

Neuroimaging of Human Memory

Linking cognitive
process to neural
systems

Edited by

Frank Roesler

Charan Ranganath

Brigitte Röder

Rainer H. Kluwe

OXFORD
UNIVERSITY PRESS

OXFORD

UNIVERSITY PRESS

Great Clarendon Street, Oxford ox2 6DP

Oxford University Press is a department of the University of Oxford.
It furthers the University's objective of excellence in research, scholarship,
and education by publishing worldwide in
Oxford New York

Auckland Cape Town Dar es Salaam Hong Kong Karachi
Kuala Lumpur Madrid Melbourne Mexico City Nairobi
New Delhi Shanghai Taipei Toronto

With offices in

Argentina Austria Brazil Chile Czech Republic France Greece
Guatemala Hungary Italy Japan Poland Portugal Singapore
South Korea Switzerland Thailand Turkey Ukraine Vietnam

Oxford is a registered trade mark of Oxford University Press
in the UK and in certain other countries

Published in the United States
by Oxford University Press Inc., New York

© Oxford University Press, 2009

The moral rights of the author have been asserted
Database right Oxford University Press (maker)

First published 2009

All rights reserved. No part of this publication may be reproduced,
stored in a retrieval system, or transmitted, in any form or by any means,
without the prior permission in writing of Oxford University Press,
or as expressly permitted by law, or under terms agreed with the appropriate
reprographics rights organization. Enquiries concerning reproduction
outside the scope of the above should be sent to the Rights Department,
Oxford University Press, at the address above

You must not circulate this book in any other binding or cover
and you must impose the same condition on any acquirer

A catalogue record for this title is available from the British Library
Data available

Library of Congress Cataloging in Publication Data
Data available

Typeset in Minion by Cepha Imaging Private Ltd., Bangalore, India
Printed in Great Britain
on acid-free paper by

Biddles Ltd., King's Lynn, UK

ISBN 978-0-19-921-7298

10 9 8 7 6 5 4 3 2 1

Contents

List of contributors 00

Abbreviations and acronyms 00

- 1** Introduction: Neuroimaging of human memory 1
Frank Rösler, Charan Ranganath, Brigitte Röder, and Rainer H. Kluwe

Part 1 **Setting the stage**

- 2** On how to reconcile mind and brain 15
Frank Rösler and Charan Ranganath
- 3** Uncovering unobservable cognitive mechanisms: The contribution of mathematical models 25
Rolf Ulrich

Part 2 **Learning and consolidation**

- 4** Reinforcement learning mechanisms in the human brain: Insights from model-based fMRI 45
John P O'Doherty
- 5** Cognitive models in learning and reward processing 65
Christian Büchel
- 6** Neuroimaging and interactive memory systems 77
Dara G. Ghahremani and Russell A. Poldrack
- 7** Contributions of functional neuroimaging to theories of category learning 89
Paul J. Reber
- 8** Declarative memory consolidation 109
Guillén Fernández and Indira Tendolkar
- 9** On the intimate relationship between neurobiology and function in the theoretical analysis of human learning and memory 127
Alan Richardson-Klavehn, Elena Magno, Gerasimos Markopoulos, Catherine M. Sweeney-Reed, and Maria Wimber

Part 3 **Working memory control processes and storage**

- 10** Toward characterizing the neural correlates of component processes of cognition 169
Matthew R. Johnson and Marcia K. Johnson

- 11** The mid-ventrolateral frontal cortex and attentional control 195
Adrian M. Owen and Adam Hampshire
- 12** Mechanisms underlying the short-term retention of information 213
Bradley R. Postle
- 13** Interrelationships between working memory and long-term memory 227
Charan Ranganath
- 14** Is there anything special about working memory? 255
Bradley R. Buchsbaum and Mark D'Esposito
- 15** Retrieving pictures from long-term memory 263
Alumit Ishai
- 16** Content specificity of long-term memory representations 281
Patrick Khader and Frank Rösler
- 17** Multivariate methods for tracking cognitive states 297
Kenneth A. Norman, Joel R. Quamme, and Ehren L. Newman
- 18** Imaging emotional influences on learning and memory 329
Kevin S. LaBar
- 19** Developing theories that bridge mind and brain: Some thoughts of a cognitive psychologist 347
Andrew P. Yonelinas

Part 4 **Control processes during encoding and retrieval**

- 20** Episodic memory storage and retrieval: Insights from electrophysiological measures 355
Axel Mecklinger and Theodor Jäger
- 21** Memory and the awareness of remembering 381
Ken A. Paller, Joel L. Voss, and Carmen E. Westerberg
- 22** Constraints on cognitive theory from neuroimaging studies of source memory 403
Jon S. Simons
- 23** Oscillatory and haemodynamic medial temporal responses preceding stimulus onset modulate episodic memory 425
Emrah Düzel and Sebastian Guderian
- 24** Functional neuroimaging and cognitive theory 441
Michael D. Rugg

Subject index 000

Name index 000

Contributors

Frank Rösler

Experimental and Biological Psychology,
Philipps-University Marburg,
Marburg, Germany

Charan Ranganath

Center for Neuroscience,
University of California at Davis,
Davis, USA

Brigitte Röder

Biological Psychology and
Neuropsychology,
University of Hamburg,
Hamburg, Germany

Rainer H. Kluwe

Helmut-Schmidt-University Hamburg,
Hamburg, Germany

Rolf Ulrich

Cognitive and Biological Psychology,
University of Tübingen

John P O'Doherty

Division of Humanities and Social
Sciences and Computation and Neural
Systems Program,
California Institute of Technology,
Pasadena, USA

Christian Büchel

NeuroImage Nord, Department of
Systems Neuroscience,
University Medical Center
Hamburg-Eppendorf,
Germany

Dara G. Ghahremani

University of California Los Angeles,
Los Angeles, USA

Russell A. Poldrackxxx**Paul J. Reber**

Department of Psychology,
Northwestern University, Evanston, USA

Guillén Fernández

Cognitive Neurology Section at the
F.C. Donders Center and the Dept. of
Neurology,
Nijmegen, The Netherlands

Indira Tendolkar

Cognitive Neurology Section at the F.C.
Donders Center and the Dept. of
Neurology and Dept. of Psychiatry,
Radboud University Nijmegen,
Nijmegen, The Netherlands

Alan Richardson-Klavehn

Memory and Consciousness Research
Group, Department of Neurology II,
Faculty of Medicine,
Otto von Guericke University,
Magdeburg, Germany

Elena Magno

Memory and Consciousness Research
Group, Department of Neurology II,
Faculty of Medicine,
Otto von Guericke University,
Magdeburg, Germany

Gerasimos Markopoulos

Memory and Consciousness Research
Group, Department of Neurology II,
Faculty of Medicine,
Otto von Guericke University,
Magdeburg, Germany

Catherine M. Sweeney-Reed

Memory and Consciousness Research Group, Department of Neurology II, Faculty of Medicine, Otto von Guericke University, Magdeburg, Germany

Maria Wimber

Memory and Consciousness Research Group, Department of Neurology II, Faculty of Medicine, Otto von Guericke University, Magdeburg, Germany

Matthew R. Johnson

Interdepartmental Neuroscience Program, Yale University, New Haven, CT, USA.

Marcia K. Johnson

Interdepartmental Neuroscience Program, and Department of Psychology, Yale University, New Haven, CT, USA.

