The Frontal Lobes

The frontal lobes and their functional properties are recognized as crucial to establishing our identity as autonomous human beings. This book provides a broad introductory overview of this unique brain region. In an accessible and readable style it covers the evolutionary significance of the frontal lobes, typical and atypical development pathways, the role played in normal cognition, memory and emotion, and in damaged states, resulting in a range of neurological syndromes and psychiatric disturbances. The coverage integrates current theoretical knowledge with observation of the both normal and disturbed behavior across the lifespan. The result is an easy-to-read review of this fascinating and involved field suitable for graduate students in neuropsychology and psychology, clinicians from the fields of neurology, neurosurgery or psychiatry, and researchers engaged in neuroscientific investigations.

Jarl Risberg is Professor of Neuropsychology at Lund University and Head of the Neuropsychology Section at the Departments of Clinical Neuroscience and Psychology, Lund University, Lund, Sweden.

Jordan Grafman is the Chief of the Cognitive Neuroscience Section at the National Institute of Neurological Disorders and Stroke in Bethesda, USA.
Series for the International Neuropsychological Society
Sponsored by the Vivian Smith Foundation

SERIES EDITOR

Andrew Papanicolaou
Director, Division of Clinical Neurosciences
University of Texas
Houston, Texas
USA
The Frontal Lobes
Development, Function, and Pathology

Edited by
Jarl Risberg and Jordan Grafman
The frontal lobes: development, function, and pathology / Jarl Risberg and Jordan Grafman, editors.

p. cm.--(Series for the International Neuropsychological Society)
Includes bibliographical references and index.
ISBN-10: 0-521-67225-2 (pbk.)
1. Frontal lobes. I. Risberg, Jarl. II. Grafman, Jordan. III. Series.
I. Title. II. Series.
QP382.F7F758 2006
612.8'2 —dc22
2006028963
ISBN-10 0-521-67225-2 paperback
Cambridge University Press has no responsibility for the persistence or accuracy of URLs for external or third-party internet websites referred to in this publication, and does not guarantee that any content on such websites is, or will remain, accurate or appropriate.

Every effort has been made in preparing this publication to provide accurate and up-to-date information which is in accord with accepted standards and practice at the time of publication. Although case histories are drawn from actual cases, every effort has been made to disguise the identities of the individuals involved. Nevertheless, the authors, editors and publishers can make no warranties that the information contained herein is totally free of error, not least because clinical standards are constantly changing through research and regulation. The authors, editors and publishers therefore disclaim all liability for direct or consequential damages resulting from the use of material contained in this production. Readers are strongly advised to pay careful attention to information provided by the manufacturer of any drugs or equipment that they plan to use.
## Contents

### Contributors

*Contributors*

*From the series editor*  
ix

*Introduction*  
xi

1. Evolutionary aspects on the frontal lobes  
   Jarl Risberg  
   1

2. Organization of the principal pathways of prefrontal lateral, medial, and orbitofrontal cortices in primates and implications for their collaborative interaction in executive functions  
   Helen Barbas  
   21

3. Human prefrontal cortex: processes and representations  
   Jordan Grafman  
   69

4. A microcircuit model of prefrontal functions: ying and yang of reverberatory neurodynamics in cognition  
   Xiao-Jing Wang  
   92

5. Prefrontal cortex: typical and atypical development  
   Maureen Dennis  
   128

6. Case studies of focal prefrontal lesions in man  
   David W. Loring and Kimford J. Meador  
   163

7. Left prefrontal function and semantic organization during encoding and retrieval in healthy and psychiatric populations  
   J. Daniel Ragland  
   178

8. Clinical symptoms and neuropathology in organic dementing disorders affecting the frontal lobes  
   Arne Brun and Lars Gustafson  
   199

*Index*  
222
Contributors

Helen Barbas, Ph.D.
Department of Health Sciences
Boston University
635 Commonwealth Ave., #431
Boston, MA 02215
USA
Phone: 617-353-5036
Fax: 617-353-7567

Arne Brun, MD, Ph.D.
Department of Pathology
University Hospital
SE-221 85 Lund
SWEDEN
Phone: +46-46-120384

Maureen Dennis, Ph.D.
Department of Psychology
The Hospital for Sick Children
555 University Avenue
Toronto, ON M5G 1X8
CANADA
Phone: 416-813-6658
Fax: 416-813-8839

Jordan Grafman, Ph.D.
Cognitive Neuroscience Section
NINDS, NIH
Building 10; Room 5C205
10 Center Drive; MSC 1440
Bethesda, Md. 20892-1440
USA
Phone: 301-496-0220
Fax: 301-480-2909

Lars Gustafson, MD, Ph.D.
Department of Psychogeriatrics
University Hospital
SE-221 85 Lund
SWEDEN
Phone: +46-46-177450

