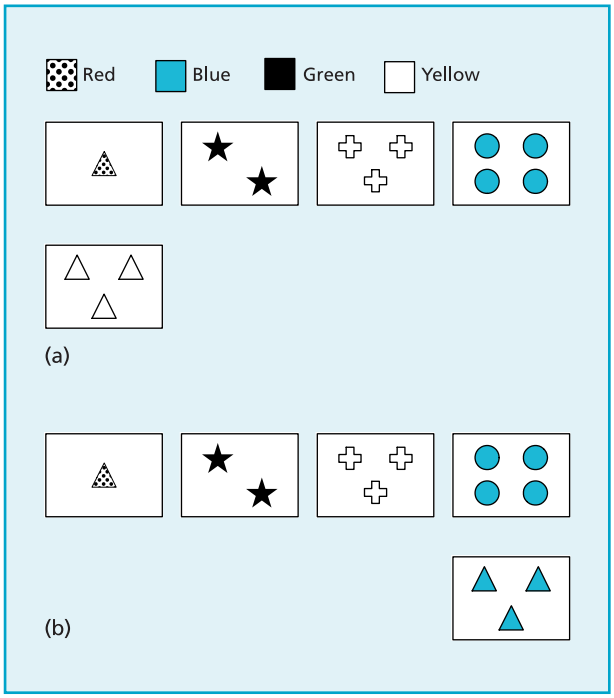


FIG. 11.2 Typical responses in the WCST. In (a) the unstated rule was "sort by colour". The participant's response is incorrect because they actually sorted by shape. In (b) the unstated rule was also "sort by colour", which the respondent did correctly even though the card differed from the matching cards in respect of both shape and number.

at a time so that each matches one of four "key" cards in some way. Each card differs in three dimensions (see Figure 11.2): the number of objects shown on the card (one, two, three, or four), the shape of the objects (circles, triangles, squares, or stars), and their colour (red, green, blue, or yellow). So, for each card, a participant can match it according to shape, number, or colour. As the participant places a card in a pile underneath one of the four key cards, they are told only whether or not the card matches according to the criterion the experimenter "has in mind". The idea is that by using this feedback, the individual will quite quickly learn (i.e., infer) the matching criterion, and sort subsequent cards according to it. After a number of correct sortings, the experimenter changes the matching criterion. (In some procedures, this is done without warning, but in the modified procedure, Nelson, 1976, participants are explicitly told that the former matching rule no longer applies.) People with frontal lobe damage generally learn to sort much more slowly than normal people but, in particular, they make many more perseverative errors, meaning that they continue to sort according to the previous matching criterion even though it no longer applies. This is most obviously apparent in Nelson's modified procedure (in which participants are specifically told that the rule has changed though not what it has changed to). Despite this instruction, some frontal patients will continue to sort according to the obsolete rule, showing an inability to think flexibly and change behaviour to adapt to the "new situation".

A variant of the WCST developed by Delis et al. (1992) required participants to sort sets of six cards each showing an object/drawing/word into two equal piles. The cards could be sorted according to several criteria including shape, shading, category of word written on each, and so on. Frontal patients struggled with this test in two characteristic ways. First, they were not very good at sorting the cards into meaningful groups at all, and second, even if they could sort as per the instructions, they struggled to describe the actual rule they were using.

Other tests that assess conceptual thinking are the Brixton and Hayling tests (Burgess & Shallice, 1997). In the Brixton test, participants must predict which of an array of numbered circles will be filled in on the next trial. This is determined by one of several simple rules and periodically the relevant rule is changed. Thus participants must learn a rule, apply it, and update it as necessary. Frontal patients make more errors on this task than controls or patients with posterior lesions (Shallice & Burgess, 1996).

The Hayling task consists of two sets of 15 sentences, each with the last word missing. The sentences are designed to strongly cue a particular final word. In the first task (Hayling A) participants must complete the sentence as quickly as

possible with an appropriate word. For example: He mailed the letter without a . . . (stamp).

In the second task (Hayling B) participants must complete the sentence with any inappropriate word. For example: He mailed the letter without a . . . (gorilla).

This second condition is much more difficult, requiring participants to inhibit a cued prepotent response and to generate an entirely novel response. Patients with frontal damage are impaired on both Haylings A and B, but it is suggested that different fundamental processes underpin the impairments (Shallice & Burgess, 1996) with Hayling B capturing important aspects of executive function.

IMPAIRMENTS IN GOAL-ORIENTED BEHAVIOUR

Goal-oriented behaviour comprises various core aspects. One component is sequencing: we must generate a sequential plan of action incorporating various subcomponents in an appropriate order. Second, successful behaviour requires self-monitoring, essentially the process of checking that we are on track to achieve the desired result. Both of these components are sensitive to frontal lobe damage.

Sequential planning

Research suggests that individuals with frontal lobe damage struggle with tasks that, for successful completion, must be broken down into a series of subroutines to be completed in the right order. Problems may arise because of composite difficulties in sequential planning, memory, self-monitoring, and of course not losing sight of the overall goal (see Box 11.1).

Box 11.1 "Tea for two"

Consider the executive components involved in making a cup of tea:

- First there is, self-evidently, an overall goal that must be borne in mind as the tea-maker goes about their task.
- The task can be broken down into a number of subcomponents. What materials and items will be needed, and where are they in the kitchen?
- What is the appropriate sequence of actions? The kettle must be filled, the tea should go in the pot, milk in the cups, and so on.
- What about contingency plans? Perhaps the milk in the jug is sour? Is there more in the fridge? Is there any powdered milk? Did anyone want sugar? Are there any sweeteners instead?

The point of this example is to illustrate the range of psychological skills implicated in even this simple task: Our tea-maker has to have a strategy: they must sequence different elements of the task in the correct order; they must remember what has already been done, and what yet needs to be done; and finally they must be able to adapt the task to changing circumstances (if needs be) to fulfil the overall goal.

The example of making a cup of tea illustrates the vital importance of "temporal" sequencing in planning many actions. A study by Milner (1982) neatly illustrates the particular difficulty some frontal patients have in distinguishing between more and less recent events. Participants viewed a sequence of simple line drawings of objects one at a time. Every so often a test card would be shown that had two objects on it. On recognition trials, the respondent had to decide which of the two objects had appeared in the preceding sequence (one had appeared but the other was new). In recency trials, the respondent had to decide which of the two objects had appeared most recently. The recognition rate of frontal patients was comparable with that of control participants, but recency judgements were significantly impaired. In other words, frontal patients could not remember the order in which the material was viewed. Incidentally, there was also a laterality effect evident in this study giving rise to a double dissociation. Patients with left frontal damage fared worse with verbal material than with drawings, and patients with right frontal damage did worse with drawings than words.

The previous study shows that frontal patients struggle to memorise sequences—but do they also struggle in planning sequential actions? Petrides and Milner (1982) developed a disarmingly simple procedure to test this. Respondents were required simply to point to any item in a 3×2 array that they had not pointed to before. The array always contained the same six items, but their location was changed on successive trials. Frontal patients made significantly more errors than controls, suggesting a marked impairment in planning of sequential actions. Of course, this task relies heavily on working memory (remembering what you have already pointed to, in order to avoid doing it again), and we saw in Chapter 7 that central executive component of working memory is mediated by the dorsolateral prefrontal cortex (DLPFC).

Impaired planning of sequential action is also seen in tasks such as the "Tower of London" puzzle (Shallice, 1982). In this test there are three coloured balls, and three prongs. One can hold three balls, the second two balls, and the third just one ball. On each trial the balls are placed in the standard starting position and the participant must move them to a different specified finishing position in the least possible number of moves. Some trials require only two moves, while others require ten or more to reach the final configuration. Frontal patients are worse than controls on both simple and complex trials, although the gap widens on complex trials. The behaviour of frontal patients seems aimless and devoid of strategy. Even when they do solve the puzzle, it is as if they have stumbled across the answer rather than thinking it through step-by-step (see Figure 11.3). A computerised variant of the Tower of London task, dubbed the "Stockings of Cambridge" (part of the CANTAB battery; see Chapter 2) has been used to show explicitly that not only do patients with frontal damage solve fewer problems than controls, but they also solve problems less efficiently, tending to take more moves than the optimum number.

Self-monitoring

When neuropsychologists refer to self-monitoring, they are really talking about the reflexive skill of self-inquiry: "How am I getting along with this task?", "What was it I just did?", "How close am I to successful completion?" Time and again, both anecdotal and experimental evidence points to frailties in this intrinsic ability

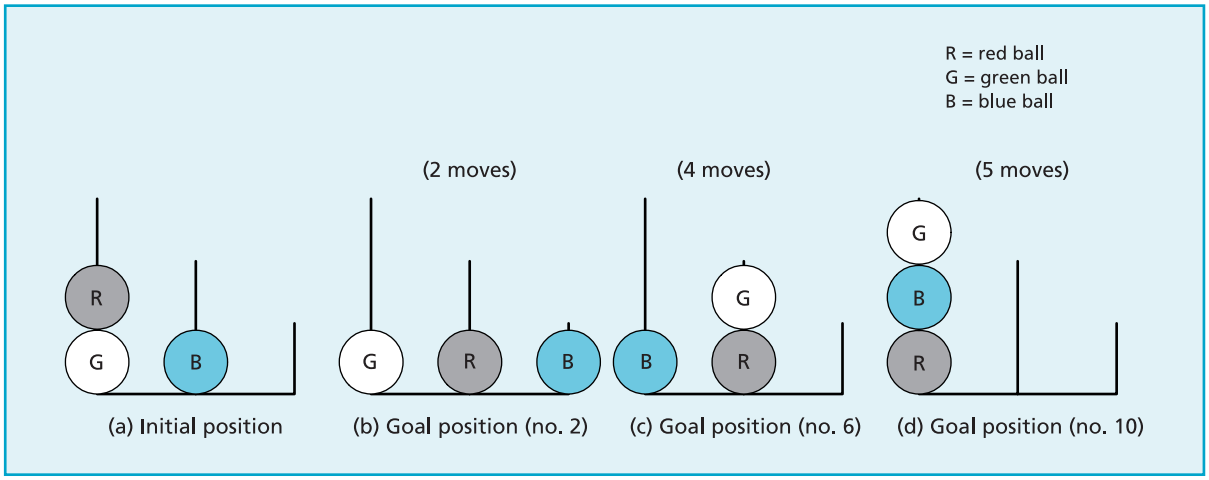


FIG. 11.3 The "Tower of London" test. Respondents may only move one ball from the top of a prong at a time. From a standard starting position (a) the participant might be asked to rearrange the balls in various ways that require two (b), four (c), or more (d) moves. Patients with dorsolateral prefrontal damage probably struggle on this test because their ability to plan a sequence of actions is compromised.

in patients with frontal damage. Anecdotally, case reports frequently allude to the frontal patient's inability to "keep on track" during prolonged tasks. When asked to copy one of several drawings on a page, they may start accurately, but then integrate material from one or more of the other drawings into their own. In a classic "real-life" study of the derailment that is seen in the goal-oriented behaviour of frontal patients, Shallice and Burgess (1991) set three patients a set of relatively simple tasks to complete. These included shopping for certain items, finding out some information about four queries (the price of a pack of tomatoes, etc.), and keeping an appointment. This was specifically not a memory test and respondents had a list of the tasks and instructions to follow. Nevertheless, each patient had difficulty completing the assignment. In one case an item could not be purchased because the shop did not stock the individual's favourite brand; in another, items were selected but not paid for; or, worse still, an entire component of the assignment was ignored. This is a particularly good illustration of the problems frontal patients have in achieving goals. They start with the best intentions, but are easily distracted, and are unable to get back on track because of an apparent lack of awareness about being blown off-course.

TASK SWITCHING AND MULTI-TASKING

The preceding section on goal-directed behaviour focuses on situations where a person has a single goal in mind and must sequence their actions to achieve that goal. However, executive functions are also thought to be called on in situations where people are required to perform more than one task, thus maintaining multiple goals. Typical examples of this are task switching (where people move between distinct tasks) and multi-tasking (where they attempt to carry out more than one task at the same time.

TASK SWITCHING

Everyday life requires frequent switching between different tasks. If I sit at my desk writing an email and the phone rings, I stop writing and pick up the phone. I must switch task from writing to one person to talking to another and it may take a moment to adjust to the change. This phenomenon can be studied in an experimental setting by using two (or more) simple tasks and switching between trials of each task. Rogers and Monsell (1995) devised a task where participants looked at a grid of four squares on a computer screen. A letter/number pairing (e.g., L4 or G9) appeared in each square of the grid in turn, moving in a clockwise direction (thus L4 top left, G9 top right, A6 bottom right, P3 bottom left, etc.). When the pair was at the top participants had to decide if the letter was a vowel or consonant, and when the pair was at the bottom they had to decide if the number was odd or even. On two of the four trials participants were doing the same task as the last trial; on the other two they were switching to a different task. On trials where participants switched, they made more errors and their reaction times were significantly longer. This reaction time difference is referred to as a "switch cost" (see Figure 11.4).

There are several interesting characteristics of the switch cost which tell us more about the nature of task switching (Monsell 2003). First, the switch cost is reduced but not eliminated if people are given a chance to prepare for the switch. Second, although the switch trials are particularly slowed, performance overall is slower in a task-switching block of trials than in a single-task block, suggesting longer-term as well as transient effects of switching. Third, switch costs are most pronounced when participants switch from a hard to an easy task, as compared with an easy to hard switch. These observations have led theorists to suggest a number of mechanisms that are important in task switching. Monsell and others have suggested that participants must undergo a process of reconfiguring their task set, a "mental gear change". However this reconfiguration must depend, in part, on presentation of the trigger stimulus, in order to explain the residual switch cost even when preparation is allowed. The finding of greater switch costs when moving from hard to easy suggests that inhibition of the old task may be more important than activating the new one when performing a switch. A harder task that requires more processing resources may be harder to inhibit.