Adrian M. Owen

Medical Research Council Cognition and Brain Sciences Unit, 15, Chaucer Road, Cambridge, CB2 2EF, U.K

Adam Hampshire

Medical Research Council Cognition and Brain Sciences Unit, 15, Chaucer Road, Cambridge, CB2 2EF, U.K

Bradley R. Postle

Department of Psychology, University of Wisconsin-Madison

Bradley R. Buchsbaum

Helen Wills Neuroscience Institute and Department of Psychology, University of California, Berkeley

Mark D'Esposito

Helen Wills Neuroscience Institute and Department of Psychology, University of California, Berkeley

Alumit Ishai

Institute of Neuroradiology, University of Zurich

Patrick Khader

Experimental and Biological Psychology, Philipps-University Marburg, Germany

Kenneth A. Norman

Department of Psychology, Princeton University, Princeton, USA

Joel R. Quamme

Department of Psychology, Princeton University, Princeton, USA

Ehren L. Newman

Department of Psychology, Princeton University, Princeton, USA

Kevin S. LaBar

Center for Cognitive Neuroscience, Duke University, Durham, NC, USA

Andrew P. Yonelinas

Department of Psychology, University of California Davis, Davis, USA

Axel Mecklinger

Experimental Neuropsychology Unit, Department of Psychology, Saarland University, Saarbrücken, Germany

Theodor Jäger

Department of Neurology, Universitätsklinikum Mannheim, University of Heidelberg, Mannheim, Germany

Ken A. Paller

Interdepartmental Neuroscience Program and Department of Psychology, Northwestern University

Joel L. Voss

Interdepartmental Neuroscience Program and Department of Psychology, Northwestern University

Carmen E. Westerberg

Interdepartmental Neuroscience Program and Department of Psychology, Northwestern University

Jon S. Simons

Department of Experimental Psychology,
University of Cambridge, Cambridge, UK

Emrah Düzel

Institute of Cognitive Neuroscience,
University College London, 17 Queen
Square, London, UK.

Sebastian Guderian

Laboratory of Neuropsychology, National
Institute of Mental Health, National
Institutes of Health, Building 49, Room
1B80, Bethesda, USA.

Michael D. Rugg

Center for the Neurobiology of Learning
and Memory and Department of
Neurobiology and Behavior

Chapter 15

Retrieving pictures from long-term memory

Alumit Ishai

Introduction

‘At the present time, one of the major deficiencies in cognitive psychology is the lack of explicit theories that encompass more than a single experimental paradigm. The lack of such theories and some of the unfortunate consequences have been discussed by Allport (1975) and Newell (1973). Two important points are made by Newell: First, research in cognitive psychology is motivated and guided by phenomena (e.g. those of the Sternberg paradigm and the Brown-Peterson paradigm). Second, attempts to theorize result in the construction of binary oppositions (e.g. serial vs. parallel, storage vs. retrieval, and semantic vs. episodic). Thus, an appreciable portion of research in cognitive psychology can be described as testing binary oppositions within the framework of a particular experimental paradigm. This style of research does not emphasize or encourage theory constructions; but without theory, it is almost impossible to relate experimental paradigms or to substantiate claims that the same processes underlie different experimental paradigms. Furthermore, the concern with binary oppositions tends to obscure the more interesting aspects of data, such as the form of functional relations’ (Ratcliff, 1978).

Three decades have passed since these words have been written. Despite the functional brain imaging revolution, which transformed cognitive psychology to cognitive neuroscience, we still do not have a theory of human memory, we are still guided by phenomena, and we still test binary oppositions. The contemporary neuroimaging literature on human memory is saturated with studies that contrast encoding with retrieval, recollection with familiarity, remembered with forgotten items, and correct with incorrect responses. These contrasts result in statistical maps that identify the location of activation in some brain areas during some experimental conditions. At best, these functional brain imaging studies are designed to test a specific hypothesis, but hypotheses do not comprise a unified theory of human memory. Perhaps the best example of how psychological theories have provided insights into functional brain imaging studies is Baddeley’s influential model of working memory and its subsequent revision due to novel neuroimaging data, from which new predictions derived (see chapters by Postle and Ranganath). It has been argued that the collection of large-scale fMRI data do not represent an intellectual integration (Savoy, 2001). It has also been suggested that we have to accept the assumption that there is a systematic mapping from cognitive function to brain structure and that neuroimaging data comprise an independent variable that can be used to construct and

test competing theories (Henson, 2005). In this chapter, several fMRI studies, designed to elucidate the neural correlates of retrieving pictorial information from long-term memory (LTM), are described. Although these studies were originally designed to test binary oppositions (e.g. perception vs. imagery; short- vs. long-term memory; old vs. new), I argue that the complex activation patterns observed when subjects generate mental images of faces and objects or perform recognition memory tasks provide us with valuable information that is essential for the formulation of any theories or models of human memory. As visual imagery and recognition memory are mediated by activation in distributed cortical networks that include visual, parietal, limbic, and prefrontal structures, I further argue that an integrative theory of human memory has to account for wide spread patterns of activation and for the dynamics and effective connectivity within these cortical networks.

Visual perception, imagery, and effective connectivity

Visual imagery is the ability to generate percept-like images in the absence of retinal input and therefore is a vivid demonstration of retrieving pictorial information from memory. The subjective similarity of seeing and imagining suggests that perception and imagery share common internal representations. Psychophysical and brain-imaging studies have demonstrated functional similarities between visual perception and visual imagery, to the extent that common mechanisms appear to be activated by both (Roland *et al.*, 1987; Farah *et al.*, 1988; Goldenberg *et al.*, 1989; Ishai & Sagi 1995). Numerous neuroimaging studies have shown that visual imagery, like visual perception, evokes activation in occipito-parietal and occipito-temporal visual association areas (Mellet *et al.*, 1996; D'Esposito *et al.*, 1997). In some studies, the primary visual cortex (Le Bihan *et al.*, 1993; Kosslyn *et al.*, 1993, 1999) and the lateral geniculate nucleus (Chen *et al.*, 1998) were activated during imagery, suggesting that the generation of mental images may involve sensory representations at the earlier processing stages in the visual pathway. Studies of patients with brain damage have demonstrated a dissociation of visual-object and visual-spatial imagery (Levine *et al.*, 1985), indicating that different parts of the visual system mediate 'where' and 'what' imagery, a dissociation that parallels the two anatomically distinct visual systems proposed for visual perception (Ungerleider & Mishkin, 1982).

Functional MRI studies have reported that within the ventral object vision pathway faces and other objects, such as outdoor scenes, houses, chairs, animals, and tools, have distinct representations (Kanwisher *et al.*, 1997; Epstein & Kanwisher, 1998; Aguirre *et al.*, 1998; Chao *et al.*, 1999). In particular, it has been shown that faces, houses, and chairs evoke maximal responses in distinct occipital and ventral temporal regions with a highly consistent topological arrangement across subjects (Ishai *et al.*, 1999, 2000a). As each category was associated with its own differential pattern of responses across a broad expanse of cortex, it has been proposed that the representation of objects in the ventral stream is not restricted to discrete, highly selective patches of cortex, but, rather, is comprised of distributed representation of information about object form (Ishai *et al.*, 1999, 2000a; Haxby *et al.*, 2001). Inspired by the consistent topology of the response to faces, houses, and chairs, we investigated whether visual imagery of these objects would evoke

content-related activation within the same extrastriate ventral regions that are activated during perception. Furthermore, we asked which brain regions, activated during imagery, provide the top-down signal to visual extrastriate cortex. To that end, we designed an fMRI study with the following experimental conditions: Perception, in which subjects viewed pictures of faces, houses, chairs; Perception-control, in which subjects viewed scrambled pictures; Imagery, in which subjects were instructed to generate vivid mental images of familiar houses, faces, and chairs from LTM while viewing a gray square, and to press a button when ready with a vivid image; and Imagery-control, in which subjects were asked to press the button from time to time while viewing the gray square. Conventional Statistical Parametric Mapping (SPM) analysis revealed differential activation in medial fusiform, lateral fusiform, and inferior temporal gyri during the perception of houses, faces, and chairs, respectively. During visual imagery, content-related patterns of activation were found, but this activity was restricted to small sectors of the regions that responded differentially during perception. Thus, the generation of mental images of familiar faces from LTM evoked activation within small subsets of the lateral fusiform gyrus, a face-responsive region, whereas generating mental images of houses and chairs evoked activation within subsets of the medial fusiform and inferior temporal gyri, respectively. Visual perception and visual imagery evoked activity with opposite patterns of hemispheric asymmetry in ventral temporal cortex, with stronger responses in the right hemisphere during perception, and stronger responses in the left hemisphere during imagery. Contrasting responses evoked by visual imagery and responses evoked during the imagery control condition revealed activation within a network of parietal and frontal regions. This 'imagery network' included the precuneus, intraparietal sulcus (IPS) and inferior frontal gyrus (IFG), regions that were implicated in various attention and retrieval from episodic memory tasks (e.g. Fletcher *et al.*, 1995; Buckner *et al.*, 1996; Mellet *et al.*, 1998). We interpreted these findings to suggest that retrieval of content-specific memory traces, stored in the ventral pathway, is top-down controlled by a parieto-frontal network that mediates the generation and maintenance of mental images (Ishai *et al.*, 2000b).

