

Springer Series in Translational Stroke Research

Selva Baltan
S. Thomas Carmichael
Carlos Matute
Guohua Xi
John H Zhang *Editors*

White Matter Injury in Stroke and CNS Disease

 Springer

Springer Series in Translational Stroke Research

Selva Baltan
S. Thomas Carmichael
Carlos Matute
Guohua Xi
John H Zhang *Editors*

White Matter Injury in Stroke and CNS Disease

 Springer

Springer Series in Translational Stroke Research

Series Editor

John Zhang

For further volumes:

<http://www.springer.com/series/10064>

Selva Baltan • S. Thomas Carmichael
Carlos Matute • Guohua Xi • John H Zhang
Editors

White Matter Injury in Stroke and CNS Disease

 Springer

Editors

Selva Baltan
Department of Neurosciences
Cleveland Clinic Lerner Research Institute
Cleveland, OH, USA

S. Thomas Carmichael
Department of Neurology
University of California, Los Angeles
Los Angeles, CA, USA

Carlos Matute
Departamento de Neurociencias, Achucarro
Basque Center for Neuroscience,
Universidad del País Vasco (UPV/EHU),
and Centro de, Investigación Biomédica
en Red en
Enfermedades Neurodegenerativas
(CIBERNED), Leioa, Spain

Guohua Xi
Department of Neurosurgery
University of Michigan
Ann Arbor, MI, USA

John H Zhang
Department of Physiology
Loma Linda University
Loma Linda, CA, USA

ISBN 978-1-4614-9122-4

ISBN 978-1-4614-9123-1 (eBook)

DOI 10.1007/978-1-4614-9123-1

Springer New York Heidelberg Dordrecht London

Library of Congress Control Number: 2013953313

© Springer Science+Business Media New York 2014

This work is subject to copyright. All rights are reserved by the Publisher, whether the whole or part of the material is concerned, specifically the rights of translation, reprinting, reuse of illustrations, recitation, broadcasting, reproduction on microfilms or in any other physical way, and transmission or information storage and retrieval, electronic adaptation, computer software, or by similar or dissimilar methodology now known or hereafter developed. Exempted from this legal reservation are brief excerpts in connection with reviews or scholarly analysis or material supplied specifically for the purpose of being entered and executed on a computer system, for exclusive use by the purchaser of the work. Duplication of this publication or parts thereof is permitted only under the provisions of the Copyright Law of the Publisher's location, in its current version, and permission for use must always be obtained from Springer. Permissions for use may be obtained through RightsLink at the Copyright Clearance Center. Violations are liable to prosecution under the respective Copyright Law.

The use of general descriptive names, registered names, trademarks, service marks, etc. in this publication does not imply, even in the absence of a specific statement, that such names are exempt from the relevant protective laws and regulations and therefore free for general use.

While the advice and information in this book are believed to be true and accurate at the date of publication, neither the authors nor the editors nor the publisher can accept any legal responsibility for any errors or omissions that may be made. The publisher makes no warranty, express or implied, with respect to the material contained herein.

Printed on acid-free paper

Springer is part of Springer Science+Business Media (www.springer.com)

Preface

Studies of cerebral white matter are arguably the stepchild of the neurobiology of disease. Accounting for over half the brain volume of the adult human, it would be surprising if cerebral white matter structure was not intimately involved in disease progression for most neurological disorders of the brain. Yet the learned reader of the scientific literature might justifiably conclude that brain insults affect neurons, and that neuronal protection and repair should be the main targets for translational neuroscience.

The field of white matter biology and disease is emerging to fill this scientific void. Fueled by new imaging modalities, molecular tools and cellular and animal models, studies of white matter development, injury, and repair are beginning to generate new concepts of disease progression in Alzheimer's disease, new descriptions and biomarkers of axonal pathology in traumatic brain injury and stroke, and a more detailed understanding of white matter health in normal aging. The chapters in this book explore these new developments in each of these categories: normal white matter structure and imaging; developmental white matter injury and its unique anatomical and temporal profile; progressive white matter degeneration as a major component of Alzheimer's disease and, surprisingly, normal aging; white matter energy dynamics, axonal support, and ischemic injury; acute structural white matter insults in stroke and head trauma; and progressive white matter injury in toxic exposures.