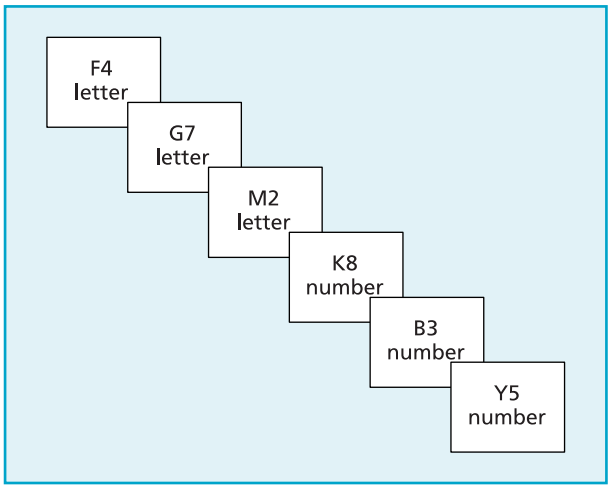


FIG. 11.4 A typical task-switching paradigm. Participants see a letter and a number on the screen and are prompted to name either the letter or the number. Where they have to switch from one to the other (on the fourth trial in this example), their reaction time is elevated, representing a so-called "switch cost".

It should be clear that task switching, requiring as it does mental flexibility and active maintenance of behavioural goals, falls within the definition of executive function, and should depend on intact frontal lobes. Rogers et al. (1998) have shown that patients with prefrontal damage (especially left-sided) have difficulties performing task-switching paradigms. Aron, Robbins, and Poldrack (2004) have suggested an interesting dissociation between left and right prefrontal regions in task switching. Patients with focal right-sided lesions appeared to have particular problems inhibiting the old task, while those with left-sided lesions were poor at maintaining control of the appropriate task set.

MULTI-TASKING

Like task switching, multi-tasking is also an integral component of everyday life. If, instead of typing an email, I am making a cup of tea when the phone rings, I am likely to continue with that while holding a conversation. Most of us can perform two tasks at once with reasonable competence as long as at least one of the tasks is relatively routine. However, as the tasks become more demanding, attempting to do two (or more) things at once typically leads to impaired performance on one or both tasks. The debate on mobile phone use while driving highlights this point. Using a hand-held mobile phone is now banned in many countries because it has been shown to impair driving performance and thus increase the likelihood of accidents. However, many experts argue that even using a hands-free system has a significant negative effect on driving performance. Although the concept of switch costs does not apply when we are performing two tasks in parallel, capacity limitations make it likely that neither task is being performed with optimum efficiency.

Burgess and colleagues (see Burgess, 2000, for review) have suggested that multi-tasking is prototypical of situations where we have to organise and structure behaviour in the face of multiple goals. They characterise certain patients as displaying "strategy application disorder", which specifically compromises their ability to multi-task. These patients are unimpaired on many laboratory tests of function, including IQ tests and the classic executive function tests, such as Wisconsin Card sorting and verbal fluency. Burgess et al. (2000) reported that patients with this specific disorder typically have lesions to the most anterior part of the prefrontal cortex, suggesting that this region is critical for coordinating multiple behavioural goals.

ISSUES WITH "EXECUTIVE TESTS"

Current research on the neuropsychology of executive function is raising a number of issues about the classic executive tests. In the previous sections, we have illustrated/described a number of features of impaired executive function in terms of characteristic performance deficits on tests undertaken both in the laboratory or clinic and in real-world settings. In Shallice and Burgess's study for example, the researchers designed tasks based on patients' real-life experiences. This raises the issue of **ecological validity**. Burgess et al. (2006) have recently argued that traditional tests of executive function are largely derived from conceptual frameworks that have become outdated. They suggest that these tests were aimed more at theoretical research than clinically useful research and, especially given that the theories in question have been substantially revised, there is a case for developing and using new measures that are more ecologically valid. Such measures have a direct relevance to the problems encountered by patients in their everyday lives. Examples from Burgess's research group include the "Multiple Errands" and "Six Elements" tasks, which simulate real-life situations where cognitive flexibility, working memory, etc. are required. In considering this issue, it is also important to distinguish between tests to characterise deficits in frontal patients and tests that engage frontal mechanisms in normal people. The best tests for one application may not be the best for the other.

Key Term
Ecological validity: Characteristic of experiments where the methods, materials and setting approximate the real-life situation that is under study.

An additional concern about traditional tests of executive function is that multiple versions of tests have often been developed. For example, Unterrainer et al. (2003) explicitly demonstrated that performance on the Tower of London task depended on the exact instructions given. The length of training sessions and the use of cueing or prompting also have significant effects on performance. These findings led Unterrainer and Owen (2006) to call for standardised versions of the classic frontal tasks to allow inter-study comparisons.

INTERIM COMMENT

In the previous sections we described three principal domains of executive dysfunction. Individuals have difficulty initiating and terminating actions, and often seem indifferent to their own "inertia". Sometimes, their behaviour is guided more by immediate circumstances than any grand plan, and we see evidence of utilisation or stimulus-driven behaviour. Dysexecutive cases also have difficulties with tasks that demand flexibility and adaptation of behaviour, and, as a result, may show marked perseveration. Finally, they seem to have particular problems with complex tasks that need to be broken down into smaller sequential tasks in order to be completed successfully.

Our list of executive dysfunctions is meant to be illustrative rather than comprehensive and, even with our examples, it is possible to argue that the domains overlap. For instance, poor planning may be linked to a tendency to engage in stimulus-driven behaviour, and perseveration may be related to "loss of goal" because both rely on impaired memory. Nevertheless, the overall impression of someone with executive dysfunction is of an individual whose thinking has undergone fundamental changes that may impact on almost every other aspect of behaviour. In the following sections we try to address these issues from a different "bottom-up" perspective, by considering in a little more detail what we know about the brain systems and regions that may be involved in executive function, and how damage or dysfunction to these areas is related to impaired executive function.

UNDERLYING MECHANISMS OF EXECUTIVE FUNCTION

When asked to define executive function, a neuropsychologist will typically resort to listing various higher-level cognitive processes that are believed to depend on "executive function". However, defining a single process that underpins all these examples has proved much more challenging. Certain influential theorists have attempted to reduce executive function to a lowest common denominator. For example, Goldman-Rakic (1987) argued that representational working memory held the key to understanding prefrontal control of behaviour. However, perhaps the prevalent view today is that executive functions are multifactorial. In fact, in studies using batteries of tests designed to assess executive function, a highly consistent finding is that the degree of correlation between different executive tests is small and often statistically insignificant. This

suggests that the concept of "executive function" is not unitary and requires further fractionation. Having reviewed the available literature, Baddeley (1996) proposed that what he termed the "central executive" served four different functions: allocating resources to perform two tasks simultaneously, the capacity to switch strategies, the capacity to selectively attend to one source of input while inhibiting the effect of others, and the capacity to manipulate information stored in long-term memory.

More recently, Miyake et al. (2000) used a statistical technique called latent variable analysis to determine the extent to which aspects of executive function may be distinct. The three processes considered (shifting, updating, and inhibition) were found to be moderately correlated but still clearly separable. The authors concluded that component processes falling under the umbrella of executive function are distinguishable but not completely independent. Subsequent work from the same group has made the situation still more complicated, as Friedman and Miyake (2004) have demonstrated that one of the previously defined components—inhibition—can itself be further fractionated into distinct but somewhat correlated subcomponents. Specifically, resistance to proactive interference (that is, the impact of previous learning on performance) was dissociated from prepotent response inhibition (the need to restrain oneself from making an established motor response). Both of these were further dissociated from distractor interference (the impact of task-irrelevant distraction on performance). Clearly the exact nature of executive function, or functions, and the inter-relationships between components are still incompletely understood. The complexity of this area of neuropsychology is exacerbated by the fact that tests of executive function are, by definition, complex cognitive tasks that almost invariably depend on non-executive as well as executive processes.

THE BRAIN AND EXECUTIVE FUNCTION/ DYSFUNCTION

In spite of the debate surrounding the definition and fractionation of executive function, the combination of traditional neuropsychology and functional neuroimaging has allowed researchers to gain more understanding about the brain basis of executive functions. To illustrate this, we will focus on three tasks tapping into the three domains of executive function discussed earlier in this chapter. Given that executive functions are thought to be subserved by the prefrontal cortex, key questions are whether executive tasks are *sensitive* to frontal function and whether they are *specific* to frontal function.

THE BRAIN AND ACTION CONTROL: VERBAL FLUENCY

Verbal fluency is a commonly used measure of executive function, in part because it is an extremely quick and simple task to administer. In the phonemic version of the task (mentioned earlier), participants are given a letter of the alphabet and asked to generate as many words as possible beginning with that letter in a set time period. Several meta-analyses (e.g., Henry & Crawford, 2004) have shown that

patients with frontal lobe lesions consistently demonstrate impaired performance on phonemic verbal fluency tasks. The impairment is typically more severe when the lesion is either bilateral or left lateralised. However, verbal fluency impairments do not seem to be specific to frontal lobe patients, as patients with non-frontal lesions also perform poorly on the task (e.g., Perret, 1974). Again left-sided lesions produce more pronounced impairments.

Neuroimaging can explore which regions within the frontal lobes are important for a task. Studies of verbal fluency have produced somewhat inconsistent results, perhaps reflecting differences in the exact nature of the cognitive activation tasks used. However, in general terms, studies suggest that key regions are the left dorsolateral prefrontal cortex (DLPFC), anterior cingulate, and left inferior frontal gyrus (e.g., Frith, 1995; Paulesu et al., 1997). Non-frontal regions have also been identified, in particular the thalamus.

THE BRAIN AND ABSTRACT/CONCEPTUAL THINKING: WCST

We described the WCST earlier in this chapter. It assesses cognitive flexibility, thought to depend on the core subprocesses of shifting and updating. A recent review (Alvarez & Emory 2006) assessed 25 studies of the effects of different brain lesions on WCST performance. Although the majority of studies found that frontal patients performed worse on the WCST than either controls or patients with non-frontal lesions, this was by no means a universal finding. In particular, there are a number of studies reporting negligible differences between the performance of patients with frontal and non-frontal damage, suggesting that the WCST may be sensitive to prefrontal damage, but not a specific index of it.

This conclusion is largely supported by the neuroimaging literature (see Barcelo & Knight, 2001, for review). Typically WCST performance is associated with widespread and bilateral activation of the prefrontal cortex, in particular the DLPFC. However, this frontal activation is part of a distributed network of activity that also includes posterior and subcortical brain regions.

THE BRAIN AND GOAL-DIRECTED BEHAVIOUR: TOWER OF LONDON

The Tower of London and related tasks were described earlier in this chapter. They are tests of planning thought to particularly assess components of executive function related to goal-directed behaviour. Unterrainer and Owen (2006) have recently reviewed the neuropsychological and neuroimaging literature on this task. Numerous studies have reported impaired planning abilities in patients with frontal lobe lesions. Indeed, a more sophisticated componential analysis of performance by Owen et al. (1995) suggests that inhibition impairments may play a crucial role. It appears that patients begin to move the coloured balls around before they have fully thought through an appropriate solution. However, once again, although the sensitivity of the task seems well established, the specificity is more debatable. For example, studies of patients with basal ganglia disorders such as Parkinson's disease show significant impairments on the task. This is consistent with the idea mentioned earlier, that executive dysfunctions may depend

on disruptions to fronto–subcortical circuitry, rather than specific frontal damage.

The neuroimaging literature supports a role for prefrontal regions in Tower of London performance (see Figure 11.5). The DLPFC seems particularly important, with similar levels of activation in the right and left hemispheres. However, once again, non-frontal regions are also involved, including basal ganglia structures, premotor cortex, and posterior parietal cortex (e.g., Van den Heuvel et al., 2003).

THE BRAIN AND TASK SWITCHING/MULTI-TASKING

Neuroimaging has also been used to study task switching and multi-tasking, again confirming the involvement of prefrontal regions but additionally implicating non-frontal regions. Lateral prefrontal cortex and anterior cingulate are critically involved in task switching, but studies also report increased posterior parietal and (sometimes) basal ganglia activation (e.g., Braver, Reynolds, & Donaldson, 2003; Liston et al., 2006; Yeung et al., 2006). Imaging studies of multi-tasking have confirmed the importance of anterior prefrontal regions, as suggested by the neuropsychological literature (e.g., Burgess, Scott, & Frith, 2003), however few imaging studies have explicitly addressed multi-tasking, not least because the physical constraints of a scanner limit the available paradigms.

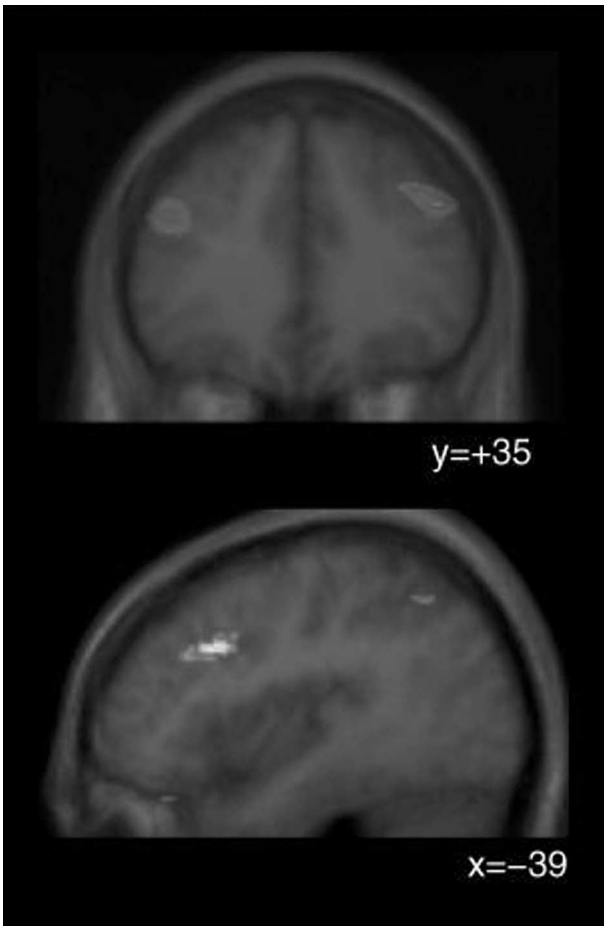


FIG. 11.5 Brain activations from a PET study of people performing a computerised Tower of London task. We are very grateful to Dr Adrian Owen of the MRC Cognition and Brain Sciences Unit, Cambridge for providing this image.

INTERIM COMMENT

In the examples discussed above it is clear that the evidence from neuropsychology and neuroimaging confirms the sensitivity of classic executive function tests to frontal lobe function. However, it is also clear that these tests are not specific to frontal function. Other regions are activated during normal performance, and non-frontal lesions can result in impairments of task performance. Two important issues arise from this brief review. First, although we have alluded to different prefrontal regions thus far, we have focused on frontal vs non-frontal. Treating the frontal lobe as a single area is obviously grossly simplistic. Neuroimaging studies have helped us address the issue of whether different aspects of executive function depend on different frontal regions. The second issue is how we refine our understanding of frontal involvement in executive function to account for the lack of specificity discussed above. In the next part of this chapter we will look at these two issues in more detail.