To investigate the neuronal interactions and effective connectivity that mediate the category-specific responses in the visual cortex, we used Dynamic Causal Modeling (DCM), a relatively new analytic approach that allows the assessment of effective connectivity within cortical networks (Friston *et al.*, 2003). The aim of DCM is to estimate and make inferences about the coupling among brain areas, and how that coupling is influenced by changes in experimental context (e.g. stimuli or tasks). Consistent with a previous DCM study, which showed that category effects in occipito-temporal cortex were mediated by forward connections from early visual areas (Mechelli *et al.*, 2003), we hypothesized that the category-specific patterns of activation observed in occipito-temporal cortex during visual perception of faces and objects could be explained by a selective enabling of forward connectivity from early visual areas. We also predicted that content-related activation observed during visual imagery would be associated with category-dependent changes in backward connectivity from parietal and frontal areas. Finally, we examined whether the DCM analysis would reveal different patterns of effective connectivity

during imagery of faces, houses, and chairs in parietal and frontal cortices, as our original SPM analysis did not show category-specific imagery activation within these regions (Ishai *et al.*, 2000b). We found that during visual perception, when subjects viewed gray-scale pictures of faces, houses, and chairs, the category-selective effects in occipito-temporal cortex were mediated by forward connections from early visual areas. In contrast, during visual imagery, when subjects generated mental images of faces, houses, and chairs from LTM, the category-selective effects in the visual cortex were mediated by backward connections from prefrontal cortex. Interestingly, the backward connections from prefrontal, but not from parietal cortex, to occipito-temporal cortex were category-selective (Figure 15.1). Thus, the DCM analysis revealed that dynamic neuronal interactions between occipito-temporal, parietal, and frontal regions are task- and stimulus-dependent. Sensory representations of faces and objects in ventral extrastriate cortex are mediated by bottom-up mechanisms arising in early visual areas during

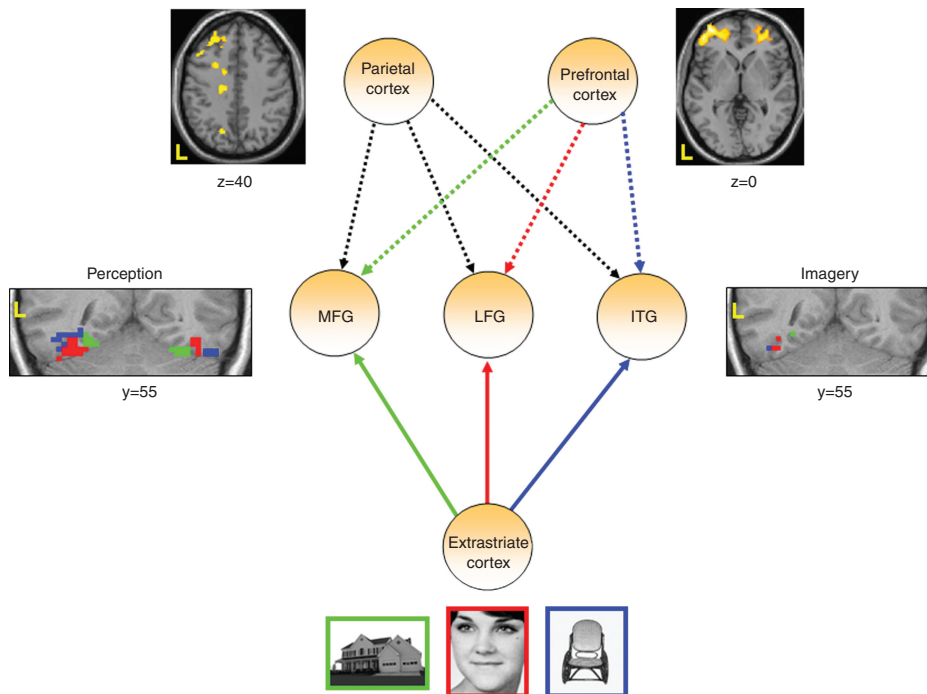


Figure 15.1 Category-selective effects during visual perception and visual imagery. Dynamic Causal Modeling (DCM) analysis revealed that category-selective effects observed in occipito-temporal cortex during perception of houses, faces, and chairs are mediated by forward connections from early visual areas (green, red, and blue arrows, respectively). During visual imagery, the backward connections from prefrontal cortex were category-selective (dashed green, red, and blue arrows), whereas the backward connections from parietal cortex (dashed black arrows) were not content-specific. MFG = medial fusiform gyrus; LFG = lateral fusiform gyrus; ITG = inferior temporal gyrus. (This figure summarizes data published in Ishai *et al.*, 1999, 2000a, 2000b; Mechelli *et al.*, 2003, 2004).

perception, and top-down mechanisms originating in prefrontal cortex during imagery. Additionally, non-selective, top-down processes, originating in superior parietal areas, contribute to the generation of mental images and their maintenance in the 'mind's eye' (Mechelli *et al.*, 2004).

Behavioural studies have reported differential effects of visual imagery on the performance of a perceptual task: visual recall from short-term memory (STM) facilitated task performance, whereas visual recall from LTM interfered with performance, suggesting that imagery-induced facilitation and interference are memory-dependent (Ishai & Sagi 1995, 1997a, 1997b). Moreover, the type of memory (short- or long-term) required for the generation of mental images seems to be a crucial factor in the 'V1 debate', namely the controversy about the extent to which the primary visual cortex is activated during visual imagery. In the vast majority of studies reporting activation during visual imagery in the primary visual cortex, the imagery tasks were based on recall from STM (e.g. Le Bihan *et al.*, 1993; Kosslyn *et al.*, 1993, 1999; Chen *et al.*, 1998; O'Craven & Kanwisher, 2000). To investigate whether similar or different cortical regions are activated during visual imagery generated from STM and from LTM, we had to use a special class of stimuli: famous faces (Ishai *et al.*, 2002). We chose faces of contemporary Hollywood celebrities, assuming that as a result of exposure to these faces in everyday life, subjects would have pictorial representations in memory that could be retrieved by way of visual imagery. Moreover, giving the same visual cue, i.e. a famous name, an image could be generated from either LTM or STM. For example, one could imagine Marilyn Monroe without seeing her picture before the imagery task (LTM), or one could memorize a specific picture of Marilyn Monroe and shortly after generate a mental image of that picture (STM). We also tested the effect of focal attention during visual imagery. Numerous fMRI studies have shown that selective attention to particular attributes of visual stimuli, such as colour or motion, enhanced the activity in regions of extrastriate cortex that process these attributes (e.g. Corbetta *et al.*, 1990). We therefore hypothesized that focusing attention on features of a mental image, rather than on the global configuration of that image, might also result in increased activation. We also speculated that focal attention to mental images would evoke activation in primary visual cortex, based on a model suggested by Sakai and Miyashita (1994), according to which visual imagery is implemented by the interactions between memory retrieval of representations stored in higher visual association areas, and the effect of focal attention on early visual areas. To test all these predictions, our experimental design included the following imagery conditions: Imagery from STM, in which subjects were presented with names of famous faces they had seen and memorized shortly before, and were instructed to generate vivid images of the exact same faces; Imagery from LTM, in which subjects were presented with names of famous faces they had not seen during the experiment, and were instructed to generate any vivid images of these faces; Imagery from STM + Attention, in which subjects were presented with names of famous faces they had seen and memorized shortly before, and were instructed to generate vivid images of these faces and then to answer questions about some facial feature (e.g. 'thick lips?'); and Imagery from LTM + Attention, in which subjects were presented with names of famous faces they had not seen during the experiment, and

