Wiley-Blackwell Handbooks of Behavioral Neuroscience

The Handbook of Alzheimer's Disease and Other Dementias

Andrew E. Budson and Neil W. Kowall

WILEY-BLACKWELL

The Handbook of Alzheimer's Disease and Other Dementias

Edited by Andrew E. Budson and Neil W. Kowall

WILEY-BLACKWELL
A John Wiley & Sons, Ltd., Publication

This edition first published 2011

Blackwell Publishing was acquired by John Wiley & Sons in February 2007. Blackwell's publishing program has been merged with Wiley's global Scientific, Technical, and Medical business to form Wiley-Blackwell.

Registered Office
John Wiley & Sons Ltd, The Atrium, Southern Gate, Chichester, West Sussex, PO19 8SQ, UK

Editorial Offices
350 Main Street, Malden, MA 02148-5020, USA

9600 Garsington Road, Oxford, OX4 2DQ, UK

The Atrium, Southern Gate, Chichester, West Sussex, PO19 8SQ, UK

For details of our global editorial offices, for customer services, and for information about how to apply for permission to reuse the copyright material in this book please see our website at www.wiley.com/wiley-blackwell.

Library of Congress Cataloging-in-Publication Data

The handbook of Alzheimer's disease and other dementias / edited by Andrew E. Budson and Neil W. Kowall.
p. ; cm. – (Wiley-Blackwell handbooks of behavioral neuroscience)
Includes bibliographical references and index.
ISBN 978-1-4051-6828-1 (hardcover : alk. paper)
1. Dementia. I. Budson, Andrew E. II. Kowall, Neil W. III. Series: Wiley-Blackwell handbooks of behavioral neuroscience.
[DNLM: 1. Dementia. WM 220]
RC521.H34 2011
616.8'3–dc22

2011010575

A catalogue record for this book is available from the British Library.

This book is published in the following electronic formats: ePDFs 9781444344080; Wiley Online Library 9781444344103; ePub 9781444344097
Set in 10.5/13 pt Minion by Toppan Best-set Premedia Limited
Printed and bound in Singapore by Markono Print Media Pte Ltd

1 2011

The Handbook of Alzheimer's Disease and Other Dementias

Wiley-Blackwell Handbooks of Behavioral Neuroscience

The rapidly expanding field of behavioral neuroscience examines neurobiological aspects of behavior, utilizing techniques from molecular biology, neuropsychology, and psychology. This series of handbooks provides a cutting-edge overview of classic research, current scholarship, and future trends in behavioral neuroscience. The series provides a survey of representative topics in this field, suggesting implications for basic research and clinical applications.

Series editor: David Mostofsky, Boston University

The Handbook of Stress: Neuropsychological Effects on the Brain
Edited by Cheryl D. Conrad

The Handbook of Alzheimer's Disease and Other Dementias
Edited by Andrew E. Budson and Neil W. Kowall

The Handbook of the Neuropsychology of Language (2 Volumes)
Edited by Miriam Faust

We wish to dedicate this book to our families:

Amy, Leah, and Danny

And

Miriam, Elisheva, Charlotte, Jenny, Mischa, and Jonah

Contributors

Carmela R. Abraham Department of Biochemistry & Alzheimer's Disease Center, Boston University School of Medicine, Boston, MA, USA

Brandon A. Ally Departments of Neurology, Psychiatry, and Psychology, Vanderbilt University, Nashville, TN, USA

Stacy L. Andersen New England Centenarian Study, Boston University School of Medicine, Boston, MA USA

Adam L. Boxer Memory and Aging Center, Department of Neurology, University of California, San Francisco, CA, USA

Marina Boziki 3rd Department of Neurology, Aristotle University of Thessaloniki, Greece