SPECIALISATION WITHIN THE PREFRONTAL CORTEX

Given the complexity of both executive function and frontal lobe neuroanatomy, it is perhaps surprising how little research effort has been dedicated to exploring the mappings between them. However, with the emergence of neuroimaging techniques more studies have attempted to localise components of executive processing. Given that there is no coherent and accepted theory that clearly fractionates executive function into separable processes, this literature is inevitably hamstrung to some extent. Nevertheless, certain important themes can be identified, some of which are reviewed briefly below.

THE SUPERVISORY ATTENTIONAL SYSTEM AND ANTERIOR CINGULATE

Norman and Shallice (1986) proposed a model of executive function that they termed the "supervisory attentional system" (see Figure 11.6). This model was proposed to explain goal-directed behaviour where achieving an overall goal depends on successful and orderly completion of several subgoals. For example, if you are decorating a room there are a number of smaller subroutines that must be completed to achieve this goal. The ordering of these subroutines is quite important: there is no point painting a wall before filling in cracks in it; and laying a new carpet before painting the walls is asking for trouble. Representations of how to complete the subroutines are stored in memory, along with thousands of other learned actions. In order to decorate the room, a decorator must inhibit irrelevant representations, and select and correctly sequence the appropriate ones. For a professional decorator, correctly ordering these representations (or "schemas" as Norman and Shallice termed them) is a relatively automatic and passive process termed "contention scheduling". For an amateur, contention scheduling alone is unlikely to be sufficient; the process will also require a higher level of planning. Norman and Shallice suggest that this depends on a supervisory attentional system (SAS). The SAS can bring order to the task in hand when a higher level of control is called for. It can also override contention scheduling, where necessary, to bring flexibility to complex task performance. For example, if our professional decorator discovers an unexpected problem, his or her SAS will come into play in order to solve the problem and complete the task.

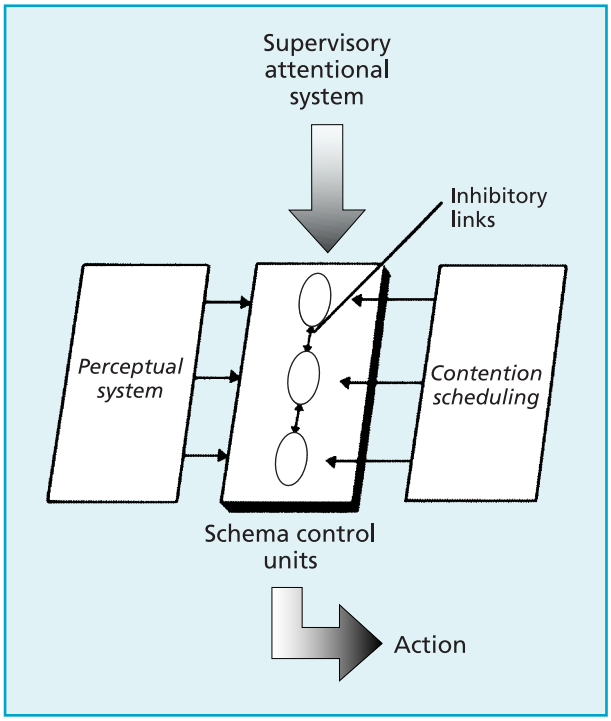


FIG. 11.6 Norman and Shallice's supervisory attentional system in which certain components within an overall plan of action are mutually inhibitory (you cannot stir the tea without already having picked up the spoon, for example). This relatively passive organisational process is known as contention scheduling. However, it can be "overridden" by a supervisory attentional process if required (if, for example, your guest advises you that he or she no longer takes milk or sugar).

Early neuroimaging experiments attempted to localise the SAS within the prefrontal cortex. PET studies in the 1990s suggested that the anterior

cingulate may be a critical region. Corbetta et al. (1991) showed that when participants had to watch for changes in one stimulus parameter (shape, colour, or movement), posterior cortical regions were activated. However, when they had to simultaneously monitor all three parameters, the region most strongly activated was the anterior cingulate. In another study (Frith et al., 1991) greater anterior cingulate activation was seen when participants had to generate a random sequence of finger movements compared to producing a cued sequence. These, and other studies, suggest a role for the anterior cingulate in action control. However, this region is also involved in many other aspects of function (see examples elsewhere in this chapter, and indeed elsewhere in this book). Moreover, the original SAS model has been re-evaluated in more recent years to explain executive function (Shallice & Burgess, 1996). This model suggests processes for examining schema as well as eight separable executive processes for implementing, monitoring, and updating schema as appropriate. Their "supervisory system" thus involves multiple components which are likely to relate to the function of multiple brain regions.

RESPONSE SELECTION AND LEFT DORSOLATERAL PREFRONTAL CORTEX

In the PET experiment of Frith et al. (1991) described above, greater anterior cingulate activation was seen when participants generated their own sequence of finger movements. The left dorsolateral prefrontal cortex was also involved. In a verbal version of the task, left DLPFC was activated when participants freely generated words rather than simply repeating them. Jahanshahi et al. (1995) showed that left DLPFC was also more activated if participants had to choose when to make a specific response. Thus choosing when to respond, as well as which response to make, seems to depend on the left DLPFC. In a later study, Jahanshahi and Rothwell (2000) asked participants to generate random response sequences (a demanding thing to do!) at faster and faster rates. Performance broke down at faster rates and there was an accompanying drop in left (but not right) DLPFC activity. These observations led Frith, Jahanshahi, and others to propose that the left DLPFC has a specific role in response selection and specification.

WORKING MEMORY AND LATERAL PREFRONTAL CORTEX

An influential hypothesis suggests that the ventrolateral prefrontal cortex (VLPFC) and DLPFC play distinct roles in working memory (Owen, 1997). Specifically the VLPFC is proposed to control the retrieval of representations from posterior cortical regions, while the DLPFC is proposed to control the monitoring and manipulation of these representations. Various imaging studies have supported this idea. For example, Wagner et al. (2001) demonstrated VLPFC activation but very little DLPFC activation associated with rote rehearsal in working memory. Elaborative rehearsal, which involves the manipulation of material in working memory, preferentially activated the DLPFC. However, other studies have argued against such a simple separation, suggesting a greater degree of functional overlap.

Neither the DLPFC nor VLPFC is uniquely activated by working memory tasks. Duncan and Owen (2000) performed a meta-analysis of neuroimaging studies of executive function (see Figure 11.7). Their analysis covered a wide range

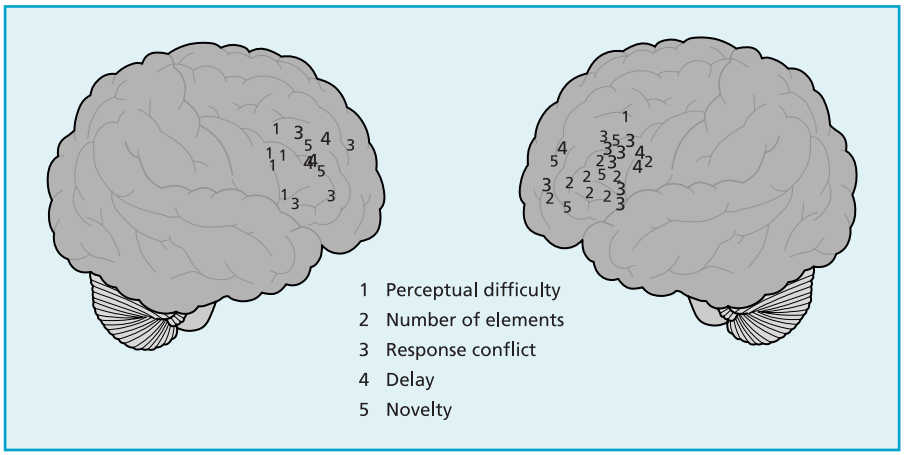


FIG. 11.7 Similar regional brain activations from various studies using different executive tasks, from a meta-analysis by Duncan and Owen (2000). We are grateful to Dr Adrian Owen of the MRC Cognition and Brain Sciences Unit, Cambridge for providing this image.

of tasks and considered the extent to which the tasks activated similar regions. In spite of the diversity of the tasks, three main clusters of activation could be identified across the studies: the dorsal anterior cingulate, mid DLPFC, and mid VLPFC. One possible interpretation of these findings is that the three regions form a common network that is recruited by diverse cognitive demands. Another explanation is that the three regions subserve distinct functions, but functions that are sufficiently abstract to be involved in different cognitive tasks. For example, working memory processes are often involved in complex tasks: the WCST is not seen as an implicit test of working memory, although participants clearly need to hold in mind the current rule and remember recent selections when working out a new rule. Similarly the Tower of London is typically seen as a test of planning, but generating a solution involves remembering previous moves in the sequence and thus working memory processes are implicitly recruited. As already discussed, DLPFC and VLPFC are both implicated in working memory and are therefore likely to be involved in any task with working memory components, explicit or implicit. Similarly, the anterior cingulate has been widely implicated in sustained attention, response selection, and inhibition of competing inappropriate responses. Some or all of these processes may be components of many complex tasks. As astute readers may have realised, there is a tendency for arguments and theories in this area to become somewhat circular, and further research is required to refine the concepts.

DISTRIBUTED CONTROL NETWORKS

As discussed above, executive function research has run into a number of difficulties. First, executive function and frontal lobe function have been used interchangeably, but it is clear that many paradigmatic tests of executive function are not specific to the frontal lobes. Second, attempts to fractionate executive functions into component subprocesses dependent on different brain regions have produced disappointing results.

Neuroimaging is beginning to suggest that the reason for these difficulties may

be that thinking about a one-to-one mapping between structure and function is inappropriate for executive functions. This is intuitively plausible as these functions are by definition extremely complex and multi-faceted. Various recent meta-analyses have suggested that executive functions are mediated by networks incorporating multiple cortical regions, both frontal and posterior, whose functions are collaborative and overlapping (Goldman-Rakic, 1998; Mesulam, 1998). Carpenter and Just (1999) showed that the component regions involved in executive task performance depended on the level of difficulty (or "cognitive load"; see our discussion of this in Chapter 8). This suggests that understanding the brain basis of executive function is by no means a simple mapping exercise. Instead it involves understanding how multiple brain regions can be flexibly combined depending on task requirements and, potentially, also on individual skills and experiences. Different people may take different strategic approaches to an executive task, and therefore recruit different brain regions.

Understanding the interaction between brain regions involves a new approach to functional imaging data. Structural equation modelling or, more recently, dynamic causal modelling can be used to look at "effective connectivity": that is, the dynamically changing functional interactions between regions in a connected network. Studies using this approach have demonstrated that the strength of connections between regions involved in executive function is modulated by task demands (Funahashi, 2001). In a further recent development, event-related fMRI has shown that the frontal activation associated with particular tasks has distinct temporal properties. Some activations are sustained while others are more transient. Understanding the brain basis of executive function must take these temporal differences into account (Collette et al., 2006).

INTERIM COMMENT

Functional neuroimaging has changed the way we think about executive function over the last 10 years. In many areas of neuropsychology, PET and fMRI have been used as tools in a mapping exercise: determining which brain regions are responsible for which functions. In the area of executive function, it has become clear that seeking one-to-one mapping between structure and function is unlikely to be a fruitful way forward. Instead researchers are using more sophisticated analysis techniques to explore the connectivity between regions in distributed networks and determine how these connections are modulated by task demands. This approach has been applied to other aspects of function too, but the need for it is perhaps clearest for the high-level functions we term "executive".

EXECUTIVE DYSFUNCTION AND PSYCHIATRIC DISORDERS

THE RISE AND FALL OF FRONTAL LOBOTOMIES

In view of what has been said so far about damage to the frontal lobes and associated impaired function, it is both ironic and (for psychiatry) somewhat

embarrassing to record that some of the earliest attempts to modify presumed brain disorder among psychiatric patients involved wholesale removal (or isolation) of frontal tissue. The development of the procedure that came to be known as the frontal lobotomy or leucotomy represents one of the darkest times in the history of psychiatry, yet merits retelling if only to serve as a reminder to avoid making the same sort of mistake ever again.

The procedure itself was introduced in the early 1930s by the respected Portuguese neurologist Egas Moniz. Of course at that time there were no effective treatments for any of the major psychiatric disorders, and in Moniz's defence it must be said that clinicians were desperate for access to any therapeutic procedures that offered hope of favourable outcome, or even a measure of effective control. Moniz heard of the work by two American researchers who reported a change to the "personality" of a chimpanzee whose frontal lobes they had removed. From being uncooperative and aggressive, the chimp became docile and pliant after surgery. Moniz reasoned that the same effect might offer relief for severely agitated mental patients. However, he was uneasy about operating on the whole of the frontal lobes so modified the procedure to encompass only the prefrontal areas.

Moniz eventually settled on a surgical procedure in which a hole was drilled in the side of the patient's forehead, and a probe with a retractable blade (a leucotome) inserted and moved through an arc, lesioning all the tissue it encountered. After World War II the technique was adopted (and simplified) by Freeman in the United States. The "lobotomy" (as it now came to be known) could be administered (under anaesthesia) in a doctor's surgery in a matter of minutes. Over the next few years thousands of lobotomies were carried out using Freeman's procedure, and, to compound insult with injury, Moniz received the Nobel prize for physiology and medicine in 1949.

It is, of course, easy to be wise after the event. Records show that a small number of aggressive agitated patients did become more cooperative and manageable after surgery. Some depressed and extremely anxious patients also showed a reduction in their symptoms, but often exchanged these for the behavioural inertia that we described earlier. Proper clinical trials were never instigated even though the procedure itself was used on an ever-wider cross-section of psychiatric patients. It was, for example, used extensively for a period as a treatment for schizophrenia, yet no formal evaluative study of its effectiveness for such patients was ever conducted, and so far as we can tell, anecdotally, it seemed to do little good and clearly made symptoms worse for some schizophrenic patients.

The procedure eventually fell out of favour, largely because of the development in the early 1950s of effective drugs for schizophrenia, and then later for depression and the anxiety disorders. Today psycho-surgical procedures are still occasionally carried out as a last-ditch treatment for intractable depression or drug-resistant obsessive-compulsive disorder. The most common procedure is anterior cingulotomy involving a small disconnecting lesion between the anterior cingulate and subcortical structures. A more recent technique that also targets the anterior cingulate is deep brain stimulation. Mayberg et al. (2005) have used implanted electrodes to disrupt cingulate activity, leading to marked improvement in severely depressed patients.