were instructed to generate vivid images of these faces and then answer questions about some facial feature (e.g. ‘big nose?’). We found that visual perception of famous faces activated the inferior occipital gyrus, lateral fusiform gyrus, the superior temporal sulcus (STS), and the amygdala, regions of the distributed network that mediates face perception (Haxby *et al.*, 2000; Ishai *et al.*, 2005; Fairhall & Ishai, 2007), whereas visual imagery of famous faces activated small subsets of these face-responsive regions. Visual imagery of famous faces activated a network of regions that included the calcarine, precuneus, hippocampus, IPS, and IFG. In all these regions, imagery generated from STM evoked more activation than imagery generated from LTM (Ishai *et al.*, 2002). Furthermore, during imagery generated from both STM and LTM, focusing attention on features of the imagined faces resulted in increased activation in the right IPS and right IFG, consistent with reports on activation in these regions during sustained attention (e.g. Pardo *et al.*, 1990).

Our findings propose a new perspective on the neural basis of visual imagery. We found evidence for content-related activation in ventral temporal cortex: small sectors of extrastriate regions that participate in visual perception of faces and objects are also involved in representing perceptual information retrieved from LTM during visual imagery of faces and objects (Ishai *et al.*, 2000b, 2002; Mechelli *et al.*, 2004). As imagery evoked activity in small portions of the regions that participate in perception, it is possible that stored information evoked by imagery is simply weaker than equivalent representations evoked by actual visual input. Alternatively, only a specific subset of cortical regions may be dedicated to mental imagery, allowing perception and imagery to operate simultaneously. These results suggest that sensory representations of faces and objects stored in ventral temporal cortex are reactivated during the generation of visual images, consistent with electrophysiological and other fMRI studies, which have reported content-specific activation in sensory areas during imagery and memory retrieval (Buckner & Wheeler, 2001; Kreiman *et al.*, 2000; Wheeler *et al.*, 2000). Interestingly, electric stimulation of regions in the temporal lobe of humans results in imagery recall, suggesting that memory traces are localized in these regions (Penfield & Perot, 1963). Similarly, studies in non-human primates indicate that the temporal lobe is the memory storehouse for visual representations of complex stimuli (Miyashita & Chang, 1988; Miyashita, 1988).

Visual imagery of faces and objects also activated several parietal and frontal regions that were previously implicated in ‘top-down’ control functions. These parietal and frontal regions may mediate the retrieval of object representations from LTM, their maintenance in a working memory ‘buffer’, and the attention required to generate those mental images. Interestingly, a similar network of prefrontal areas was activated during motion imagery (Goebel *et al.*, 1998). On the basis of our effective connectivity analysis, we suggest that this ‘imagery network’ is composed of a general attentional mechanism arising in parietal cortex, and a content-sensitive mechanism originated in prefrontal cortex. Numerous studies of spatial and non-spatial attention tasks have shown activation in parietal cortex (e.g. Corbetta *et al.*, 1998; Kastner *et al.*, 1999; Wojciulik & Kanwisher, 1999). Moreover, parietal activation has been reported in a variety of mental imagery tasks (Mellet *et al.*, 2000; Ishai *et al.*, 2002). It is therefore reasonable to assume that

regions in parietal cortex mediate the attentional processes required to perform the imagery task, irrespective of stimulus-content. Electrophysiological and lesion studies have shown that the prefrontal cortex is not only crucial for object recognition (Bechevalier & Mishkin, 1986), but importantly, that category-selective responses exist in the monkey prefrontal cortex (Freedman *et al.*, 2001). Current models of visual working memory (Miller *et al.* 1996; Fuster & Bauer, 1974) posit that visual working memory is mediated by neuronal interactions between prefrontal and occipito-temporal cortices. Evidence for the existence of similar mechanism in the human brain comes from working memory studies showing that the retrieval of visual information is mediated by a top-down flow of information from prefrontal cortex to category-selective regions in the ventral stream (e.g. Druzgal & D'Esposito, 2003). Our visual imagery studies further show that content-specific imagery effects in the ventral stream are mediated by top-down mechanisms arising in prefrontal cortex (Ishai *et al.*, 2000b, 2002; Mechelli *et al.*, 2004).

Recognition memory and visual similarity

The neural mechanism that mediates the retrieval of newly learned pictures from memory is currently unknown. We conducted a series of event-related fMRI studies to investigate how novel pictorial representations are formed in the cortex and retrieved from LTM. As recognition memory requires matching new items with stored ones, we tested whether matching between new and old pictures depends on their visual similarity. In the first study, the experimental approach combined explicit category learning with a recognition memory task, and original sets of stimuli, namely portraits, landscapes, and abstract compositions by six painters with a unique style (Modigliani, Renoir, Pissarro, Van Gogh, Kandinsky, and Miro). In the training session, subjects were told that paintings from each artist belonged to a category of paintings with a characteristic style and were instructed to memorize these pictures. Four days later, a memory retrieval session was conducted in the MR scanner. Subjects were presented with old and new pictures and indicated whether they had seen these pictures before. The new paintings were either visually similar to the old ones, somewhat similar (ambiguous), or visually different (Figure 15.2). We predicted fast and accurate responses to the new, visually different items, and slower, less accurate responses to the new, similar and ambiguous pictures, due to their visual resemblance to the old items. Moreover, we predicted that activation in the visual cortex and in parietal and prefrontal regions would be modulated by the degree of visual similarity and expected reduced activity with decreased visual similarity between the new and the old pictures. The behavioural data showed that about 70% of the old paintings were correctly recognized and that responses to the new pictures depended on their visual similarity to the old ones. Subjects responded faster and more accurately to new, visually different items, and longer latencies were associated with the new, similar pictures. We found activation in a distributed cortical network that included regions in visual, parietal, and prefrontal cortices, where responses evoked by the new items were modulated by their visual similarity to the old pictures (Figure 15.2). In the visual cortex, the paintings evoked activation in face- and object-responsive regions, where old pictures elicited stronger

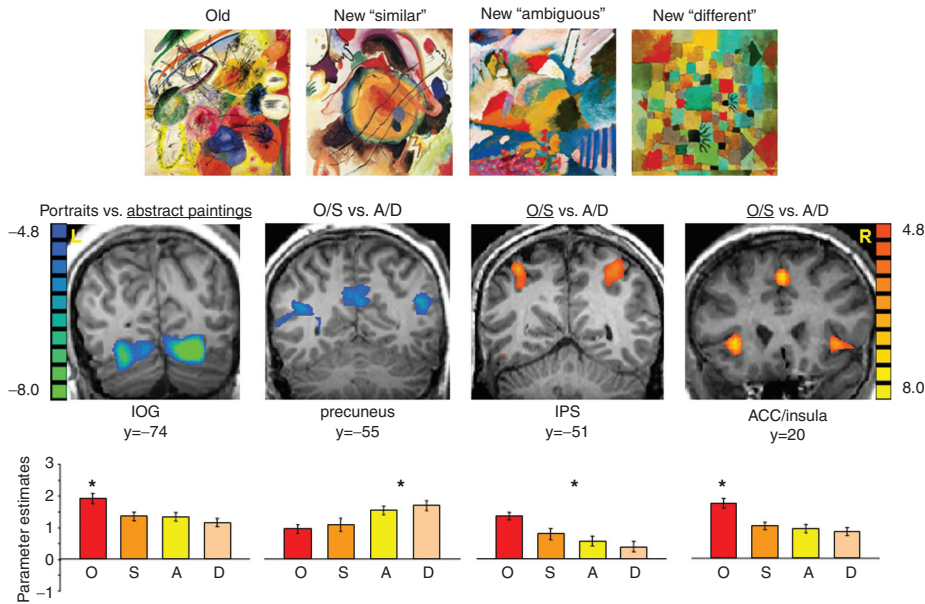


Figure 15.2 Recognition memory is modulated by visual similarity. Subjects memorized art paintings and four days later, a memory retrieval session was conducted in the MR scanner. The old paintings (O) were mixed with new ones that were visually similar (S), ambiguous (A), or different (D), and subjects indicated whether they had seen each picture before. The fMRI data analysis revealed activation within a distributed cortical network. In the inferior occipital gyrus (IOG), an extrastriate visual region, the old pictures evoked stronger activation than the all new items, regardless of their visual similarity. When the old and new, visually similar pictures were contrasted with the new, visually ambiguous and different pictures (O+S vs. A+D), modulation by visual similarity was found in the precuneus, where the new, visually different items evoked the strongest activation, and in the intraparietal sulcus (IPS), where activation was reduced with decreased visual similarity to the old paintings. In the insula and the anterior cingulate cortex (ACC), the old paintings evoked stronger activation than all the new ones. The paintings: 'Black Lines' (old); 'Panel' (new, visually similar); 'Church' (new, ambiguous) by Kandinsky; 'Tunisian Garden' by Klee (new, different).