Andrew E. Budson Department of Neurology & Alzheimer's Disease Center, Boston University School of Medicine, Boston, MA, USA; Center for Translational Cognitive Neuroscience and Geriatric Research Education Clinical Center, VA Boston Healthcare System, Boston, MA, USA; Memory Disorders Unit, Division of Cognitive and Behavioral Neurology, Department of Neurology, Brigham & Women's Hospital, Boston, MA, USA; Harvard Medical School, Boston, MA, USA

Alice Cronin-Golomb Department of Psychology, Boston University, Boston, MA, USA

Bradford C. Dickerson Department of Neurology, Athinoula A. Martinos Center for Biomedical Imaging, and the Alzheimer's Disease Research Center, Massachusetts General Hospital, Boston, MA, USA; Memory Disorders Unit, Division of Cognitive and Behavioral Neurology, Department of Neurology, Brigham & Women's Hospital, Boston, MA, USA; Harvard Medical School, Boston, MA, USA

Tamara G. Fong Aging Brain Center, Hebrew SeniorLife, Boston, MA. USA; Department of Neurology, Beth Israel Deaconess Medical Center, Boston, MA. USA; Harvard Medical School, Boston, MA. USA

Brandon E. Gavett Department of Neurology & Alzheimer's Disease Center, Boston University School of Medicine, Boston, MA, USA

Amanda M. Gentile Department of Neurology & Alzheimer's Disease Center, Boston University School of Medicine, Boston, MA, USA

Robert C. Green Division of Genetics, Department of Medicine, Brigham and Women's Hospital, Boston, MA. USA; Harvard Medical School, Boston, MA. USA

Murray Grossman Department of Neurology, University of Pennsylvania School of Medicine, Philadelphia, PA, USA

David G. Harper Department of Psychiatry, Harvard Medical School, Boston, MA, USA; Department of Psychology, McLean Hospital, Belmont, MA, USA

Paul Hollingworth Medical Research Council (MRC) Centre for Neuropsychiatric Genetics and Genomics, Department of Psychological Medicine and Neurology, School of Medicine, Cardiff University, Cardiff, UK

Angela L. Jefferson Department of Neurology & Alzheimer's Disease Center, Boston University School of Medicine, Boston, MA, USA

Ravi Kahlon Department of Neurology & Alzheimer's Disease Center, Boston University School of Medicine, Boston, MA, USA

Ronald J. Killiany Department of Anatomy and Neurobiology, Laboratory for Cognitive Neurobiology, Center for Biomedical Imaging, Boston University School of Medicine, Boston, MA, USA

Neil W. Kowall Departments of Neurology and Pathology & Alzheimer's Disease Center, Boston University School of Medicine, Boston, MA, USA; Neurology Service and Geriatric Research Education Clinical Center, VA Boston Healthcare System, Boston, MA, USA; Harvard Medical School, Boston, MA, USA

Alan M. Mandell Departments of Neurology and Psychiatry, and Alzheimer's Disease Center, Boston University School of Medicine, Boston, MA, USA; Geriatric Research Education Clinical Center, Bedford VA Hospital, Bedford, MA, USA

Ann C. McKee Departments of Neurology and Pathology, Alzheimer's Disease Center, Boston University School of Medicine, Boston, MA, USA; Geriatric Research Education Clinical Center, Bedford VA Hospital, Bedford, MA, USA

Peter J. Morin Department of Neurology & Alzheimer's Disease Center, Boston University School of Medicine, Boston, MA, USA; Geriatric Research Education Clinical Center, Bedford VA Hospital, Bedford, MA, USA

Vassilis Papaliagkas 3rd Department of Neurology, Aristotle University of Thessaloniki, Greece

Maija Pihlajamäki Department of Neurology, Kuopio University Hospital, Kuopio, Finland

Daniel Z. Press Department of Neurology, Beth Israel Deaconess Medical Center, Boston, MA, USA; Harvard Medical School, Boston, MA, USA

Jamie Reilly Department of Speech, Language, and Hearing Sciences, University of Florida, Gainesville, FL, USA