PSYCHIATRIC DISORDERS, THE FRONTAL LOBES, AND NEUROIMAGING

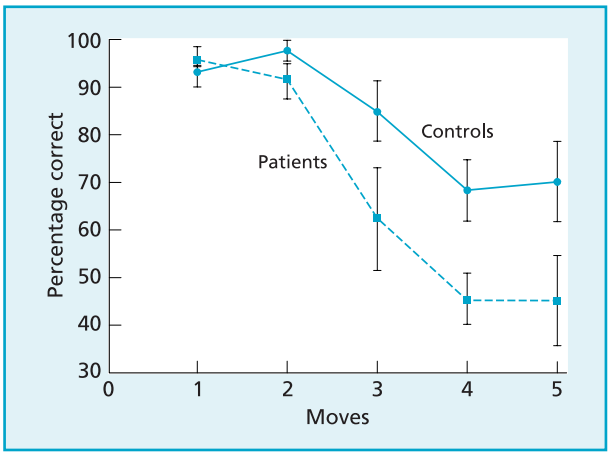


FIG. 11.8 Tower of London performance in schizophrenia. The performance of a group of 12 patients and 12 age- and IQ-matched controls on a computerised Tower of London task. In spite of relatively preserved general intellectual function, this group of patients performed poorly on more difficult problems (those requiring more moves) suggesting executive dysfunction. Data acquired in collaboration with Professor Barbara Sahakian and Dr Peter McKenna, University of Cambridge.

The link between psychiatry and the frontal lobes is evident when psychiatric symptoms are compared to those caused by frontal lobe lesions. The term pseudo-psychopathy has been coined to identify some of the disinhibited features, especially in the social domain, that frontal patients may exhibit. A second syndrome, called pseudo-depression, was also characterised by Blumer and Benson (1975) to encompass the apathy, indifference, withdrawal, and loss of initiative seen in some frontal patients. These descriptors are, of course, also applicable to many people with chronic schizophrenia. Patients with schizophrenia have been reliably shown to have impairments on classic tests of frontal function; for example, Figure 11.8 shows performance on a Tower of London task. Neuroimaging research has confirmed that people with this diagnosis often have functional abnormalities indicative of frontal impairment (Stirling, Hellewell, & Quraishi, 1998). Underactivation of the frontal lobes (during the completion of tasks that lead to activation in control respondents) is now a relatively robust finding in schizophrenia and seems most closely linked to the presence of negative symptoms. However, many classic imaging studies of schizophrenia are plagued by confounds (Weinberger, Berman, & Frith, 1996) and the general consensus today is that there is no clear focal pathology. Instead, connectivity models of schizophrenia have gained more and more credence (Andreasen, Paradiso, & O'Leary, 1998; Frith, 1997). Effective connectivity analyses have clearly demonstrated abnormalities in schizophrenic patients performing executive tasks (Fletcher et al., 1999; Meyer-Lindenberg et al., 2001). Newer techniques of white matter and diffusion tensor imaging have confirmed the presence of connectivity disruption even in very young patients (White et al., 2007) and those with new-onset illness (Federspiel et al., 2006). These observations underpin a new generation of neurodevelopmental and neuropathological theories of schizophrenia (e.g., Carlsson & Carlsson, 2006; Rubia, 2002; Stephan, Baldeweg, & Friston, 2006).

In the case of clinical depression, as with schizophrenia, functional changes are apparent in the frontal lobes but the picture is more complicated than was first thought (Drevets et al., 1997). Regions of the prefrontal cortex may be hypo- or hyperactive in response to cognitive challenges. Again, it seems that a model of depression based on an interconnected network with frontal, limbic, and subcortical components provides a more complete picture (Mayberg, 2003)

CHAPTER SUMMARY

The raft of well-documented impairments of executive function can be categorised in a variety of ways. Nevertheless, the list will include problems in the initiation and

cessation of actions, impaired strategy formation, and loss of goal-oriented behaviour.

No single theory of frontal lobe impairment can currently account for the range of dysfunctions associated with them. Impairments in action control, abstract thinking, and goal-oriented behaviour are all observed in patients with prefrontal damage. Patients may also have difficulties with task switching and multi-tasking. However, although there are plenty of examples, there is no clear theoretical framework for understanding whether the concept of executive function can be broken down into separable components.

Neuroimaging research has demonstrated, unsurprisingly, that classic executive functions are mediated by prefrontal regions. However, attempts to localise specific components of executive function to specific frontal regions have met with limited success. Further, many studies find that executive functions involve posterior and subcortical regions, as well as prefrontal cortices. Influential recent research is therefore moving away from a functional segregation approach to prefrontal mapping and concentrating instead on functional integration. In other words, researchers are not looking for one-to-one mappings between structure and function, but identifying interconnected networks of regions that mediate these complex functions. This approach is in its infancy but promises significant advances in our understanding of the brain's most complicated activities.

Surgical lesioning of frontal regions of the brain was introduced as a treatment for severe mental illness in the 1930s. Although no properly controlled evaluation studies of the procedure were ever conducted, the lobotomy continued to be employed until the mid-1950s. More recently it has become apparent that a significant proportion of people meeting diagnostic criteria for either schizophrenia or depression show abnormalities of prefrontal function. A new generation of neuroanatomical models of psychiatric disorders propose that they are characterised by disrupted connectivity with networks involving frontal, limbic, and subcortical structures.

APPENDIX

CONTENTS

A primer of nervous system structure and function

INTRODUCTION

Almost all recent textbooks of physiological or biopsychology (many of which are listed in the "Further reading" section after this appendix) provide up-to-date detailed and well-illustrated accounts of the "workings" of the mammalian nervous system. Rather than reiterate this material in full here, we aim to provide the minimum grounding to help contextualise the material covered in the preceding chapters. We have pitched this appendix at a level to suit readers not already familiar with nervous system structure and function so, if what follows whets your appetite to learn more about the brain, spinal cord, and other components of the nervous system, so much the better. If, on the other hand, you are approaching this appendix with some trepidation, remember that many important ideas in neuropsychology pre-date our current level of understanding of brain physiology. Thus, an encyclopaedic knowledge of the nervous system is not a prerequisite for the neuropsychologist, although a basic understanding probably is.

We know that, like other parts of the nervous system, the brain and spinal cord are made up of different types of component nerve cell, so a starting point is to learn how these work and communicate with each other. Inevitably, our prime interest is the brain—a structure that has been described as the most complicated known to man. It therefore makes sense to divide it up into separate regions, each of which will be briefly considered in turn. Since neuropsychology is usually concerned with functions and operations that have cortical origins, the cortex clearly deserves special consideration. This structure is the outer surface of the brain, and, in evolutionary terms, the most recently developed region. It too is usually divided up, first in terms of left or right side (or cortical hemisphere), and then, in relation to the particular bones of the skull that cover and protect it, into lobes. As you will see, cortical lobes can also be distinguished in terms of some of the psychological functions they mediate (see Figure A1).

Knowing some of the basic terminology about the layout of the nervous system will also be advantageous. For example, brain regions are often described

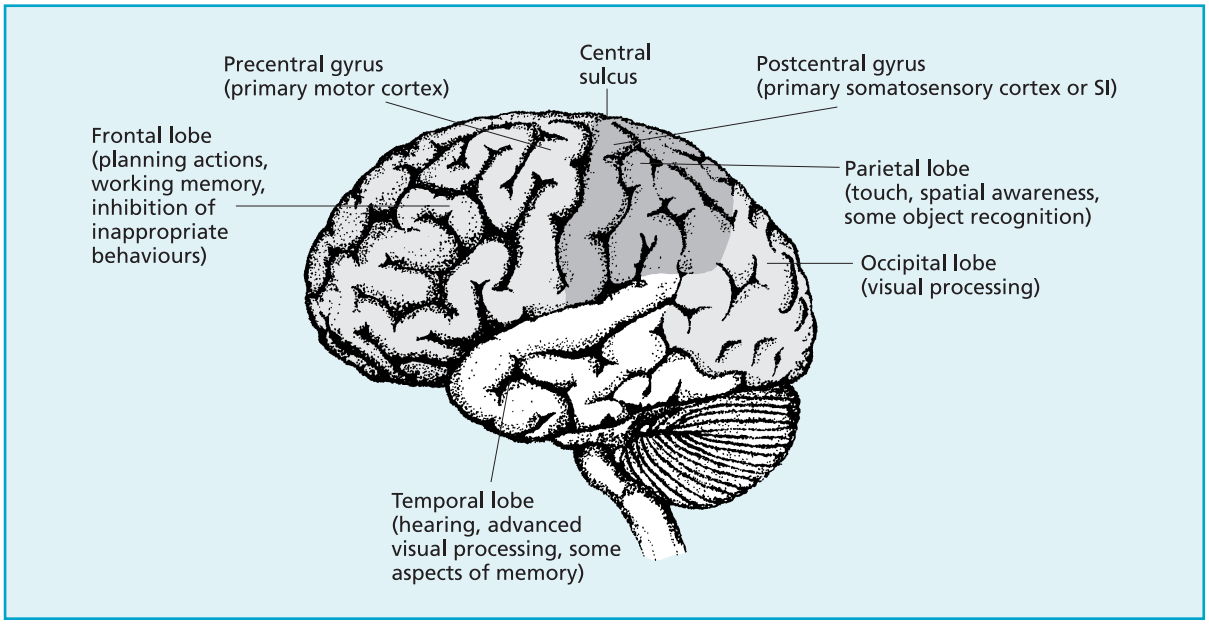


FIG. A1 The lobes of the cortex, showing the anatomical locations (and some functional specialisms) of the four cortical lobes.

in terms of their location, particularly in relation to other regions. So, allowing for the fact that humans walk upright rather than on all fours, dorsal means towards the back, and ventral the underside. Rostral means towards the front (head end), and caudal towards the bottom or tail end. Lateral is to the side, whereas medial is to the middle. If a particular structure has a front and rear section, we might refer to these as the anterior and posterior (pituitary gland for example). Finally, inferior means below, and superior above.

NEURONS AND GLIA

Our entire nervous system is made up of two fundamentally different classes of cell: neurons and neuroglia or just glia (which is the plural of glial cell) (see Figure A2). Neurons are responsible for conveying tiny electrical (or nerve) impulses around the nervous system and communicating, via synaptic transmission, with other neurons or, in the periphery, with muscles. Neurons themselves do not move, but they can convey nerve impulses along their length very efficiently and quickly (see Figure A3).

Although no one has ever actually counted them, it is estimated that the adult human brain contains between 100 and 150 billion neurons (1 billion = 1000 million), and glia are thought to outnumber neurons by 10 to 1! Glia play a range of vital supporting roles but are probably not directly involved in either conveying nerve impulses or in synaptic transmission. For example, in the central nervous system one type of glial cell (known as an oligodendrocyte) literally wraps itself around the "cable" part of a neuron (the axon), rather like a carpet is wrapped round a central cardboard tube, to provide a form of insulation known as a **myelin sheath**. (Schwann cells do a similar job in the peripheral nervous system.)

KEY TERM
Myelin sheath: A wrapping of insulation found on axons of many neurons giving a characteristic white appearance and leading to faster nerve impulse propagation.

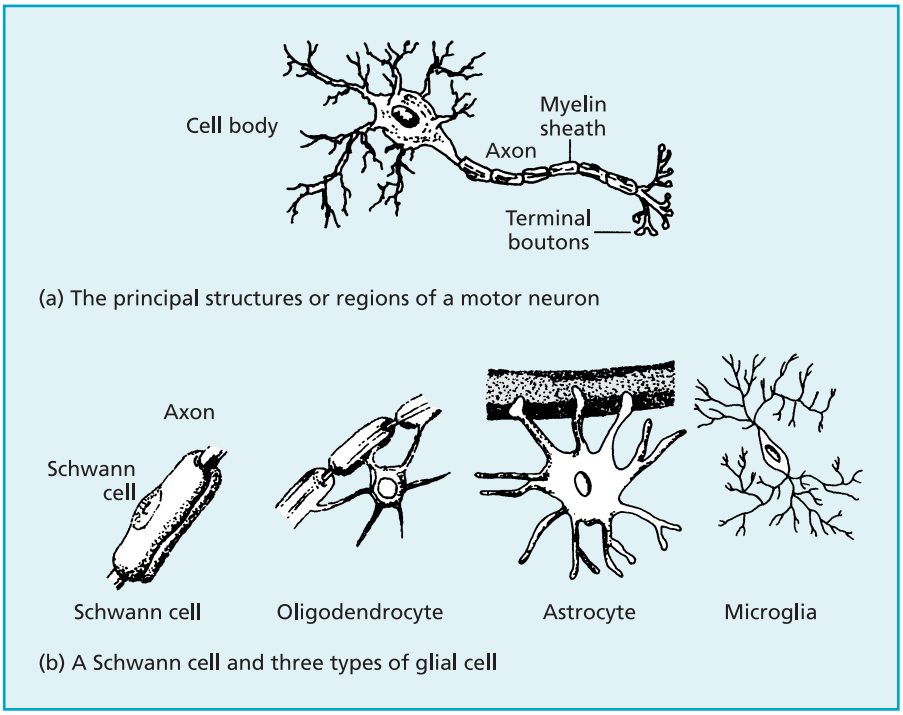


FIG. A2 A neuron (a) and glia (b). Not all neurons look like the one shown (a), but all have a cell body, an axon (that usually branches), and terminal boutons. This neuron is myelinated, and several dendrites are apparent as processes (outgrowths) of the cell body. A Schwann cell and three types of glial cell are illustrated (b). See the text for an explanation of their principal functions.

Another type of glial cell (known as microglia) *can* move around the nervous system, and they act rather like vacuum cleaners, removing (and digesting) dead or damaged tissue, and filling what would otherwise be empty space with scar tissue (see Raivich, 2005). Astrocytes surround blood vessels in the brain, and are involved in regulating the transfer of substances (glucose, oxygen, hormones, and potentially harmful toxins) between blood and brain.

As with glial cells, there are a variety of different types of neuron, some of which are found throughout the nervous system, and others that are only found in very discrete locations. For example, amacrine cells are found only in the retina, whereas interneurons are widespread throughout the brain and spinal cord. However, because most neurons carry nerve impulses and engage in synaptic transmission, it is helpful (though not entirely accurate) to think of them as all working in the same way.