activation than all new pictures, regardless of their visual similarity. Consistent with our hypothesis, in the IPS and superior parietal lobule (SPL), responses evoked by new pictures were reduced with decreased similarity to the old ones. In memory-related areas, two patterns of activation were observed: in the caudate, insula, and anterior cingulate cortex (ACC), the old pictures elicited stronger activation than the new items, whereas in the precuneus, superior temporal, and superior frontal gyri (STG and SFG) the new, visually different pictures evoked stronger activation than both the old and the new, visually similar pictures. Finally, in the hippocampus, the new, similar pictures evoked weaker activation than the new, ambiguous, and different items. These findings suggest that recognition memory is mediated by activation in a cortical network that includes regions in visual cortex where stimulus-specific representations are stored, attention-related areas where visual similarity to old pictures is detected, and memory-related areas where new

items are classified as a match or a mismatch based on their similarity to the old pictures (Yago & Ishai, 2006).

Our old-new recognition memory tasks did not address the issue of memory processes and the extent to which the observed behavioural and neural responses were due to recollection- or familiarity-based memory decisions. To test whether recollection and familiarity judgments were influenced by the degree of visual similarity between old and new pictures, we conducted a behavioural study. A new group of subjects memorized the paintings and four days later returned for a memory test in which they had to indicate whether they remembered the picture, the picture looked familiar, or the picture was new. Consistent with our hypothesis, subjects correctly recognized more new, visually different items and the response latency was significantly shorter than responses to the new, similar, or ambiguous paintings. We found that the proportion of false alarms, namely Remember and Know responses to new pictures, was reduced with reduced visual similarity between the new pictures and the old ones. The number of Know responses to the new, similar items was significantly higher than the number of Know responses to the ambiguous and different paintings. It therefore seems that mistaking new pictures for old ones is associated with feelings of familiarity, not recollection (Ishai & Wiesmann, 2007).

Our study with art paintings has shown that recognition memory of newly learned, visually similar items is associated with many false alarms, namely erroneous responses subjects make, mistaking new items for old ones. To further investigate the neural correlates of false memory, we conducted a second study with unfamiliar South Korean faces. Caucasian subjects, who had limited exposure to Asian faces in their environment, memorized unfamiliar neutral and happy South Korean faces, and four days later performed a recognition memory task in the MR scanner. Previously seen faces were recognized faster and more accurately than new faces. Response latencies for misses were significantly longer than the response latencies for hits, and response latencies for hits were significantly longer than the latencies for false alarms. These behavioural data suggest that it took subjects longer to decide whether a face was new, probably due to the high visual similarity between the South Korean faces. The recognition memory task elicited activation within a distributed cortical network that included visual, parietal, and prefrontal regions. Within all regions, previously seen faces evoked stronger activation than new faces and the response to happy faces was very similar to the response to neutral faces. In parietal and prefrontal cortices, activation during correct trials was stronger than activation during incorrect trials. Finally, in the hippocampus, false alarms to happy faces evoked stronger activation than false alarms to neutral faces (Ishai & Yago, 2006).

Recognition memory of portraits, landscapes, abstract paintings, and South Korean faces evoked activation in face- and object-responsive regions in the visual cortex. In the lateral fusiform gyrus, a face-responsive region (Kanwisher *et al.*, 1997), portraits elicited stronger activation than landscapes and abstract paintings. In the medial fusiform and parahippocampal gyri, regions that respond to houses and places, respectively (Aguirre *et al.*, 1998; Epstein & Kanwisher, 1998; Ishai *et al.*, 1999), landscapes evoked stronger activation than portraits and abstract paintings. In the posterior fusiform gyrus, abstract paintings evoked stronger activation than portraits and landscapes. Finally, landscapes

and abstract paintings evoked stronger responses than portraits in dorsal occipital cortex. Within these face- and object-selective regions, previously seen pictures evoked stronger responses than the new items. The patterns of activation observed in the visual cortex indicate that explicit encoding of pictures results in stimulus-specific representations, consistent with numerous category learning (Reber *et al.*, 1998), visual imagery (Ishai *et al.*, 2000b; Mechelli *et al.*, 2004), working memory (Druzgal & D'Esposito, 2003) and associative memory retrieval (Ranganath *et al.*, 2004) studies, which showed stimulus-specific memory traces in the human visual ventral stream.

Activation in parietal cortex during recognition memory of paintings revealed stronger responses to the old pictures than to the new items. Furthermore, confirming our hypothesis, activation within these regions was reduced with decreased similarity between the new paintings and the old ones. The IPS and the SPL, regions of the dorsal frontoparietal attention network, were implicated in many cognitive studies of attention. In particular, both regions were activated in target detection tasks (Corbetta *et al.*, 2000; Shulman *et al.*, 2001; Kincade *et al.*, 2005). The old items, for which the correct response was 'Yes, I had seen these pictures before', were randomly mixed with new, never seen before pictures. It is highly likely that subjects were searching for and detecting these old paintings as 'targets'. We observed shorter reaction times and decreased amplitudes of the fMRI signal with decreased similarity to the old items. The enhanced activation evoked by the old pictures and the reduced activity elicited by the new, visually different pictures suggest that the IPS and SPL process the segmentation of old from new items (Pollmann *et al.*, 2003). Thus, recognition of familiar pictures and target detection seem to be mediated by similar neural correlates within the attentional network. Numerous recognition memory studies have further shown that posterior parietal cortex does not merely 'detect old items' but, rather, mediates higher order cognitive processes associated with memory retrieval (Konishi *et al.*, 2000; Wheeler & Buckner, 2003; Shannon & Buckner, 2004). Our data also support the 'mnemonic accumulator' hypothesis, according to which recognition memory decisions are based on the integration of sensory signals (Wagner *et al.*, 2005).

Explicit encoding and recognition of the paintings, revealed activation in multiple memory-related areas, with two distinct patterns of response: stronger activation for the old pictures in the caudate, ACC and the insula, and stronger activation for new, visually different items in the precuneus, STG, and the SFG. Some of these regions were implicated in previous studies of category learning (e.g. Reber *et al.*, 2002; Vogels *et al.*, 2002). Our study revealed differential activation within these regions as a function of visual similarity between old and new pictures. In the caudate, ACC, and insula, the old paintings evoked stronger activation than all new items, regardless of their visual similarity. These regions therefore likely mediate the correct classification of the old items, consistent with previous reports about their role in memory retrieval, target detection, and category learning (Poldrack *et al.*, 1999; Seger & Cincotta, 2002). It is of interest that the pattern of activation in the caudate, ACC, and insula resembles that of the face- and object-responsive regions in the visual cortex, where old pictures evoked stronger responses than new ones. The enhanced activation elicited by the old items is consistent with visual categorization studies in monkeys that showed stronger responses to familiar

prototypes in IT and PFC (Freedman *et al.*, 2003). Moreover, it has been shown that during associative learning in monkeys, rapid learning-related responses in the caudate precedes slower responses in the PFC, further suggesting that output from the basal ganglia also modulates PFC activation during learning (Pasupathy & Miller, 2005). An fMRI study in humans has shown that the caudate has two functional roles in category learning: the body and tail mediate classification, whereas the head processes feedback during learning (Seger & Cincotta, 2005). It therefore seems that in addition to stimulus-specific representations stored in visual and prefrontal regions, recognition of familiar pictures requires output signals from the striatum. In the precuneus, STG, and SFG, regions implicated in many studies of memory retrieval (e.g. Fletcher *et al.*, 1995; Shannon & Buckner, 2004; Yonelinas *et al.*, 2005), the new, visually different exemplars evoked stronger activation than both the old and the new, visually similar pictures. Behaviourally, responses to the new, visually different pictures were faster and more accurate than responses to the visually similar ones. It is likely that the visually different, or mismatch items were classified as new within these regions.