Neuroscience is a field driven by technology. Our emerging understanding of white matter health, disease, and repair is no exception to this principle. Chapters in this book review the MRI sequences that have provided structural insight into white matter tracts, such as diffusion tensor imaging, high angular resolution MRI, NMR spectroscopy, and their combination in multimodal MRI in humans and preclinical models. These approaches clearly provide indices of white matter structure in ischemia, head injury, and neurodegenerative diseases and might provide biomarkers for clinical stratification of patients for treatment.

One of the most important areas of study in white matter disease is the field of white matter progenitor biology. The most abundant progenitor cell in the brain, the

oligodendrocyte progenitor cell (OPC), is a card-carrying member of the white matter club. Originally and literally described as a precursor to mature oligodendrocytes, these cells have in fact a far more complicated biology, with multipotent potential to differentiate into neurons, with an ability to form synapses, and a capacity to recognize injury, migrate, and participate in scar formation (the “reactive OPC”). These principles are reviewed and the tools necessary for detailed study of the OPC are discussed.

Though it is tempting in the Preface to this book to push the “white matter-centric” view far so as to draw out distinct and neglected biological principles of CNS disease, the study of white matter injury reaches its most important points when integrated back into a more whole neurobiology of disease. Several principles discussed in these chapters illustrate this point. At a system’s level, in Alzheimer’s disease the integrated function of white matter tracts and overlying neuronal areas are key to understanding disease progression. On a cellular level the myelinated axon interacts with its neighboring oligodendrocyte to form an axoglial unit. This unit interconnects metabolic shuttling, cell-adhesion signals, and triggers compartmentalization in both the axon and its nodes with the oligodendrocyte that is key to normal signal propagation. In traumatic brain injury, stroke, periventricular leukomalacia, and other brain injuries the axoglial unit is disturbed, and this can be progressive even after the initial insult is completed. These points are clearly made throughout this book.

If the Preface as a beginning is anything it leads into the chapters and then beyond, in this case to the more robust study of white matter structure, function, disorder and recovery. The latest tools for this journey are described, from genetic cellular fate-mapping to MRI imaging and network analysis. New principles are set, and these now need future examination, such as the cognitive dysfunction of aging, acute injury, and progression; white matter progenitor biology and tissue repair; and subcellular energy dynamics and signaling. The reader, like the editors and authors before him, is set on this journey. A more famous beginning lead into a journey and an examination of the principles beyond, "Somewhere in La Mancha, in a place whose name I do not care to remember, a gentleman lived not long ago, one of those who has a lance and ancient shield on a shelf and keeps a skinny nag and a greyhound for racing." With a relatively new conception of the importance and role of white matter disease it is time to lower the lance and charge.

Cleveland, OH, USA
 Los Angeles, CA, USA
 Leioa, Spain
 Ann Arbor, MI, USA
 Loma Linda, CA, USA

Selva Baltan
 S. Thomas Carmichael
 Carlos Matute
 Guohua Xi
 John H Zhang

Contents

Part I White Matter and Evaluation

1 White Matter: Basic Principles of Axonal Organization and Function	3
Alexander Velumian and Marina Samoilova	
2 White Matter Injury and Potential Treatment in Ischemic Stroke	39
Mingke Song, Anna Woodbury, and Shan Ping Yu	
3 CADASIL and Animal Models	53
Francesco Blasi, Anand Viswanathan, and Cenk Ayata	
4 Neuroimaging of White Matter Injury: A Multimodal Approach to Vascular Disease	67
Gary A. Rosenberg, Branko Huisa, Fakhreya Y. Jalal, and Yi Yang	
5 Diffusion MRI Biomarkers of White Matter Damage in Traumatic Brain Injury	91
Maria Ly, Samuel Ji, and Michael A. Yassa	