NERVE IMPULSES AND SYNAPTIC TRANSMISSION

Most physiological or biopsychology textbooks include elegant descriptions of these processes, and the interested reader should consult these sources for detailed information. However, the points summarised in Boxes A1 and A2 may help to provide a clearer idea of the basics of both "within" and "between" neuron

communication. When considering these points, remember that nerve impulses can travel the length of your body (2 metres or so) within about 20 ms, and that synaptic transmission can occur in an even shorter period of time. So, although our account of the processes may seem long winded, they actually happen incredibly quickly. Remember, too, that scientists estimate that the average central nervous system neuron (not that any such thing really exists) probably receives several thousand converging inputs, and can in turn influence about the same number of neurons (i.e., several thousand) via its dividing axon (**divergence**). For some neurons whose role is specifically to control the activity levels of others (such as neurons in our brainstem that modulate overall brain arousal level), the degree of divergence is such that a single neuron may synaptically influence at least a quarter of a million other neurons. See Figure A3 for an illustration of an active neuron and a schematic synapse, and Figure A4 for an illustration of "summation" of excitatory and inhibitory influences on a receiving (post-synaptic) neuron.

KEY TERM
Divergence: In the nervous system, the principle that because axons may branch many times, a single neuron can influence a large number of targets (usually other neurons).

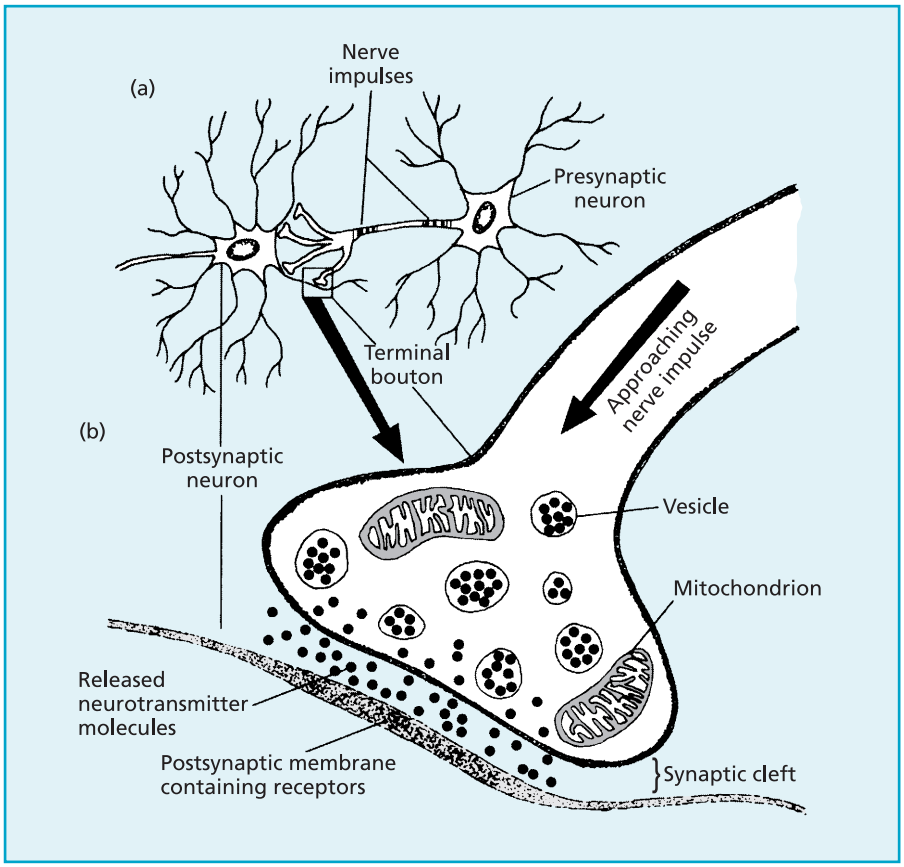


FIG. A3 A neuron conveying a volley of nerve impulses (a) and a schematic synapse (b). When nerve impulses arrive in the terminal bouton region, a sequence of events is triggered culminating in the release of neurotransmitter into the synaptic cleft.

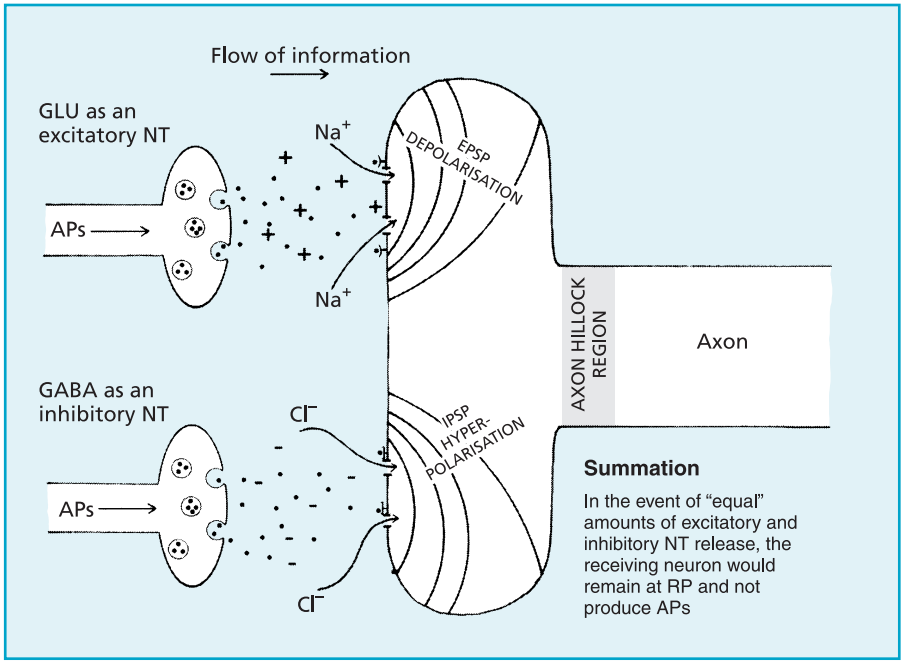


FIG. A4 The convergence of an excitatory and inhibitory input onto a receiving neuron, grossly simplified. Two neurons converge on a single "receiving" neuron. One releases the excitatory neurotransmitter (GLU) and the other releases the inhibitory neurotransmitter (GABA). Whether or not the receiving neuron fires will depend on the relative influences of the two competing inputs.

Box A1 Nerve impulses

- Think of nerve impulses as tiny electrical "blips" that travel along the surface of the cable part (the axon) of neurons. Most are formed at the axon hillock—a region where the cell body "becomes" the axon. This type of conduction is regarded as "active" in comparison with the "passive" conduction of information that occurs along dendrites and over a neuron's cell body.
- A neuron is able to generate its own nerve impulses (when stimulated), which, once formed, travel at a fixed speed and amplitude (size) in a given neuron, although speed and size of nerve impulse may vary between neurons. In fact, many neurons actually display spontaneous excitability or firing, so the critical issue is how this rate changes as the neuron itself is influenced by other neurons, events, or stimuli.
- In the human nervous system large myelinated neurons (such as motor neurons) can convey nerve impulses at over 100 metres per second; small diameter non-myelinated neurons (such as interneurons in the spinal cord) may propagate nerve impulses at less than 1 metre per second.
- Nerve impulses tend to occur in volleys (bursts) rather than alone. Thus a few nerve impulses may indicate a weak stimulus; more will signal a strong stimulus. Frequency coding, as this is known, appears to be a general feature of nervous system functioning. However, note that inverse frequency coding

operates at some locations in the nervous system—for example, the firing of some neurons in the retina is inhibited by strong light.

- Nerve impulses conform to the "all or none" law, meaning they either occur fully or not at all. You cannot have a partial action potential.
- When a nerve impulse is at a particular point along an axon, its presence "excites" the region of axon just in front of it, effectively causing the impulse to move on to the next region of axon. This is analogous to a "domino" effect where a falling domino in one position causes the domino next to it to fall, and so on. The main difference is that, in neurons, "fallen" dominoes quickly pick themselves up ready to be knocked down again by the next passing nerve impulse.
- A variety of factors can influence a neuron and determine whether or not it produces nerve impulses, but in the brain and spinal cord the most likely influence is from other neurons via synaptic transmission.

Box A2 Synaptic transmission

- Action potentials arriving at the terminal bouton region of a neuron induce the neuron to discharge chemical messengers (called neurotransmitters) into the space between it and the "receiving" neuron. This extremely narrow gap (typically, about 30 nanometres) is called the synaptic cleft, and it contains extra-cellular fluid (water with ions and enzymes).
- Neurotransmitters are stored ready for release in tiny sacks called vesicles, present in the terminal bouton region of neurons. Neurons manufacture their own neurotransmitters from the breakdown products of food.
- There are many different neurotransmitters (some researchers have estimated over 1000 exist in our own nervous systems) but the vast majority of synapses are mediated by one of a core group of about 10, which includes acetylcholine (ACh), noradrenaline (NA), serotonin (5HT), dopamine (DA), gamma-aminobutyric acid (GABA), and glutamate (GLU). Some neurons release more than one neurotransmitter: a phenomenon called "co-release". This is most likely to involve one of the core neurotransmitters mentioned above plus a specialised (and probably localised) second substance from the "peptide" class of neurotransmitters. Substance P and VIP are two examples.
- Some released molecules of neurotransmitter diffuse across the cleft and find their way to particular receptor sites on the surface of the receiving neuron into which they fit (like a key in a lock). This diffusion is passive: the neurotransmitter molecules are not propelled in any way to the other side of the cleft.
- Their presence in the receptor can cause the receiving neuron to become excited, making it more likely to generate its own nerve impulses (an excitatory synapse). This is often mediated by the opening of channels in the receiving neuron's membrane that permit the influx of positively charged Na (sodium) ions.
- At other synapses, a neurotransmitter may have the opposite effect, causing the receiving neuron to become less excited, reducing the likelihood of it producing action potentials (an inhibitory synapse). This effect is mediated

either by the influx of negatively charged Cl (chloride) ions or the efflux (movement out) of positively charged K (potassium) ions.

- Some neurotransmitters (such as GLU) seem to be exclusively excitatory, and others such as GABA exclusively inhibitory (see Figure A4). Other neurotransmitters can be excitatory at certain synapses and inhibitory at others. Such opposite effects are possible because there are different receptor types for certain neurotransmitters. For example, ACh has an excitatory influence at so-called nicotinic ACh receptors and an inhibitory influence at muscarinic ACh receptors. There are thought to be at least five DA receptors and as many as nine 5HT receptors in our own nervous systems.
- The action of a neurotransmitter is quickly terminated either by it being broken down by enzymes present in the cleft, or by being pumped back into the terminal bouton of the sending neuron (a process called re-uptake).

DEVELOPMENTAL AND AGEING ASPECTS

Where do neurons and glia come from and how do they end up where they are? The answer to the first question is straightforward. Like all cells in our body, neurons and glia are the products of cell division, ultimately traceable back to the single fertilised egg which begins to divide shortly after conception. However, the second part of the question is, with a few exceptions, currently unanswerable, except to say that during development, cells migrate (move), divide, and in certain cases selectively die (Toga, Thompson, & Sowell, 2006). The neurons and glia remaining are our nervous system!

One thing we can be sure of is that the maximum number of neurons an individual ever has reaches a peak relatively early in life—there is little evidence of further widespread neuron proliferation after the age of 2. The fact that many neurons are already present explains (in part) why a newborn baby's head is large in comparison with the rest of its body. The number of neurons appears to remain relatively static throughout childhood and then begins to decline in adolescence, and it has been estimated that by the age of 15 or so, humans are losing thousands of neurons every day (up to 85,000 according to Pakkenberg & Gundersen, 1997). This apparently alarming figure must be set alongside the vast number we start off with. If you consider a lifespan of 80 years, you will find that the loss of neurons at age 80 is less than 10% of the total, assuming a normal healthy life. Accelerated cell loss is, of course, a feature of several neurological disorders including Alzheimer's and Parkinson's diseases.

Unlike neurons, glial cells do increase in number throughout childhood and adolescence, and even in adulthood. In the corpus callosum (a structure in the middle of the brain that was discussed in Chapter 3), the amount of myelination increases (i.e., more oligodendrocytes form myelin sheaths) annually, with the structure only reaching full maturity at about 18 years. Incidentally, on a more sinister note, most brain tumours arise as a result of uncontrolled division of glial cells, not neurons.

In the last few years it has become clear that certain neurons in the adult mammalian nervous system may also undergo cell division to produce new cells. In rodents this has now been established at two locations: the olfactory bulb and

the dentate gyrus in the hippocampus (see Ziv et al., 2006; and Hack et al., 2005). Although it is unlikely that cell proliferation here does much to counter the overall loss of neurons, the finding is important because it raises the possibility of being able to control (particularly, to switch on) cell division in other brain regions where marked loss of tissue has occurred (see below). At time of writing, neurogenesis in the adult human brain is assumed, rather than unequivocally proved, to occur at the same sites (Eriksson et al., 1998).

Before we leave the issue of lifespan changes, it is important to realise that for a nervous system to work effectively it is not just the number of neurons that is important, but how they interconnect with each other. We know that in the mammalian nervous system (including our own), neurons communicate predominantly via chemical synapses. Although the absolute number of neurons declines with age from adolescence onwards, the number of connections or synapses between neurons *can* increase, and certainly does not follow the declining neuron count. Some researchers estimate that most of the physical growth of the human brain after the age of about 2, not attributable to myelination, reflects the formation of new connections, and synaptic contacts (Toga et al., 2006).

Certainly, when there is brain damage later in life, loss of cells may be compensated for by the formation of new synapses (called synaptogenesis). In Parkinson's disease (discussed in Chapter 5), there is progressive loss of a particular type of neuron, but it is not until about three-quarters of these cells have died that the characteristic symptoms of tremor and rigidity appear. Researchers think that in the period of disease prior to symptom onset the remaining healthy cells continually form new synapses onto target cells, in effect replacing the inputs from the neurons that have died. This is known to involve axonal sprouting, meaning that existing neurons produce new shoots or branches that, in turn, make new synaptic contacts. Thus when we said earlier that neurons do not move, this is not strictly true for a neuron's axon, which may grow new branches several millimetres long to extend its sphere of influence.