Recognition memory of South Korean faces revealed activation in the IFG, insula, and ACC. Within these regions, responses during correct trials, regardless of stimulus type (old or new faces) were stronger than responses during incorrect trials. Previous functional brain imaging studies have implicated the prefrontal cortex in memory formation (Buckner *et al.*, 1999) and monitoring during retrieval (Buckner & Wheeler, 2001). Enhanced activation in parietal and prefrontal regions in response to old items has been reported in numerous fMRI studies (Kahn *et al.*, 2004). This 'old-new' parieto-frontal effect is also consistent with the ERP correlates of recollection, namely a positive shift in waveforms elicited by correctly classified old items relative to the waveforms evoked by new items in the left parietal cortex, and a sustained positive shift elicited by old items in the right prefrontal cortex (Rugg *et al.*, 2002). Most functional brain imaging studies of episodic memory retrieval have used written words, and not pictures, as stimuli (Cabeza *et al.*, 2003; Rugg & Wilding, 2000). Moreover, our task required a simple 'Yes-No' recognition, whereas other studies of episodic retrieval employed the 'Remember-Know' procedure (Rugg & Yonelinas, 2003). Finally, the ERP and fMRI techniques detect different signals, namely scalp electrical activity and the haemodynamic response, which reflect direct and indirect measures of neuronal activity, respectively. Hemispheric asymmetries should therefore be carefully interpreted.

In both recognition memory studies we found differential patterns of activation in the hippocampus. The new, visually similar paintings evoked less activation than both the old and the new, visually different items. Moreover, activation evoked by false alarms to happy South Korean faces was stronger than activation elicited by false alarms to neutral faces, suggesting that emotional faces are more susceptible to be mistaken as familiar faces and are therefore likely to induce illusory memories. Activation in the hippocampus has been observed in various memory-related processes, including recognition memory (Stark & Squire, 2001), maintenance in working memory (Ranganath & D'Esposito, 2001), source memory (Davachi *et al.*, 2003), generation of visual images from STM (Ishai *et al.*, 2002), and explicit categorization (Reber *et al.*, 2003). Although it is currently

unclear to what extent the hippocampus mediates the recovery of true and false memory traces (Cabeza *et al.*, 2001; Slotnick & Schacter, 2004), our findings suggest that true and false memories result in differential patterns of activation within this region. It has been reported that false memory can be induced by way of visual imagery. When subjects generate mental images of objects based on a corresponding word-cue and on some trials pictures of these objects are presented after the imagery task, some words are later falsely remembered as pictures. Interestingly, these false memories are associated with more positive posterior brain potentials (Gonsalves & Paller, 2000).

Taken collectively, our recognition memory studies have shown that retrieving pictures from LTM is mediated by a distributed cortical network, where activation is modulated by the visual similarity between old and new pictures: Face- and object-responsive regions in the visual cortex store stimulus-specific representations; parietal, and prefrontal regions mediate the retrieval and classification of old and new items; and the hippocampus mediates the recovery of true memory traces.

Conclusions

Retrieving pictures from LTM is mediated by a distributed neural system that includes visual, limbic, parietal, and prefrontal regions. Cognitive factors such as memory type (short- or long-term), attention, and visual similarity modulate the neural responses within these regions. The identification of distributed patterns of activation and their effective connectivity provides useful clues for theory building, however, bridging the gap between correlational data and a theory of human memory is not trivial and remains a challenge. Although my own research was tailored to test binary oppositions, the empirical findings described here clearly demonstrate the importance of understanding and integrating large-scale fMRI data. Thus, regardless of whether mental images are 'pictorial' or 'propositional', or whether 'recollection' and 'familiarity' are independent memory processes, the wide spread patterns of activation in the human brain during memory retrieval suggest that we should pursue cortical connectivity instead of dichotomies. Cognitive theories should therefore take into account the dynamics and modulation of neural coupling among nodes in distributed networks.

In order to develop functional, testable theories that go beyond mere localization of cognitive functions, we need new cognitive models. A few years ago, Mel has written: 'The need for modeling in neuroscience is particularly intense because what most neuroscientists ultimately want to know about the brain is the model – that is, the laws governing the brain's information processing functions. The brain as an electrical system, or a chemical system, is simply not the point. In general, the model as a research tool is more important when the system under study is more complex. In the extreme case of the brain, the most complicated machine known, the importance of gathering more facts *about* the brain through empirical studies must give way to efforts to relate brain facts to each other, which requires models matched to the complexity of the brain itself.' (Mel, 2000). With the advent of brain-imaging technology and novel analytic tools, mapping higher cognitive functions is a feasible task, and better understanding of brain-imaging data would hopefully lead to the formulation of refined network models of the human brain.

Acknowledgments

The author is supported by the Swiss National Science Foundation grant 3200B0-105278 and by the Swiss National Center for Competence in Research: Neural Plasticity and Repair.

References

- Aguirre, G. K., Zarahn, E., & D'Esposito, M. (1998). An area within human ventral cortex sensitive to "building" stimuli: Evidence and implications. *Neuron*, *21*, 1–20.
- Bachevalier, J. & Mishkin, M. (1986). Visual recognition impairment follows ventromedial but not dorsolateral prefrontal lesions in monkeys. *Behavioural Brain Research*, *20*, 249–261.
- Buckner, R. L., Raichle, M. E., Miezin, F. M., & Petersen, S. E. (1996). Functional anatomic studies of memory retrieval for auditory words and visual pictures. *Journal of Neuroscience*, *16*, 6219–6235.
- Buckner, R. L. & Wheeler, M. E. (2001). The cognitive neuroscience of remembering. *Nature Reviews Neuroscience*, *2*, 624–634.
- Cabeza, R., Rao, S. M., Wagner, A. D., Mayer, A. R., & Schacter, D. L. (2001). Can medial temporal lobe regions distinguish true from false? An event-related functional MRI study of veridical and illusory recognition memory. *Proceedings of the National Academy of Sciences, USA*, *98*, 4805–4810.
- Cabeza, R., Locantore, J. K., & Anderson, N. D. (2003). Lateralization of prefrontal activity during episodic memory retrieval: evidence for the production-monitoring hypothesis. *Journal of Cognitive Neuroscience*, *15*, 249–259.
- Chao, L. L., Haxby, J. V., & Martin, A. (1999). Attribute-based neural substrates in posterior temporal cortex for perceiving and knowing about objects. *Nature Neuroscience*, *2*, 913–919.
- Chen, W., Kato, T., Zhu, X. H., Ogawa, S., Tank, D. W., & Ugurbil, K. (1998). Human primary visual cortex and lateral geniculate nucleus activation during visual imagery. *Neuroreport*, *9*, 3669–3674.
- Corbetta, M., Miezin, F. M., Dobmeyer, S., Shulman, G. L., & Petersen, S. E. (1990). Attentional modulation of neural processing of shape, color, and velocity in humans. *Science*, *248*, 1556–1559.
- Corbetta, M., Akbudak, E., Conturo, T. E., Snyder, A. Z., Ollinger, J. M., *et al.* (1998). A common network of functional areas for attention and eye movements. *Neuron*, *21*, 761–773.
- Corbetta, M., Kincade, J. M., Ollinger, J. M., McAvoy, M. P., & Shulman, G. L. (2000). Voluntary orienting is dissociated from target detection in human posterior parietal cortex. *Nature Neuroscience*, *3*, 292–297.
- Davachi, L., Mitchell, J. P., & Wagner, A. D. (2003). Multiple routes to memory: distinct medial temporal lobe processes build item and source memories. *Proceedings of the National Academy of Sciences, USA*, *100*, 2157–2162.
- Druzgal, T. J. & D'Esposito, M. (2003). Dissecting contributions of prefrontal cortex and fusiform face area to face working memory. *Journal of Cognitive Neuroscience*, *15*, 771–784.
- D'Esposito, M., Deter, J. A., Aguirre, G. K., Stallcup, M., Alsop, D. C., Tippet, L. J., & Farah, M. J. (1997). A functional MRI study of mental image generation. *Neuropsychologia*, *35*, 725–730.
- Epstein, R. & Kanwisher, N. (1998). A cortical representation of the local visual environment. *Nature*, *392*, 598–601.
- Fairhall, S. L. & Ishai, A. (2007). Effective connectivity within the distributed cortical network for face perception. *Cerebral Cortex*, *17*, 2400–2406.
- Farah, M., Peronnet, F., Gonon, M. A., & Giard, M. H. (1988). Electrophysiological evidence for a shared representational medium for visual images and visual percepts. *Journal of Experimental Psychology: General*, *117*, 248–257.
- Fletcher, P. C., Frith, C. D., Baker, S. C., Shallice, T., Frackowiak, R. S. J., & Dolan, R. J. (1995). The mind's eye – precuneus activation in memory-related imagery. *Neuroimage*, *2*, 195–200.