Reisa A. Sperling Department of Neurology, Brigham and Women's Hospital, Boston, MA, USA; Harvard Medical School, Boston, MA, USA

Robert A. Stern Department of Neurology & Alzheimer's Disease Center, Boston University School of Medicine, Boston, MA, USA

Joshua Troche Department of Speech, Language, and Hearing Sciences, University of Florida, Gainesville, FL, USA

Magda Tsolaki 3rd Department of Neurology, Aristotle University of Thessaloniki, Greece

Julie Williams Medical Research Council (MRC) Centre for Neuropsychiatric Genetics and Genomics, Department of Psychological Medicine and Neurology, School of Medicine, Cardiff University, Cardiff, UK

Christopher I. Wright Laboratory of Aging and Emotion, Department of Psychiatry, Athinoula A. Martinos Center for Biomedical Imaging, Massachusetts General Hospital, Charlestown, MA, USA; Division of Cognitive and Behavioral Neurology, Department of Neurology, Brigham and Women's Hospital, Boston, MA, USA; Harvard Medical School, Boston, MA, USA

Foreword

In 1903, Emil Kraeplin recruited Alois Alzheimer to join his department at the Nervenklinik in Munich. Kraeplin challenged Alzheimer, who was known for his clinical and pathological research, to uncover the biological basis of mental illness. In 1906, Alzheimer hit pay dirt, when he described the neuritic plaques and neurofibrillary tangles in the brain of Auguste D., his 53-year-old patient with dementia. Alzheimer's presentation at the 37th Assembly of Southwest German Psychiatrists in Tubingen apparently generated very little interest from the attendees, who included such prominent figures as Nissl, Jung, and Binswanger; the *Tubinger Chronik* newspaper carried a single line on the case in reporting the meeting. Kraeplin's influential textbook eventually accepted this condition of pre-senile dementia and proposed the name Alzheimer's disease. Growing from this single case report, Alzheimer's disease is now widely recognized as one of the most common neurological diseases, but it was not always so.

Between 1906 and 1966, there was very little clinical or research interest in Alzheimer's disease as it was widely viewed as a rare form of pre-senile dementia. Neurology textbooks rarely allotted it more than a page or two, there were only a handful of papers published in the literature, and almost nothing heard at the annual neurology meetings.

Interest began to pick up with Sir Martin Roth's report in 1966 that neuritic plaques occurred in brains of the elderly, and that their number roughly correlated with the extent of dementia severity. In 1976, Robert Katzman's seminal article on the epidemiology of Alzheimer's disease stressed that pre-senile and senile dementia were similar pathologically. His conclusion that we faced a silent epidemic of staggering proportions was a stunning wake-up call to action. Three other events occurred in the 1970s that catalyzed the modern era wave of clinical and scientific research into the causes, mechanisms, and treatment of Alzheimer's disease and related dementias. The first of these was establishing the National Institute on Aging at the National Institutes of Health, and the strategic plan for Alzheimer's

disease under the direction of the Institute's first director, Robert Butler and the associate director Zaven Khachaturian. This Institute cast Alzheimer's disease as a priority on the national health stage, and provided federal funds for research. The second important step was led by Jerry Stone, who founded the Alzheimer's Disease and Related Disorders Association (now renamed the Alzheimer's Association). This private foundation spread from its base in Chicago to establish chapters across the country dedicated to raising awareness about Alzheimer's disease and raising money to support research. The third event was a scientific breakthrough: Indices of acetylcholine metabolism, a neurotransmitter in the brain linked to memory capacities, were decreased in brains of patients with Alzheimer's disease. This advance was crucial because it opened a new approach to Alzheimer's disease that justified expenditure of public and private dollars for research. Further, this discovery sparked hope for a cure because drugs can be developed that alter the neurochemical milieu of the brain, whereas the anatomic pathological features of Alzheimer's disease – the neuritic plaques and tangles – have always seemed immutably fixed. Indeed, this discovery paved the way for developing acetylcholinesterase inhibitors, the first class of drugs approved by the FDA for treating Alzheimer's disease. In 1984, the first clinical criteria for the diagnosis of Alzheimer's disease was published, and the first five Alzheimer's Disease Research Centers were established with funding from the National Institute on Aging. These Centers, which now number 30 across the United States, are the focal point for much of the clinical and scientific research conducted on Alzheimer's disease. This volume highlights many of the advances generated by investigators in these Centers and underscores the multidisciplinary approach in clinical science that is the hallmark of modern dementia research.