DIVIDING UP THE NERVOUS SYSTEM

Because the nervous system stretches from the top of your head to the tip of your toes, it makes sense to divide it up into more manageable chunks. One important distinction is between the central (CNS) and peripheral nervous system (PNS). For mammals, the CNS is the brain and spinal cord, and the PNS is everything else. Sometimes it is useful to further subdivide the peripheral nervous system into the branch in which neurons carry nerve impulses to voluntary muscles (i.e., ones you can consciously control), and the branch carrying nerve impulses to muscles such as the heart and gut, which are not under voluntary control. The former is referred to as the skeletal nervous system and the latter as the autonomic nervous system (ANS).

Another way of subdividing the nervous system is to take into account the direction of nerve impulses conveyed along particular neurons. Afferent (or sensory) neurons carry nerve impulses towards the brain. Efferent neurons carry impulses away from the brain, and in the case of motor neurons, towards muscles.

A further useful distinction differentiates neurons with and without myelin sheaths. The sheath (which actually only covers the axon part of the neuron) dramatically improves speed of conduction, and the myelin gives these neurons a

characteristic pinky-white appearance, hence the term "white matter". Incidentally, this structure is not continuous, being broken every 1–2 mm of axon at regions known as nodes of Ranvier, where the exchange of ions (mainly Na and K) necessary to propagate the nerve impulse can occur. Unmyelinated neurons convey action potentials much more slowly, and have a pinky-grey appearance. So too do cell bodies, giving rise to the term "grey matter".

Quite often, cell bodies of neurons will be clumped together in one location. (They don't actually touch one another but lie in very close proximity to each other.) These clumps are known as ganglia or nuclei. Similarly, the cable parts of neurons (the axons) often run side-by-side from one part of the nervous system to another. Once again, they don't actually merge into a single structure, but they do lie next to each other. Bundles of axons are known as tracts or nerves. It is important to remember just how small and densely packed axons can be. The human optic nerve is made up almost exclusively of myelinated axons, and is about the same diameter as a piece of cooked spaghetti. Yet it comprises axons of over 2 million individual retinal ganglion cells conveying information in the form of nerve impulses from the retina into the brain.

THE CENTRAL NERVOUS SYSTEM

In mammals, the central nervous system (CNS) includes all nerve tissue that is encased in bone. Although neuropsychology is understandably preoccupied with the cortex and its functions, it is important to realise that the cortex itself is only one part of the brain (many other brain structures in addition to cortex are highlighted in Figure A5). We will consider the brain shortly, but for completeness, we need briefly to consider the other major element of the CNS: The spinal cord nestles within the vertebrae, and is made up of both grey and white matter. It is a continuous structure but is also highly segmented, meaning that there is very precise delineation of input and output at each level (or vertebra). Sensory

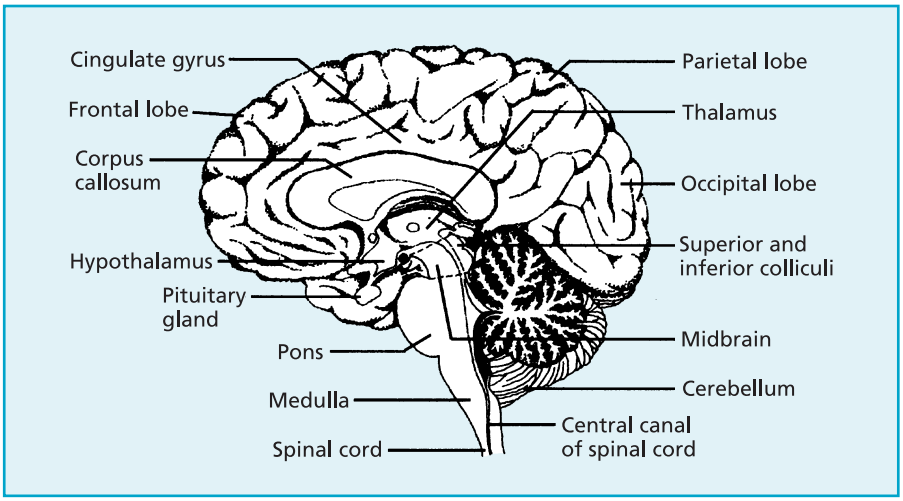


FIG. A5 A medial sagittal view of the adult human brain. The dotted lines represent the anatomical positions of the notional divisions between the hindbrain, midbrain, and forebrain. Clearly, the latter has expanded at the expense of the former two regions in the course of evolution for many higher mammals.

information from a clearly mapped-out region of body (known as a dermatome) enters towards the rear (or dorsal regions) of the spinal cord, at the particular level (vertebra). Motor output from the cord leaves via the ventral (frontal) roots, again to innervate muscles predominantly within the specified dermatome.

The grey matter comprises, for the most part, unmyelinated interneurons. These tend to influence other neurons only locally, either at the level in question, or perhaps in an adjacent segment. The white matter, on the other hand, surrounds the central grey matter, and comprises vast tracts of myelinated axons conveying both afferent and efferent information. Some of these run the entire length of the spinal cord although any given neuron only carries information in one direction. As we saw in Chapter 4, the dorsal columns carry relatively precise "sensory" information from the periphery towards the brain, and the ventral columns carry "motor" output in the opposite direction to muscles.

THE HINDBRAIN

This comprises the medulla, pons, and cerebellum. The medulla is, in effect, the continuation of the spinal cord in the cranium. However, in addition to the pathways to and from the cord it contains a series of regions that control basic vegetative processes such as respiration, heart rate, and certain reflexes. Brain death is assessed by the absence of electrical activity in this lowest region of the brain. More ventrally are found the pyramidal decussations: bundles of axons in pyramidal shapes that convey output signals from the brain to motor neurons whose cell bodies are located in the spinal cord itself. The term "decussation", meaning "crossing", reminds us that descending fibres cross from the left side to the right (and vice versa) at this level in the brainstem to bring about the familiar pattern of contralateral control.

The pons lies just rostral to (above) the medulla, and is ventral to the cerebellum. It is the main link between the cerebellum and the rest of the brain, particularly the cortex. It also has a role in certain aspects of both visual and auditory processing and, among other things, helps to coordinate eye movements in relation to balance. Several of the cranial nerves "exit" from this structure, including the trigeminal nerve, a mixed nerve that carries sensory information from the face and innervates muscles in the lower face and jaw. This region of brainstem also contains a significant portion of the reticular formation, which plays a key role in mediating the level of excitability (arousal) of large swathes of cortex.

The cerebellum is the large bilaterally symmetrical "walnut"-like structure on the dorsal (back) part of the brainstem roughly at the level of the ears. It is connected to the pons by three contiguous stalks called the cerebellar peduncles, two of which convey information into the cerebellum, and a third which conveys output via the thalamus to the cortex, and additionally to the brainstem. Structurally, the cerebellum comprises a midline region called the vermis and lateral regions comprising a wrinkled outer cortex and underlying white matter. This has a characteristic matrix-like appearance consequent on the way two major classes of intrinsic cerebellar neuron—Purkinje cells and the parallel fibres of granule cells—interact here. A series of four pairs of deep cerebellar nuclei are embedded in the cerebellum, serving as relay points for both inputs to and outputs from it.

Among other functions, this structure is concerned with balance, and the

learning and execution of skilled movements, particularly those "enacted" through time: in other words, skills such as playing a piano, or performing some complex gymnastic routine, in which the sequence of controlling muscles has to be precisely coordinated. People with bilateral damage to their cerebellum often appear drunk, even to the point of slurring their speech, which after all depends on the coordination (in time) of muscles in the throat and mouth. They may also display a "staggering" gate. People with unilateral damage display these problems too, but usually just on the ispilateral (same) side as the damage.

THE MIDBRAIN

Here, we find the thalamus and hypothalamus, the tegmentum, and the tectum, the latter comprising four little bumps on the dorsal surface of the brainstem above the cerebellum. The bottom two (the inferior colliculi) are concerned with auditory processing, and especially in turning the head towards an auditory stimulus. The top two (the superior colliculi) do a similar job, but for visual processing (see Chapter 8). The tegmentum (the brainstem region immediately beneath the tectum) contains a diverse set of structures and nuclei including the frontal (rostral) section of the reticular formation, the periaqueductal grey area (PAG), the ventral tegmental area (VTA), the red nucleus, and the substantia nigra (SN).

The hypothalamus is involved in controlling behaviours that help the body to maintain an equilibrium or satisfy its needs. It will be no surprise to learn that it is the nerve centre (no pun intended) for the control of eating, drinking, temperature regulation, and sex. It also includes control regions for the autonomic nervous system and, in collaboration with the pituitary gland, helps to coordinate much of the endocrine (hormone) system. Not only does it secrete so-called releasing-factor hormones to control the anterior pituitary, but it also produces and supplies the hormones released by the posterior pituitary, and additionally controls their release from it.

The thalamus—a bilateral structure resembling (in adult humans) two avocado stones joined side by side, at a point called the massa intermedia—is a relay station for sensory information coming into the brain. By relay station we mean that input from a particular modality such as vision enters the thalamus, or more specifically a particular nucleus of it, where it may undergo some preliminary/intermediate processing, before being sent on to the cortex for further detailed analysis. The lateral geniculate nuclei receive input from the eyes, and relay it to the occipital lobes; the medial geniculate nuclei receive auditory input and relay it on to the temporal lobes.

THE FOREBRAIN

The basal ganglia and limbic system

Two other systems of neurons need mention at this point. The basal ganglia (see Chapter 5) comprise not one but several interconnected structures (the caudate, putamen, globus pallidus, the subthalamic nucleus, and substantia nigra). While it is not necessary to remember their names, it is helpful to have an idea of how this network of structures collectively helps to control movement, and we describe this in Chapter 5. The basal ganglia do not, for example, directly initiate movement;

rather, in combination with the motor cortex, they determine which possible actions actually get put into effect, by permitting some and inhibiting others. Researchers now think that the basal ganglia serve as a sort of gatekeeper for motor plans that originate in the cortex, and damage to any of the component structures (or the pathways that connect them) will impair the control of movement.

The limbic system, named by MacLean (1949), comprises—in addition to the cingulate gyrus which is a region of cortex just above the corpus callosum—several different interconnected subcortical structures, including the hippocampus, amygdala, septum, and hypothalamus. It is, in certain respects, the *emotional* equivalent of the *motor* basal ganglia: Activity in the limbic system selectively imbues behaviour with emotional tone (fear, anger, pleasure, and so on). Like the basal ganglia, the limbic system seems not to work in isolation, but rather in collaboration with both lower (brainstem) and higher (cortical) brain centres. Damage or abnormal functioning in the limbic system may be associated with both inappropriate emotional responding and impaired detection and/or identification of emotion-laden stimuli. In higher mammals, including man, certain limbic structures seem to have evolved to additionally mediate learning and memory (the hippocampus) and attention (the anterior cingulate gyrus). Damage to the limbic system may be related to certain psychiatric disorders including schizophrenia, depression, and anxiety. Like the basal ganglia, the limbic system is conventionally regarded as a "forebrain" structure.

The cortex

Viewing the external surface of an intact human brain, you might expect to see the brainstem, the cerebellum, and cortex. The cortex seems to cover much of the rest of the brain, although it is actually a forebrain (front) structure. It has a bumpy, folded appearance. The bumps are called gyri (singular: gyrus), the shallower folds or indents are called sulci (singular: sulcus), and the deeper ones are called fissures. Gyri, sulci, and fissures dramatically increase the surface area of the cortex. In fact, about two-thirds of cortical tissue is hidden in these folds. If you could flatten out the human cortex, it would cover an area of about 2500 square centimetres.

"Cortex" means bark, and it is a very apt term in this case, for the adult human cortex is between 1.5 and 4.5 mm thick. Its pinky-grey appearance tells us that it is made up primarily of cell bodies (remember cell bodies do not have myelin sheaths), which are usually arranged in a series of between four and six layers parallel to the surface. Immediately underneath the cortex the appearance changes to white, indicating vast tracts of myelinated neuron axons conveying information to and from the cortex and between one cortical region and another.

Like many other brain structures the cortex is often described as being "bilaterally symmetrical", which means that the left and right sides are like mirror images of each other. However, as we mention in Chapter 3, this is only approximately true, and several important anatomical distinctions between the left and right side are apparent on closer inspection. The two sides of the cortex are sometimes referred to as hemispheres, and again the term is apt: taken as a whole, the cortex looks a little like a partly inflated ball. However, it is important to note that each hemisphere contains many subcortical structures as well. The hemispheres are connected to each other by a number of pathways, of which the largest by far is the corpus callosum (see Figure A6). This structure is actually a massive band of

axons running from one side of the cortex to the other. Although it is only about 10 cm long and no more than 1 cm in thickness, it comprises well over 500,000,000 myelinated axons. The relative isolation of the two hemispheres is best demonstrated by the observation that it is possible to insert a thin probe at any point along the longitudinal fissure (which separates them) and the first thing you would touch is the corpus callosum about 3 to 4 cm down.

We mentioned earlier that the cortex itself is made up primarily of cell bodies, and one of the largest and most prominent types of cortical cell is the so-called pyramidal cell (see Figure A7). This type of neuron has a very extensive branch-like structure. The branches are known as dendrites, and are the part of the neuron most likely to receive inputs from other neurons. Under a microscope these pyramidal cells look a little like Christmas trees, with the top branches corresponding to dendrites, and the lower, broader, part comprising a cell body and further sideways-pointing dendrites. The stem and roots of the tree would be the axon, which leaves the cortex to form a strand of white matter. Pyramidal cells are oriented at 90 degrees to the surface of the cortex, and clusters of these cells are sometimes called columns. Indeed, a regular feature of cortical organisation is its so-called column structure.

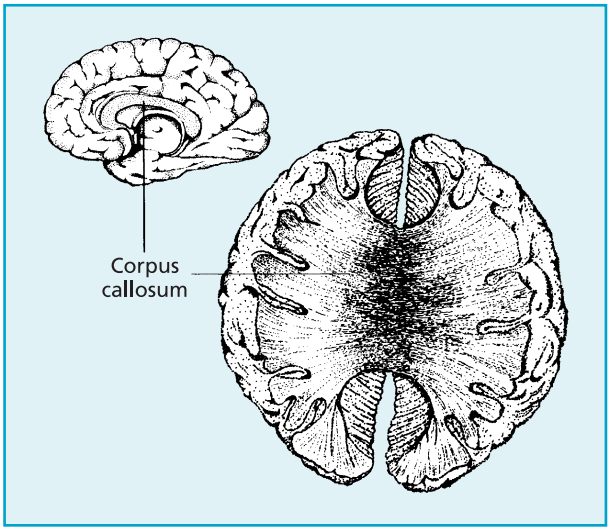


FIG. A6 The corpus callosum.