David Loring, Ph.D.
Departments of Neurology and Clinical & Health Psychology
Center for Neuropsychological Studies
McKnight Brain Institute
University of Florida
P.O. Box 100236
Gainesville, FL 32610-0236
Phone: 352-273-5550/273-5621
<table>
<thead>
<tr>
<th>List of Contributors</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Kimford Meador, Ph.D.</strong></td>
</tr>
<tr>
<td>Departments of Neurology and Clinical &amp; Health Psychology</td>
</tr>
<tr>
<td>Center for Neuropsychological Studies</td>
</tr>
<tr>
<td>McKnight Brain Institute University of Florida</td>
</tr>
<tr>
<td>P.O. Box 100236</td>
</tr>
<tr>
<td>Gainesville, FL 32610-0236</td>
</tr>
<tr>
<td>USA</td>
</tr>
</tbody>
</table>

<table>
<thead>
<tr>
<th><strong>J. Daniel Ragland, Ph.D.</strong></th>
<th><strong>Xiao-Jing Wang, Ph.D.</strong></th>
</tr>
</thead>
<tbody>
<tr>
<td>Imaging Research Center</td>
<td>Department of Neurobiology and Kavli Institute for Neuroscience</td>
</tr>
<tr>
<td>University of California at Davis</td>
<td>Yale University School of Medicine</td>
</tr>
<tr>
<td>4701 X Street</td>
<td>333 Cedar Street</td>
</tr>
<tr>
<td>Sacramento, CA 95817</td>
<td>New Haven, CT 06510</td>
</tr>
<tr>
<td>USA</td>
<td>Phone: 916-734-3230</td>
</tr>
<tr>
<td></td>
<td>Fax: 916-734-8750</td>
</tr>
</tbody>
</table>
From the series editor

This volume inaugurates a collection of books on topics of current interest in neuropsychology and systems neuroscience. The series is a natural extension of the annual Advanced Studies Institute, which operates under the auspices of the International Neuropsychological Society (INS) with the support of the Vivian L. Smith Foundation of Houston, Texas.

The purposes of the Institute and of the book series are to promote dissemination of knowledge in the fields of systems neurosciences and clinical neuropsychology; to promote the formation of professional bonds among current and future leaders in these fields from across the world; to encourage in-depth study of fundamental issues and evaluation of current advances in these fields, and to seek solutions to unresolved problems under conditions designed to optimize the efficiency of the above named endeavors. This series will, we hope, extend this message to the academic and professional community at large.

In my capacity as organizer and director of the Institute and editor of this series, I wish to express my indebtedness to the president and board of the Vivian L. Smith Foundation of Houston for their abiding support, to the secretary of the INS and to the succession of its board members and presidents since the inception of these projects, for embracing them, to Drs Jarl Risberg and Jordan Grafman who graciously volunteered to edit the present volume and to all the friends and colleagues who contributed its excellent chapters.

I also wish to thank Dr. Marcia Barnes who is editing the second volume of the series focusing on issues of mental retardation, as well as Drs Linas Bieliauskas and Kenneth Adams who have volunteered to prepare the third volume on Neuropsychology Across the Life Span.

Andrew C. Papanicolaou
Houston, February 2006
Introduction

The frontal lobes are crucial to understanding our identity as autonomous beings and this significance is now reflected in the number and importance of neuropsychological, biological, and philosophical papers and books on the functions of the frontal lobes published over the last 40 years. This research effort has identified many of the functional properties of the frontal lobes but there are still numerous unsolved problems and controversies regarding its evolutionary, biological and functional status. Based on the theme of the International Neuropsychological Society’s (INS) Summer Institute, this volume reviews this fascinating area of study. The Director of the Vivian Smith Advanced Studies Institute of the INS, Professor Andrew Papanicolaou, presents the background of the Institute in his foreword to this volume. He is also the editor of this new series of INS books starting with the present volume.

As the editors of this first book in the series, we are very proud to introduce you to the contents of the volume with the admittedly broad title The Frontal Lobes: Development, Function, and Pathology. While our volume does not cover every detailed aspect of this theme, we hope that the eight chapters will offer everyone interested in the frontal lobes an overview and some new and intriguing insights. The book is intended for graduate students in psychology and neuropsychology, as well as postdoctoral fellows and faculty members in departments of psychology, psychiatry, neurology, and related fields. The content of the volume should be of value to both practicing clinicians, who see patients with frontal disturbances, and to scientists engaged in neuroscience research.

The first chapter is written by one of the editors (Jarl Risberg) and is entitled Evolutionary Aspects on the Frontal Lobes. The chapter gives an introduction to the fascinating story about the evolution of the human brain and especially of its frontal lobes. Special focus is on the development of modern behavior and mental abilities like symbolic language and creative thinking. Disadvantages linked to the dangers and demands of a large size brain are also dealt with and
the anatomical differences between the human brain and that of our close relatives, the African great apes, are discussed. Our still very limited knowledge about what changes in the human genome made it possible to develop modern behavior is summarized. The chapter ends by viewing two very old and specifically human mental disturbances, schizophrenia and attention deficit hyperactivity disorder, from an evolutionary perspective.