Part II White Matter Injury in Stroke and Other CNS Disorders

6 Mechanisms Underlying the Selective Vulnerability of Developing Human White Matter	109
Paul A. Rosenberg	
7 Neonatal Experimental White Matter Injury	143
Zhengwei Cai	
8 Focal Ischemic White Matter Injury in Experimental Models	169
Robert Fern	

9	White Matter Injury in Global Cerebral Ischemia	181
	Shinichi Nakao and Yan Xu	
10	Experimental Global Ischemia and White Matter Injury	197
	Ji Hae Seo, Kazuhide Hayakawa, Nobukazu Miyamoto, Takakuni Maki, Loc-Duyen D. Pham, Eng H. Lo, and Ken Arai	
11	White Matter Injury After Experimental Intracerebral Hemorrhage	219
	Kenneth R. Wagner	
12	White Matter Repair in Subcortical Stroke	257
	Elif G. Sözmen and S. Thomas Carmichael	
13	White Matter Injury in Subarachnoid Hemorrhage in Humans	271
	Gian Marco De Marchis and Stephan A. Mayer	
14	Degenerative Brain Diseases and White Matter Injury	281
	George Bartzokis and Po H. Lu	
15	Unmyelinated and Myelinated Axons Exhibit Differential Injury and Treatment Responses Following Traumatic Injury	321
	Thomas M. Reeves, Adele E. Doperalski, and Linda L. Phillips	
16	Age-Dependent Mechanisms of White Matter Injury After Stroke	373
	Selva Baltan	
17	White Matter Damage in Multiple Sclerosis	405
	María Victoria Sánchez-Gómez, Fernando Pérez-Cerdá, and Carlos Matute	
Part III Pathophysiology of White Matter Injury		
18	Calcium Dyshomeostasis in White Matter Injury	433
	Elena Alberdi, Asier Ruiz, and Carlos Matute	
19	Inflammation and White Matter Injury in Animal Models of Ischemic Stroke	461
	Lyanne C. Schlichter, Sarah Hutchings, and Starlee Lively	
20	Oxidative Stress in White Matter Injury	505
	Hideyuki Yoshioka, Takuma Wakai, Hiroyuki Kinouchi, and Pak H. Chan	

21 Acute Axonal Injury in White Matter Stroke 521
Jason D. Hinman and S. Thomas Carmichael

Part IV Other White Matter Injuries

**22 The Interplay Between White Matter, Mitochondria,
and Neuroprotection** 539
R. Anne Stetler, Rehana K. Leak, Zheng Jing,
Xiaoming Hu, Yanqin Gao, Guodong Cao, and Jun Chen

23 Heavy Metals and White Matter Injury 555
Yang V. Li

24 Anesthesia and White Matter Injury 571
Phillip Vlisides and Zhongcong Xie

About the Editors 585

Index 589

Contributors

Elena Alberdi Departamento de Neurociencias, Achucarro Basque Center for Neuroscience, Universidad del País Vasco (UPV/EHU), Leioa, Spain

Centro de Investigación Biomédica en Red en Enfermedades Neurodegenerativas (CIBERNED), Leioa, Spain

Ken Arai Neuroprotection Research Laboratory, Departments of Radiology and Neurology, Massachusetts General Hospital/Harvard Medical School, Charlestown, MA, USA

Cenk Ayata, M.D. Neurovascular Research Laboratory, Department of Radiology, Massachusetts General Hospital, Harvard Medical School, Boston, MA, USA

Stroke Service and Neuroscience Intensive Care Unit, Department of Neurology, Massachusetts General Hospital, Harvard Medical School, Boston, MA, USA

Selva Baltan Department of Neurosciences, Cleveland Clinic Lerner Research Institute, Cleveland, OH, USA