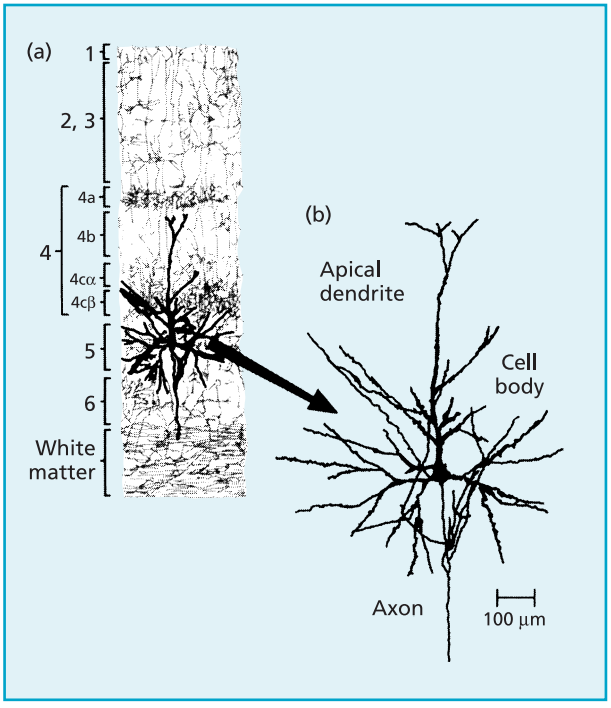


FIG. A7 The layers of the cortex (a) and a pyramidal neuron (b). Most regions of cortex appear laminated; neuroanatomists typically identify six layers. In this figure, one pyramidal neuron has been highlighted. It has an extensive dendritic structure that permeates several cortical layers, a centrally located cell body, and an axon, which descends and ultimately leaves the cortex via layer six. Adapted from Rosenzweig et al. (1999). *Biological psychology*. Sunderland, MA: Sinauer Associates Inc. Reproduced with permission.

Sensory, motor, and association cortex

Another way of distinguishing between different parts of the cortex has, historically, been according to function. Some (discrete) cortical regions clearly have primary sensory or motor responsibilities—for example, Brodmann's areas 1, 2, 3a, and 3b constitute the primary somatosensory cortex (see Chapter 4), and BA 4 is the primary motor strip (see Chapter 5). Other (more extensive) regions don't have primary sensory or motor responsibilities, and the term "association cortex" has been used for many years as a "catch-all" for these cortical areas. Yet research shows that relatively little associating (or combining) of sensory input actually takes place here. Rather, much association cortex is involved in what amounts to a more elaborate processing of information. For example,

the primary visual cortex deals with sensory registration, while regions of visual association cortex ("modules" in Fodor's terms) are concerned with (among other things) colour perception, object recognition, and movement (see Chapter 8). However, some associating *does* occur in association cortex, in the following sense at least: regions of the temporal lobe association cortex enable us to "imagine" the appearance of a person whose voice we hear, and parts of our parietal association cortex enable us to "draw" images of objects we cannot see, but can feel.

THE LOBES OF THE CORTEX

Another way of identifying cortical regions is in relation to the cranial bones that they lie beneath. In the higher mammals, including man, we differentiate between four lobes, or eight if you include both hemispheres (see Figure A1). Not only can the lobes be distinguished by their anatomical location, but they also separate *to some extent* in terms of the psychological processes with which they are concerned.

Frontal lobes

If you think of the human brain as looking a little like a boxing glove from the side, then the frontal lobes comprise the part of the glove that the fingers would occupy. They account for more than 30% of the entire complement of cortical brain cells, and are the part of the cortex that is more highly developed in humans than in any other primate. The frontal lobes are also the last to mature and there is evidence of continuing synaptogenesis and myelination into late adolescence.

At one time, the main function of these lobes was thought to be that of controlling movement, which they achieve in a highly organised hierarchical manner. The primary motor strip (BA 4) sends outputs that ultimately "drive" motor neurons controlling individual muscles: fine movements in the fingers and joints of your hand, for example. The region of frontal lobe anterior to (in front of) BA 4, called the supplementary area and merging into the premotor cortex has control over BA 4, so can organise concerted (bilateral) movements, such as holding a bottle and twisting off the cap. The region anterior to it is known as prefrontal cortex. This area is also involved in movement but only in terms of planning, intending, and "willing" it.

As we have learned more about frontal lobe function, it has become clear that, in addition to their key role(s) in movement control, they are also involved in many other aspects of behaviour including planning (in an abstract sense: for example, strategy), generating ideas, problem solving, working memory, and personality (see Chapter 11). Specialised compartments of the frontal lobe also contribute to the control of voluntary eye movements (the frontal eye fields) and expressive language (Broca's area). We describe the role of the frontal lobes in movement in Chapter 5 and some of their "executive" functions in Chapter 11.

Parietal lobes

The parietal lobes are located immediately posterior to (behind) the frontal lobes, and are separated from them by the central sulcus, the groove running across the top of the brain (roughly from ear to ear but by no means in a straight line). These lobes have important sensory functions, especially in relation to somatosensation,

and also vision, and on the left, language, which we describe in some detail in Chapters 4 and 6; they are also critical for attention (see Chapter 8).

The first strip of parietal lobe (the gyrus furthest forward) is the primary somatosensory cortex (also known as S1, encompassing BA 1, 2, and 3). Neurons here respond to touch sensation from very discrete body regions, and the entire body is "mapped" contralaterally onto this cortical strip. For example, touch receptors in your right hand will send nerve impulses that end up in your left primary somatosensory strip. Different adjacent columns of neurons here will respond to input from each finger (and each part of each finger!). Further back (i.e., further away from the central sulcus), more posterior regions of parietal lobe are involved in more "integrative" sensory functions: linking, for example, touch with visual information or with memory. Damage here can lead to a disorder known as astereognosis, which is marked by the inability to recognise objects by touch. The parietal lobes are also involved in visuospatial processing, some aspects of language processing, and attention. The left parietal lobe also has a motor function.

Parietal damage, particularly on the right side, can give rise to the condition known as neglect of the left visual field (see Chapter 8). More discrete damage is associated with difficulties in object recognition, spatial orientation, and even basic geographic knowledge/memory. Left parietal damage is associated with apraxia. As discussed in Chapter 1, the precuneus (posterior medial parietal lobe) may have a particular role in referencing "the self" in 3D space, and perhaps even in self-consciousness.

Occipital lobes

The left and right occipital lobes are tucked behind and underneath the parietal lobes at the back of the cortex. Visual input from the lateral geniculate nucleus of the thalamus terminates in V1 (so-called striate occipital cortex). Damage here almost always results in a marked visual impairment, and can lead to cortical blindness. For example, extensive damage to V1 on the right will result in blindness in the left visual field (everything to the left of centre as you look straight ahead). Surrounding V1, the "extrastriate" areas of the occipital lobe (V2, 3, and 4) comprise modules (Fodor's term again) concerned with the perception of form, movement, movement direction, location, and colour; at least 30 such modules can be found here according to Zeki et al. (1991). V2 is also the starting point for two major processing routes projecting into the dorsal parietal, the ventral parietal, and temporal lobes, and dubbed (respectively) the "where" and "what" streams by Ungerleider and Mishkin (1982). Some of these functions are described in more detail in Chapter 8.

Temporal lobes

In our boxing glove analogy, the temporal lobe would be the thumb (except you have one lobe on each side). The anterior part of this lobe is separated from the frontal lobe (which it lies to the side of), but the rear (posterior) sections are bounded by the parietal and occipital lobes, and the actual boundaries are not clearly defined by sulci. Three gyri can be identified in the temporal lobe, known as the superior (upper), medial (mid), and inferior (lower) gyri respectively. The posterior region of the superior temporal gyrus is the primary auditory cortex,

also known as Heschl's gyrus, with input coming mainly from the ear on the opposite side of the body. On the left side, adjacent regions, especially behind the primary auditory cortex, are involved in the recognition of language sounds. On the right side, the equivalent regions are involved in interpreting non-verbal speech sounds such as tone, rhythm, and emotion.

However, the temporal lobes are not just concerned with auditory processing. Lower (inferior) regions, for example, are involved in visual object recognition. In general, cells in different parts of the inferior temporal gyrus respond to rather specific visual stimuli such as faces, objects, or types of animal, suggesting that stored representations (memories) of items may be located in a highly organised and compartmentalised way here. We consider some of the evidence in support of this idea in Chapter 8. An illustration of the range of functions with which the temporal lobes are involved is that a tumour here can give rise to auditory, visual, or even olfactory (smell) hallucinations (Liddle, 1997).

CHAPTER SUMMARY

The brain, like other parts of the nervous system, is made up of neurons and glia, although neurons alone carry nerve impulses around the nervous system. To begin to understand how the brain works it makes sense to divide it up, and the principal component parts of the hindbrain, midbrain, and forebrain have been introduced. It is also helpful to divide up the cortex in terms of both the anatomical location of the lobes and their diverse functions. However, it is very important to remember that a "hallmark" feature of brain function is, in fact, the interactivity and collaboration between different regions. The brain *does not* work as a series of independent functioning elements, as the localisationists once believed. Rather, even the most simple of behaviours (wiggling one of your fingers for example) will involve the collaborative activation and interaction of multiple cortical and subcortical regions. Obviously, such collaboration can be doubled and redoubled (several times) when we consider neuronal control of more sophisticated behaviours such as "willed action selection" (see Chapter 5), expressive language (see Chapter 6), or risk taking (see Chapter 10).

No matter how many times we describe the brain to our students, we both still marvel at the sheer complexity of it, and we hope you share our sense of wonder. We are also amazed that such a complicated structure goes wrong so infrequently. However, when brain damage, disorder, or disease does occur it can sometimes shed considerable light on the functioning of the normal intact brain. You only have the one, so take care of it!

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NEUROPSYCHOLOGY ON THE WORLD WIDE WEB

There is a wealth of information about neuropsychology to be accessed via the internet. A simple GOOGLE search using a key term such as *Parkinson's disease* or *aphasia* will produce hundreds of "hits" to explore. The GOOGLE images option permits access to thousands of figures, photographs, and diagrams: These can be downloaded although some will be subject to copyright. GOOGLE Scholar will be useful if you want to start a literature search: It gives access to many full-text journal articles of interest to neuropsychologists. WIKIPEDIA is also worth browsing as a first step, although in our experience, entries are of more variable quality. However, for more detailed information we have provided below a selection of specific sites for you to explore. At time of writing all of these were fully functional, and offered open-access to most contents.

http://www.neuroguide.com
A links page with a comprehensive search facility, table of contents, and opportunities to sign up for newsletters—many useful links.

http://neuropsychologycentral.com
Mainly links, but the site also offers an in-house and web search facility.

http://home.epix.net/~tcannon1/Neuropsychology.htm
Professor Cannon's homepage with lots of links to journals, other neuropsychology information pages, and links and information on specific brain disorders.

http://www.lib.uiowa.edu/hardin/md/neuro.html
A links page to many other neuropsychology sites regularly updated by staff at the Hardin Library, University of Iowa. Lots of information about neurological disorders.

http://lbc.nimh.nih.gov
The website of the laboratory of brain cognition, National Institute for Mental Health (NIMH), with lots on functional neuroimaging, and other neuroscience material.

http://www.brainsource.com
A web site prepared by neuropsychologist Denis Swiercinsky, offering numerous links. Particularly good for information on neuropsychological testing.

http://faculty.washington.edu/chudler/ehc.html
Prof Eric Chudler's webpage which contains links to search engines, information about neuropsychological disorders, and much more. A link to the kids-page is also worth a visit!

http://www.cogneuro.ox.ac.uk/links/
Links to many other academic sites from the McDonnell Centre for Cognitive Science, University of Oxford.

http://www.psychology.org/links/Underlying_Reductionistic_Machinery/Neuropsychology/
This takes you to an Encyclopedia of Psychology, with many useful links to research methods and clinical disorders.

http://neurophys.wisc.edu/neurosci.html
More links from the University of Wisconsin.

http://mindbrain.ucdavis.edu/labs/Whitney-new/
Many useful links to brain imaging, and other current neuroscience research at U. C. Davis.

http://www.med.harvard.edu/publications/On_The_Brain/
Access to the Harvard-Mahoney Neuroscience Institute newsletters (with an extensive back catalogue).

http://www.ion.ucl.ac.uk/national_hospital/national_hospital.htm
The homepage of the Institute of Neurology, Queens Square, London. Many useful and interesting links.

http://www.neuropsychologyarena.com
The Neuropsychology Arena provides researchers, instructors, and students in neuropsychology with information on the range of books and journals produced by Psychology Press, LEA, Taylor & Francis, and Routledge. It also offers other helpful resources, such as information about conferences, societies, and blogs.

GLOSSARY

Ablation: the surgical removal of brain tissue.

Acquired alexia: loss of reading ability in a previously literate person.

Agnosia: loss of ability to recognise objects, persons, sounds, shapes, or smells in spite of intact sensory function.

Alexia: inability to read.

Allocentric neglect: consistent processing errors on one side of individual stimuli (either right or left) regardless of location with respect to the viewer.

Alzheimer's disease: a form of dementia involving progressive loss of psychological functions as a result of widespread loss of cortical and subcortical neurons.

Amnesia: general term for loss of memory. Anterograde amnesia is loss of memory following some trauma. Retrograde amnesia is loss of memory for a period of time prior to trauma.

Aneurysm: a form of stroke caused by a blood vessel in the brain suddenly expanding and then bursting.

Angular gyrus: a region of cortex on the temporal/parietal border roughly equivalent to Brodmann's area 39. The left side is probably involved in reading (sentences).

Anomia: inability to name objects or items.

Anosognosia: a condition in which a person who suffers impairment following brain damage seems unaware of or denies the existence of their handicap, even if the handicap is severe (blindness or paralysis).

Anterior cingulate: a midline frontal lobe structure implicated in attention, response inhibition, and emotional response (especially to pain).

Anterograde amnesia: a form of memory loss where new events are not stored in long-term memory.

Anti-saccade: inhibition of a reflexive eye movement towards a light target.

Aphasia: deficit in the production and/or comprehension of language.

Apraxia: the inability to carry out certain motor acts on instruction without evident loss of muscle tone (acts may be performed spontaneously, for example).

Arborial structure: the branching pattern of neuronal dendrites.