Alzheimer's disease is the most prevalent cause of dementia, but not the only cause. Dementia due to multiple strokes has always been appreciated, but clinicians now routinely diagnose degenerative conditions such as frontal temporal dementia and diffuse Lewy body disease that were previously lumped with Alzheimer's disease. As pointed out in chapters of this volume, these related neurodegenerative diseases have clinical and neuropsychological features that aid in the diagnosis and that distinguish them from Alzheimer's disease. In this sense, the field of cognitive neuroscience has improved the diagnosis of dementia syndromes; in turn, the study of neurodegenerative diseases has helped boost neuropsychological research. Neuroimaging also helps distinguish Alzheimer's disease, frontal temporal dementia, and dementia with Lewy bodies, as brain scans in each of these conditions have a typical anatomic, functional and molecular signature. Their separate identities are reinforced by neuropathological findings that confirm the clinical diagnoses, and that also drive scientific research into the causes of each disease. Advances in this area now permit molecular classification of diseases due to accumulation of misfolded proteins in brain that are distinctive for each condition. Thus, we speak of Alzheimer's disease as an "amyloidopathy"; some cases of frontal temporal dementia as a "tauopathy"; and dementia with Lewy bodies as an "alpha-syncleinopathy." Uncovering the molecular signature of these diseases is as

important to the field now as the discovery of acetylcholine deficiency was in the 1970s, as research into the cellular mechanisms leading to accumulation of toxic protein fragments may hold the key to developing protective and even curative therapies.

John H. Growdon, M.D.
Professor of Neurology, Harvard Medical School
Massachusetts Alzheimer's Disease Research Center
Massachusetts General Hospital, Boston, MA USA

Preface

This book provides a comprehensive review of Alzheimer's disease and other dementias from both basic and clinical neuroscience perspectives. Scientists and medical professionals will find both a broad introduction and an up-to-date review of important scientific advances in a single volume. Those working in the areas of Alzheimer's disease and dementia will find this book of interest, including physicians, medical students, psychologists, scientists, graduate students, and allied health professionals including nurses, social workers, and therapists. Part I, "Common Dementias," is designed to provide an overview of Alzheimer's disease and other dementias including a brief discussion of pathology, pathophysiology, clinical manifestations, diagnosis, and treatment. It also provides background for later chapters. Part II, "Pathogenesis and Disease Mechanisms," provides an update on the current genetic risk factors and pathophysiological mechanisms related to dementia. Part III, "Cognitive and Behavioral Dysfunction," reviews the disruption of different cognitive and other functions, including emotion and sleep. Part IV, "Neuroimaging in Dementia," provides an update on this exciting and fast-paced field. The book is designed such that readers can either peruse a chapter of interest or read the book cover to cover. In either case, we believe that you will find this book a useful tool for school, research, or clinical practice.

We would like to thank all of our authors for their excellent contributions and the series editor Professor Mostofsky for his constant encouragement. It is they who deserve the credit for the value in this book; any errors contained herein are our fault alone. Lastly, we would like to note that this book was completed entirely on our own time, during late nights, early mornings, weekends, and vacations.

Andrew E. Budson and Neil W. Kowall
Boston MA

Acknowledgments: Preparation of this book was supported, in part, by P30-AG13846 (Boston University Alzheimer's Disease Core Center) and the Department of Veterans Affairs GRECC program and Research Service.

Contents

Part I
Common Dementias