- Freedman, D. J., Riesenhuber, M., Poggio, T., & Miller, E. K. (2001). Categorical representation of visual stimuli in the primate prefrontal cortex. *Science*, *291*, 312–316.
- Freedman, D. J., Riesenhuber, M., Poggio, T., & Miller, E. K. (2003). A comparison of primate prefrontal and inferior temporal cortices during visual categorization. *Journal of Neuroscience*, *23*, 5235–5246.
- Friston, K. J., Harrison, L., & Penny, W. (2003). Dynamic causal modeling. *NeuroImage*, *19*(4), 1273–1302.
- Fuster, J. M. & Bauer, R. (1974). Visual short-term memory deficit from hypothermia of frontal cortex. *Brain Research*, *81*, 393–400.
- Goebel, R., Khorrarn-Sefat, D., Muckli, L., Hacker, H., & Singer, W. (1998). The constructive nature of vision: Direct evidence from functional magnetic resonance imaging studies of apparent motion and motion imagery. *European Journal of Neuroscience*, *10*, 1563–1573.
- Goldenberg, G., Poderka, I., Steiner, M., Willmes, K., Suess, E., & Deecke, L. (1989). Regional cerebral blood flow patterns in visual imagery. *Neuropsychologia*, *27*, 641–664.
- Gonsalves, B. & Paller, K. A. (2000). Neural events that underlie remembering something that never happened. *Nature Neuroscience*, *3*, 1316–1321.
- Haxby, J. V., Hoffman, E. A., & Gobbini, I. M. (2000). The distributed human neural system for face perception. *Trends in Cognitive Sciences*, *4*, 223–233.
- Haxby, J. V., Gobbini, M. I., Furey, M. L., Ishai, A., Schouten, J. L., & Pietrini, P. (2001). Distributed and overlapping representations of faces and objects in ventral temporal cortex. *Science*, *293*, 2425–2430.
- Henson, R. (2005). What can functional neuroimaging tell the experimental psychologist? *The Quarterly Journal of Experimental Psychology*, *58A*, 193–233.
- Ishai, A. & Sagi, D. (1995). Common mechanisms of visual imagery and perception. *Science*, *268*, 1772–1774.
- Ishai, A. & Sagi, D. (1997a). Visual imagery facilitates visual perception: Psychophysical evidence. *Journal of Cognitive Neuroscience*, *9*, 476–489.
- Ishai, A. & Sagi, D. (1997b). Visual imagery: Effects of short- and long-term memory. *Journal of Cognitive Neuroscience*, *9*, 734–742.
- Ishai, A., Ungerleider, L. G., Martin, A., Schouten, J. L., & Haxby, J. V. (1999). Distributed representation of objects in the human ventral visual pathway. *Proceedings National Academy of Sciences USA*, *96*, 9379–9384.
- Ishai, A., Ungerleider, L. G., Martin, A., & Haxby, J. V. (2000a). The representation of objects in the human occipital and temporal cortex. *Journal of Cognitive Neuroscience*, *12*, 35–51.
- Ishai, A., Ungerleider, L. G., & Haxby, J. V. (2000b). Distributed neural systems for the generation of visual images. *Neuron*, *28*, 979–990.
- Ishai, A., Haxby, J. V., & Ungerleider, L. G. (2002). Visual imagery of famous faces: effects of memory and attention revealed by fMRI. *NeuroImage*, *17*, 1729–1741.
- Ishai, A., Schmidt, C. F., & Boesiger, P. (2005). Face perception is mediated by a distributed cortical network. *Brain Research Bulletin*, *67*, 87–93.
- Ishai, A. & Yago, E. (2006). Recognition memory of newly learned faces. *Brain Research Bulletin*, *71*, 167–173.
- Ishai, A. & Wiesmann, M. (2007). Recollection, familiarity, and visual similarity. *Perception*, *36*(Supplement), 1001–1001,
- Kahn, I. Davachi, L., & Wagner, A. D. (2004). Functional-neuroanatomic correlates of recollection: implications for models of recognition memory. *Journal of Neuroscience*, *24*, 4172–4180.
- Kanwisher, N., McDermott, J., & Chun, M. M. (1997). The fusiform face area: A module in human extrastriate cortex specialized for face perception. *Journal of Neuroscience*, *17*, 4302–4311.