Arcuate fasciculus: fibre bundle connecting Broca's and Wernicke's areas in the brain.

Aspiration pneumonia: bronchial infection and congestion that affects ability to breathe and can lead to death.

Astereognosis: an agnosic condition in which objects cannot be recognised by touch alone.

Autism: a developmental disorder characterised by aloofness, automaticity, and aphasia.

Axon: long, thin projection from a neuron that carries electrical impulses from the cell body.

Behaviourism: the school of psychology founded by Thorndike and popularised by Skinner, which places emphasis on the acquisition of behaviour through learning and reinforcement.

Beta blocker: a drug that blocks the effects of adrenaline and noradrenaline.

Biopsy: the removal of tissue (in a living individual) for analysis.

Brainstem: the lower part of the brain, adjoining and structurally continuous with the spinal cord.

Brodmann area: a region of the cortex defined on the basis of cytoarchitecture.

Cerebellum: region at the base of the brain that is important in sensory and motor functions.

Cerebral cortex: the outer surface of the brain which has, in higher mammals, a creased and bumpy appearance

Classical conditioning: a simple form of learning where a previously neutral stimulus (e.g., a light) becomes associated with a motivationally salient stimulus (e.g., food) through repeat presentation.

Clinical neuropsychology: a branch of clinical psychology that specialises in the assessment of patients with focal brain injury or neuro-cognitive deficits.

Clot: a solid deposit in the blood that may block a narrow blood vessel leading to a form of stroke.

Cognitive neuropsychology: a branch of neuro-psychology that studies how brain structure and function relate to specific psychological processes.

Conduction aphasia: aphasia in which the principal deficit is an inability to repeat spoken language.

Convergence: in the nervous system, the process of many (converging) inputs influencing one component (for example, a neuron).

Converging operations: the use of several research methods to solve a single problem so that the strengths of one method balance out the weaknesses of the others.

Coronal (as in section): the orientation of a brain slice if you were looking "face on" and the brain was sliced vertically.

Critical periods: the early stages of an organism's life during which it displays a heightened sensitivity to certain environmental stimuli, and develops in particular ways.

D_1 receptors: a class of dopamine receptor found particularly in the frontal lobes and striatum.

D_2 receptors: another class of dopamine receptor found particularly in the striatum and pituitary.

Descartes: French philosopher famous for his ideas about the separate identities of mind and body.

Diaschisis: sudden loss of function in a region of the brain connected to, but at a distance from, a damaged area.

Disconnection: the general term for a group of disorders thought to be caused by damage to a pathway between two undamaged regions (e.g., split-brain syndrome).

Distal: far away; as opposed to proximal, meaning near to.

Divergence: in the nervous system, the principle that because axons may branch many times, a single neuron can influence a large number of targets (usually other neurons).

Dopamine: a catecholamine neurotransmitter found in the brain.

Dyslexia: a specific reading difficulty found in a person with otherwise normal intelligence.

Echoic trace: a form of very short-term auditory memory (a sort of acoustic after-image) thought to last no more than 1 or 2 seconds.

Ecological validity: characteristic of experiments where the methods, materials and setting approximate the real-life situation that is under study.

Egocentric neglect: consistent errors to one side of the viewer (right or left).

Epilepsy: the term for a group of neurological disorders characterised by synchronised but excessive neuronal activity.

Equipotentiality: the term associated with Lashley, broadly meaning that any region of cortex can assume responsibility for a given function (memory being the function of interest for Lashley).

Excito-toxicity: the process by which nerve cells are killed by excitatory substances.

Figure (as in figure and ground): the figure is the prominent or core feature of an array.

Finger maze: a piece of apparatus in which the (usually blindfolded) respondent must negotiate a route from A to B. Typically the maze comprises a grooved piece of wood with one correct route and a series of blind alleys. The respondent pushes their finger along the "correct" path.

Fluent aphasia: another name for Wernicke's aphasia. Language is fluent but nonsensical.

Free will: a philosophical term for the capacity of rational agents to choose a course of action from among various alternatives.

Gestalt: a collection of physical, biological, psychological, or symbolic entities that creates a unified concept, configuration, or pattern.

Ground (as in figure and ground): the ground is the background or peripheral element of an array.

Gyri: elongated bumps (convexities) in the cortex (singular: gyrus).

Haemorrhage: a general term for bleeding. In the brain, this may occur following an aneurysm, or other damage to a blood vessel.

Hallucinations: perceptual experiences unrelated to physical sensation. They may occur in any sensory modality, and are often associated with mental illness.

Hemiparesis: partial or complete loss of movement in one side of the body.

Hemiplegia: loss of sensory awareness from, and muscle control of, one side of the body.

Herpes simplex: infection with this virus can affect brain function, leading to permanent damage.

Homotopical: occurring at the same relative location.

Huntington's disease: a rare, genetically determined, neurological disorder causing dementia and death due to progressive loss of neurons in the striatum.

Hyperactivity: in neurological terms, excess functional activity. In behavioural terms, a developmental disorder marked by excess excitability, inattentiveness, restlessness, and reckless/antisocial behaviour.

Ictal focus: the point of origin of epileptic activity, often a discrete region of damaged cortical tissue.

Inhibition of return: when attention is directed to a location, there is a brief period of when processing at that location is facilitated. Following facilitation, there is a period during which attention is inhibited from returning to that location. This is inhibition of return (IOR).

Instrumental learning: a type of learning where an animal learns to perform an action to obtain reinforcement.

Integrative agnosia: a condition characterised by impaired object recognition due to problems in integrating or combining elements of objects.

Interneurons: the name for neurons that receive input from neurons and send their output to other neurons, found throughout the CNS.

In-vivo imaging techniques: a range of imaging techniques that explore structure and/or function in living subjects.

Ipsilateral: same-sided. An unusual anatomical "wiring" arrangement in which brain function is linked to behaviour function on the same side (the norm being contralateral or opposite side control).

Kinaesthetic: anything related to the sensation of body movement/location. Sensory information about the status of joints and muscles.

Kluver-Bucy syndrome: a collection of emotional impairments resulting from amygdala damage in animals.

Lateral inhibition: a relatively common feature of nervous system "wiring" in which active neurons tend to suppress activity of adjacent neurons.

Lesion: a cut in (or severing of) brain tissue. This may occur as the result of an accident or may be part of a surgical procedure.

Lexicon: loosely equates to stored vocabulary, that is, one's long-term memory of native-tongue words (estimated to be about 50,000 for English speakers).

Likert scales: a simple measure of subjective experience. Participants must make a mark on a line that corresponds to how they feel.

Lobectomy: surgical removal of all or part of a cortical lobe (as in temporal lobectomy for removal of the temporal lobe).

Localisation of function: the concept that different parts of the brain carry out different functions and, conversely, that not all parts of the brain do the same thing.

Long-term potentiation: the enduring increase in functional activity (at synapses) that may be related to memory storage in the brain.

Mass-action: the principle (alongside equipotentiality) that cortical regions of the brain are inherently non-specialised, and have the capacity to engage in any psychological function.

Meninges: the system of membranes that enclose the central nervous system.

Meta-analysis: a research technique in which data from similar but separate projects are pooled into a single data set to increase statistical power.

Midline: anatomically, in mammals, the imaginary line separating the left from the right side.

Mind–body problem: explaining what relationship, if any, exists between mental processes and bodily states.

Modularity: the idea (attributed to Fodor) that psychological functions such as language and perception can be broken down into multiple components that may, in turn, depend on the effective processing of discrete brain regions.

Module: a core unit in an integral modular system (see above).

Motor neuron disease: one of a group of disorders characterised by progressive destruction of the motor neurons that control voluntary action.

Multiple sclerosis: a disease in which progressive loss of myelin leads to loss of function.

Myelin sheath: a wrapping of insulation found on axons of many neurons giving a characteristic white appearance and leading to faster nerve impulse propagation.

Neurogenesis: the process by which neurons are generated.

Neuron cell bodies: the central parts of neurons (nerve cells) that contain the nucleus.

Neurotransmitters: a heterogeneous group of chemical messengers usually manufactured by, stored in, and released by neurons that can influence the excitability of other neurons (or muscles).

Ocular apraxia: the inability to move the eyes voluntarily to objects of interest despite unrestricted eye movements and normal visual fields

Open head injuries: head injuries involving damage to the cranium so that the brain is exposed or visible. Often compared with "closed head injury" in which brain damage has occurred although the cranium has not been penetrated: for example, dementia pugilistica (brain damage associated with boxing).

Optic ataxia: a deficit in reaching under visual guidance that cannot be explained by motor, somatosensory, or primary visual deficits

Optical aphasia: a deficit in naming objects viewed visually in spite of intact semantic knowledge of them.

Orienting response: a spontaneous reaction to a stimulus in which the head and/or body are moved so that the source of the stimulus may be examined.

Parallel information processing: the idea that the brain processes two sources of information simultaneously.

Paralysis: loss of movement in a body region (such as a limb).

Parietal lobe: region of cortex behind the frontal lobes and above the occipital lobes. It plays key roles in spatial function and attention.

Parkinson's disease: a neurological disorder in which movements become slowed or are lost altogether. Rigidity and tremor are also found. Associated with loss of cells in and around the basal ganglia.

Parkinsonism: signs and symptoms that resemble Parkinson's disease. Certain drugs (such as neuroleptics) can induce these as a side effect.

Percept: the "whole" that is perceived by putting together the constituent parts.

Perseveration: the tendency to repeat the same (or similar) response despite it no longer being appropriate.

Perseverative (see above): a response may be perseverative in the sense of being an unnecessary or inappropriate regurgitation of an earlier response.

Poliomyelitis (polio): a viral disease where motor neurons are damaged resulting in muscle weakness and/or paralysis.

Polysensory: responsive to input from several modalities.

Priming: the (possibly subconscious) influence of some preliminary event or stimulus on subsequent responding.

Prosodic: an adjective to describe emotionally intoned language. (Aprosodic speech is devoid of emotional intonation, or monotone.)

Prosopagnosia: the form of agnosia in which the ability to perceive faces is affected.

Psychoanalysis: the school of psychology initiated by Freud that emphasises the role(s) of unresolved subconscious conflicts in psychological disorder.

Punishment: in animal learning, anything an animal will work to avoid.

Radio-ligand: a radioactive biochemical marker that binds to a specific receptor type in the brain.

Receptive fields: the area of external influence on any given internal sensory element. Typically, for example, cells in your fovea (central field of vision) have much smaller receptive fields than those in the periphery.

Receptor sites: molecular structures on (or in) the membranes of neurons that neurotransmitter substances (and hormones) can "influence" when they occupy them, usually by making the neuron more or less excited.

Reinforcement: typically some form of reward (positive reinforcement) or punishment (negative reinforcement) that affects the likelihood of a response being repeated.

Reinforcer: a stimulus that elicits a change in behaviour.

Retrograde amnesia: a form of memory loss where people are unable to remember events that happened before the onset of amnesia.

Reward: in animal learning, anything that an animal will work to obtain.

Sagittal: sideways, as in sagittal brain scans taken from the side of the head.

Sensory nerves: nerves carrying action potentials from sensory receptors towards the CNS (e.g., the optic nerve).

Signal to noise ratio: degree to which relevant information can be perceived against a background of irrelevant information.

Signs: the indications of some abnormality or disturbance that are apparent to the trained clinician/observer (as opposed to symptoms, which are things an individual describes/complains of).

Silent synapses: synapses that are not currently transmitting neuronal signals.

Simultanagnosia: inability to recognise multiple elements in a simultaneously displayed visual presentation.

Somatosensory: sensation relating to the body's superficial and deep parts, as contrasted to specialised senses such as sight.

Spatial neglect: a condition in which damage to one side of the brain causes a deficit in attention to the opposite side of space.

Speech apraxia: a characteristic sign of Broca's aphasia in which articulatory problems are apparent and speech is peppered with neologisms or paraphasias.

Stroke: a catch-all term for disturbances of the blood supply to the brain. Most commonly, strokes are caused by obstruction to, or rupture of, blood vessels in the brain.

Striatum: a collective name for the caudate and putamen, key input regions in the basal ganglia.

Subcortical: the portion of the brain immediately below the cerebral cortex.

Substantia nigra: another component of the basal ganglia. Neurons originating in the substantia nigra terminate in the striatum, where they release the neurotransmitter dopamine.

Sulci: the smaller folds or indents on the surface of the cortex (singular: sulcus). Larger ones are called fissures.

Supranuclear palsy: one of the so-called subcortical dementias in which there is progressive tissue loss in the basal ganglia and midbrain structures such as the superior and inferior colliculi.

Symptoms (see Signs above): symptoms are the features of a disorder or disease that the individual reports/complains of.

Synapses: the tiny fluid-filled gaps between neurons where synaptic transmission (see below) may occur. Typically 20–30 nanometres (millionths of a millimetre) wide.

Syndromal: a feature of a syndrome, the latter being a term for a disorder or condition (such as split-brain syndrome) characterised by a cluster of interrelated signs and symptoms rather than one defining feature.

Syntax: the rules governing the structure of sentences.

Tachistoscope: an item of psychological equipment with which visual material can be presented to respondents for very brief exposure times (these days often replaced by digital computers).

Telegraphic speech: a name to describe the non-fluent "stop–start" agrammatic speech associated with Broca's aphasia.

Temporal lobe: the region of the cortex (on both sides of the brain) running forward horizontally above and in front of the ear, known to be involved in language, memory, and visual processing.

Thalamus: a multi-functional subcortical brain region.

Theory of mind: the ability to attribute mental states to others and to understand that others have beliefs that are different from one's own.

Transduction: process by which a cell converts one kind of signal or stimulus into another.

Trinucleotide repeats: stretches of DNA in a gene that contain many repeats of the same three-nucleotide sequence. A genetic cause of neurological disorders.

Ultrasound: an antenatal procedure for generating images of unborn children.

Voluntary gaze: intentional adjustments of eyes in the deliberate process of attending to a feature in the visual field.

Wada test: a test that involves the administration of a fast-acting barbiturate (via the carotid artery) to one hemisphere at a time, to determine, among other things, the hemisphere that is dominant for language.

White matter: parts of the brain comprising axons of nerve cells, mainly responsible for neuronal transmission rather than information processing.

Working memory: a form of short-term memory, first characterised by Alan Baddeley, which allows a person to hold "on-line" (and manipulate) a certain amount of information for a few seconds after it has been presented: for example, keeping a phone number in mind until you have dialled it.

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