The second chapter is authored by Helen Barbas and has the title *Organization of the Principal Pathways of Prefrontal Lateral, Medial, and Orbifrontal Cortices in Primates and Implications for their Collaborative Interaction in Executive Functions*. This chapter describes how the prefrontal cortex in primates guides by selecting relevant information, disregarding irrelevant information, and accessing motor control systems for action. Evidence is explored indicating that highly organized pathways link distinct prefrontal sectors with structures underlying sensory perception, cognition, and emotions. The topographically ordered pathways show consistent patterns in their laminar organization and interface with excitatory and inhibitory brain systems. The chapter ends by discussing how different sectors of the prefrontal cortex communicate with each other, inextricably linking pathways associated with cognition and emotions that guide actions.

The third chapter *Human Prefrontal Cortex: Processes and Representations* is written by the other editor of this volume (Jordan Grafman), and has its focus on what strategies you can use when characterizing the functions of the human prefrontal cortex like language, abstract reasoning, problem solving, social interactions, planning, action generation, and self-recognition. Five criteria that a theory should meet if it is to provide a useful framework for understanding the functions of the prefrontal cortex are described. An overview of the key theories about the function of the prefrontal cortex is given and their ability to stand critical experimental testing is evaluated. The main claims of each key theory are specified and a review of data addressing these claims is given. Theories that take a processing approach as well as theories that take a representational approach are discussed and evaluated.

The fourth chapter, entitled *A Microcircuit Model of Prefrontal Functions: Ying and Yang of Reverberatory Neurodynamics in Cognition*, is written by Xiao-Jing Wang. This chapter introduces the basic concepts and methods in computational neuroscience, develops intuitions about complex and recurrent circuits, and discusses biologically based models for working memory and other cognitive functions of the frontal lobes. Theories of simple and complex networks are described together with the use of these concepts for characterizing the connectivity of the frontal lobes. Behavioral data and mathematical models of working memory and task switching are also covered. The chapter ends by showing how
modeling results shed insights into the cellular/circuit basis of cognitive impairments in mental diseases like schizophrenia.

The fifth chapter, written by Maureen Dennis, is entitled *Prefrontal Cortex: Typical and Atypical Development*. This chapter provides a review of the typical development of the frontal lobes with respect to brain microstructure, brain macrostructure, and functions such as working memory, inhibitory control, intentionality, and social cognition. The atypical development of the frontal lobes in children with congenital or acquired neurodevelopmental disturbances is also covered focusing on disturbances of working memory, inhibition, theory of mind, and social comportment and the theoretical implications of these disturbances. The emphasis is on how these early disturbances impact subsequent maturation and development of the frontal lobes.

The sixth chapter is authored by David Loring and Kimford Meador and entitled *Case Studies of Focal Prefrontal Lesions in Man*. The chapter starts with an introduction to the history of clinical neuropsychology and continues with a review of some classical as well as some more recent case studies of frontally damaged patients. A detailed account of the Phineas Gage story is given followed by the case KM, described by Donald Hebb and coworkers. The patent EVR, described by Eslinger and Damasio, is then reviewed as well as patients displaying utilization as described by Lhermitte. Finally the impact of early prefrontal injury is illustrated.

The seventh chapter is authored by Daniel Ragland and has the title *Left Prefrontal Function and Semantic Organization during Encoding and Retrieval in Healthy and Psychiatric Populations*. The chapter begins with definitions of episodic and declarative memory and an overview of the role that the prefrontal cortex plays in these forms of long-term memory. The focus then narrows to the function of semantic organization, with an explication of how semantic organizational processes facilitate word encoding and retrieval in healthy subjects. This explication includes neuropsychological data showing how semantic organization improves performance, and neuroimaging data demonstrating the role of left prefrontal cortex. Schizophrenia is then introduced to illustrate how prefrontal dysfunction caused by a psychiatric illness can impact these same memory functions. Finally, levels-of-processing data are presented to demonstrate that memory performance and left prefrontal function can be normalized when patients are provided with organizational strategies.

The final and eighth chapter is authored by Arne Brun and Lars Gustafson and has the title *Clinical Symptoms and Neuropathology in Organic Dementing Disorders Affecting the Frontal Lobes*. In this chapter the authors offer some possible explanations for why the frontal lobes are such frequent targets for a variety of damaging processes. This is followed by a discussion of some general
mechanisms of importance for understanding the relationship between symptoms and brain changes. The authors conclude their chapter with a description of neuropathological findings and clinical symptoms in some of the most common dementing disorders affecting the frontal lobes: frontotemporal dementia forms, Alzheimer’s disease with frontal lobe symptoms, Huntington’s disease, and vascular dementia with frontal features.

We wish to thank all the chapter authors for participating in the Xylocastro INS Summer Institute and for their dedication to studying the functions of the frontal lobes. We also hope that the book will stimulate your frontal lobes and entice you to join us in exploring its many mysteries.

Jarl Risberg and Jordan Grafman