- Kastner, S., Pinsk, M. A., De Weerd, P., Desimone, R., & Ungerleider, L. G. (1999). Increased activity in human visual cortex in the absence of visual stimulation. *Neuron*, 22, 751–761.
- Kincade, J. M., Abrams, R. A., Astafiev, S. V., Shulman, G. L., & Corbetta, M. (2005). An event-related functional magnetic resonance imaging study of voluntary and stimulus-driven orienting of attention. *Journal of Neuroscience*, 25, 4593–4604.
- Konishi, S., Wheeler, M. E., Donaldson, D. I., & Buckner, R. L., (2000). Neural correlates of episodic retrieval success. *NeuroImage*, 12, 276–286.
- Kosslyn, S. M., Alpert, N. M., Thompson, W. L., Maljkovic, V., Weise, S. B., Chabris, C. F., Hamilton, S. E., Rauch, S. L., & Buonanno, F. S. (1993). Visual mental imagery activates topographically organized visual cortex: PET investigations. *Journal of Cognitive Neuroscience*, 5, 263–287.
- Kosslyn, S. M., Pascual-Leone, A., Felician, O., Camposano, S., Keenan, J. P., Thompson, W. L., Ganis, G., Sukel, K. E., & Alpert, N. M. (1999). The role of area 17 in visual imagery: Convergent evidence from PET and rTMS. *Science*, 284, 167–170.
- Kreiman, G., Koch, C., & Fried, I. (2000). Category-specific visual responses of single neurons in the human medial temporal lobe. *Nature Neuroscience*, 3, 946–953.
- Le Bihan, D., Turner, R., Zeffiro, T., Cuendo, C., Jezzard, P., & Bonnerot, V. (1993). Activation of human primary visual cortex during visual recall: A magnetic resonance imaging study. *Proceedings National Academy of Sciences USA*, 90, 11802–11805.
- Levine, D. N., Warach, J., & Farah, M. (1985). Two visual systems in mental imagery: Dissociation of “what” and “where” in imagery disorders due to bilateral posterior cerebral lesions. *Neurology*, 35, 1010–1018.
- Mechelli, A., Price, C. J., Noppeney, U., & Friston, K. J. (2003). A dynamic causal modeling study on category effects: bottom-up or top-down mediation? *Journal of Cognitive Neuroscience*, 15, 925–934.
- Mechelli, A., Price, C. J., Friston, K. J., & Ishai, A. (2004). Where bottom-up meets top-down: neuronal interactions during perception and imagery. *Cerebral Cortex*, 14, 1256–1265.
- Mel, B. W. (2000). In the brain, the model is the goal. *Nature Neuroscience*, 3, 1183.
- Mellet, E., Tzourio, N., Crivello, F., Joliot, M., Denis, M., & Mazoyer, B. (1996). Functional anatomy of spatial mental imagery generated from verbal instructions. *Journal of Neuroscience*, 16, 6504–6512.
- Mellet, E., Petit, L., Mazoyer, B., Denis, M., & Tzourio, N. (1998). Reopening the mental imagery debate: Lessons from functional anatomy. *Neuroimage*, 8, 129–139.
- Mellet, E., Tzourio-Mazoyer, N., Bricogne, S., Mazoyer, B., Kosslyn, S. M., & Denis, M. (2000). Functional anatomy of high-resolution visual mental imagery. *Journal of Cognitive Neuroscience*, 12, 98–109.
- Miller, E. K., Erickson, C. A., & Desimone, R. (1996). Neural mechanisms of visual working memory in prefrontal cortex of the macaque. *Journal of Neuroscience*, 16, 5154–5167.
- Miyashita, Y. (1988). Neural correlate of visual associative long-term memory in the primate temporal cortex. *Nature*, 335, 817–820.
- Miyashita, Y. & Chang, H. S. (1988). Neural correlate of pictorial short-term memory in the primate temporal cortex. *Nature*, 331, 68–70.
- O’Craven, K. & Kanwisher, N. (2000). Mental imagery of faces and places activates corresponding stimulus-specific brain regions. *Journal of Cognitive Neuroscience*, 12, 1013–1023.
- Pardo, J. V., Fox, P. T., & Raichle, M. E. (1990). Localization of a human system for sustained attention by positron emission tomography. *Nature*, 349, 61–64.
- Pasupathy, A. & Miller, E. K. (2005). Different time courses of learning-related activity in the prefrontal cortex and striatum. *Nature*, 433, 873–876.
- Penfield, W. & Perot, P. (1963). The brain’s record of auditory and visual experience. *Brain* 86, 595–697.

- Poldrack, R. A., Prabhakaran, V., Seger, C. A., & Gabrieli, J. D. (1999). Striatal activation during acquisition of a cognitive skill. *Neuropsychology, 13*, 564–574.
- Pollmann, S., Weidner, R., Humphreys, G. W., Olivers, C. N., Muller, K., Lohmann, G., Wiggins, C. J., & Watson, D. G. (2003). Separating distractor rejection and target detection in posterior parietal cortex – an event-related fMRI study of visual marking. *NeuroImage, 18*, 310–323.
- Ranganath, C. & D'Esposito, M. (2001). Medial temporal lobe activity associated with active maintenance of novel information. *Neuron, 31*, 865–873.
- Ranganath, C., Cohen, M. X., Dam, C., & D'Esposito, M. (2004). Inferior temporal, prefrontal, and hippocampal contributions to visual working memory maintenance and associative memory retrieval. *Journal of Neuroscience, 24*, 3917–3925.
- Ratcliff, R. (1978). A theory of memory retrieval. *Psychological Review, 85*, 59–108.
- Reber, P. J., Stark, C. E., & Squire, L. R. (1998). Contrasting cortical activity associated with category memory and recognition memory. *Learning and Memory, 5*, 420–428.
- Reber, P. J., Wong, E. C., & Buxton, R. B. (2002). Comparing the brain areas supporting nondeclarative categorization and recognition memory. *Brain Research, Cognitive Brain Research, 14*, 245–257.
- Reber, P. J., Gitelman, D. R., Parrish, T. B., & Mesulam, M. M. (2003). Dissociating explicit and implicit category knowledge with fMRI. *Journal of Cognitive Neuroscience, 15*, 574–583.
- Roland, P. E., Eriksson, L., Stone-Elander, S., & Widen, L. (1987). Does mental activity change the oxidative metabolism of the brain? *Journal of Neuroscience, 7*, 2373–2389.
- Rugg, M. D. & Wilding, E. L. (2000). Retrieval processing and episodic memory. *Trends in Cognitive Sciences, 4*, 108–115.
- Rugg, M. D., Otten, L. J., & Henson, R. N. (2002). The neural basis of episodic memory: evidence from functional neuroimaging. *Philosophical Transactions of the Royal Society of London: Series B, Biological Sciences, 357*, 1097–1110.
- Rugg, M. D. & Yonelinas, A. P. (2003). Human recognition memory: a cognitive neuroscience perspective. *Trends in Cognitive Sciences, 7*, 313–319.
- Sakai, K. & Miyashita, Y. (1994). Visual imagery: An interaction between memory retrieval and focal attention. *Trends in Neuroscience, 17*, 287–289.
- Savoy, R. (2001). History and future directions of human brain mapping and functional neuroimaging. *Acta Psychologica, 107*, 9–42.
- Seger, C. A. & Cincotta, C. M. (2002). Striatal activity in concept learning. *Cognitive, Affective and Behavioral Neuroscience, 2*, 149–161.
- Seger, C. A. & Cincotta, C. M. (2005). The roles of the caudate nucleus in human classification learning. *Journal of Neuroscience, 25*, 2941–2951.
- Shannon, B. J. & Buckner, R. L. (2004). Functional-anatomic correlates of memory retrieval that suggest nontraditional processing roles for multiple distinct regions within posterior parietal cortex. *Journal of Neuroscience, 24*, 10084–10092.
- Shulman, G. L., Ollinger, J. M., Linenweber, M., Petersen, S. E., & Corbetta, M. (2001). Multiple neural correlates of detection in the human brain. *Proceedings National Academy of Sciences USA, 98*, 313–318.
- Slotnick, S. D. & Schacter, D. L. (2004). A sensory signature that distinguishes true from false memories. *Nature Neuroscience, 7*, 664–672.
- Stark, C. E. & Squire, L. R. (2001). Simple and associative recognition memory in the hippocampal region. *Learning and Memory, 8*, 190–197.
- Ungerleider, L. G. & Mishkin, M. (1982). Two cortical visual systems. In: D.J. Ingle, M.A. Goodale, & R.J.W. Mansfield (Eds), *Analysis of Visual Behavior*. Cambridge, MA: MIT Press.
- Vogels, R., Sary, G., Dupont, P., & Orban, G. A. (2002). Human brain regions involved in visual categorization. *NeuroImage, 16*, 401–414.

- Wagner, A. D., Shannon, B. J., Kahn, I., & Buckner, R. L. (2005). Parietal lobe contributions to episodic memory retrieval. *Trends in Cognitive Sciences*, 9, 445–453.
- Wheeler, M. E., Petersen, S. E., & Buckner, R. L. (2000). Memory's echo: Vivid remembering reactivates sensory-specific cortex. *Proceedings National Academy of Sciences USA*, 97, 11125–11129.
- Wheeler, M. E., & Buckner, R. L. (2003). Functional dissociation among components of remembering: control, perceived oldness, and content. *Journal of Neuroscience*, 23, 3869–3880.
- Wojciulik, E. & Kanwisher, N. (1999). The generality of parietal involvement in visual attention. *Neuron*, 23, 747–764.
- Yago, E. & Ishai, A. (2006). Recognition memory is modulated by visual similarity. *NeuroImage*, 31, 807–817.
- Yonelinas, A. P., Otten, L. J., Shaw, K. N., & Rugg, M. D. (2005). Separating the brain regions involved in recollection and familiarity in recognition memory. *Journal of Neuroscience*, 25, 3002–3008.