George Bartzokis, M.D. Department of Psychiatry, Semel Institute for Neuroscience and Human Behavior, The David Geffen School of Medicine at UCLA, Los Angeles, CA, USA

Greater Los Angeles VA Healthcare System, West Los Angeles, CA, USA

Francesco Blasi, Pharm.D., Ph.D. Neurovascular Research Laboratory, Department of Radiology, Massachusetts General Hospital, Harvard Medical School, Boston, MA, USA

Zhengwei Cai, Ph.D. Department of Pediatrics, University of Mississippi Medical Center, Jackson, MS, USA

Guodong Cao, Ph.D. Department of Neurology and Center of Cerebrovascular Disease Research, University of Pittsburgh School of Medicine, Pittsburgh, PA, USA

State Key Laboratory of Medical Neurobiology and Institute of Brain Sciences, Fudan University Shanghai Medical College, Shanghai, China

Geriatric Research, Educational and Clinical Center, Veterans Affairs Pittsburgh Health Care System, Pittsburgh, PA, USA

S. Thomas Carmichael, M.D. Department of Neurology, University of California, Los Angeles, Los Angeles, CA, USA

Pak H. Chan, Ph.D. Department of Neurosurgery, Stanford University School of Medicine, Stanford, CA, USA

Department of Neurology and Neurological Sciences, Stanford University School of Medicine, Stanford, CA, USA

Program in Neurosciences, Stanford University School of Medicine, Stanford, CA, USA

Jun Chen, M.D. Department of Neurology and Center of Cerebrovascular Disease Research, University of Pittsburgh School of Medicine, Pittsburgh, PA, USA

State Key Laboratory of Medical Neurobiology and Institute of Brain Sciences, Fudan University Shanghai Medical College, Shanghai, China

Geriatric Research, Educational and Clinical Center, Veterans Affairs Pittsburgh Health Care System, Pittsburgh, PA, USA

Adele E. Doperalski, Ph.D. Department of Anatomy and Neurobiology, Virginia Commonwealth University, Richmond, VA, USA

Robert Fern, Ph.D. Cell Physiology and Pharmacology, University of Leicester, Leicester, UK

Yanqin Gao, M.D. State Key Laboratory of Medical Neurobiology and Institute of Brain Sciences, Fudan University Shanghai Medical College, Shanghai, China

Kazuhide Hayakawa Neuroprotection Research Laboratory, Departments of Radiology and Neurology, Massachusetts General Hospital/Harvard Medical School, Charlestown, MA, USA

Jason D. Hinman Department of Neurology, University of California, Los Angeles, Los Angeles, CA, USA

Xiaoming Hu, Ph.D. Department of Neurology and Center of Cerebrovascular Disease Research, University of Pittsburgh School of Medicine, Pittsburgh, PA, USA

State Key Laboratory of Medical Neurobiology and Institute of Brain Sciences, Fudan University Shanghai Medical College, Shanghai, China

Geriatric Research, Educational and Clinical Center, Veterans Affairs Pittsburgh Health Care System, Pittsburgh, PA, USA

Branko Huisa, M.D. Department of Neurology, University of New Mexico Health Sciences Center, Albuquerque, NM, USA

Sarah Hutchings Genes & Development, Toronto Western Research Institute, University Health Network, Toronto, Canada

Department of Physiology, University of Toronto, Toronto, ON, Canada

Fakhreya Y. Jalal, Ph.D. Department of Neurology, University of New Mexico Health Sciences Center, Albuquerque, NM, USA

Samuel Ji Department of Psychological and Brain Sciences, Johns Hopkins University, Baltimore, MD, USA

Zheng Jing, Ph.D. Department of Neurology and Center of Cerebrovascular Disease Research, University of Pittsburgh School of Medicine, Pittsburgh, PA, USA
Geriatric Research, Educational and Clinical Center, Veterans Affairs Pittsburgh Health Care System, Pittsburgh, PA, USA

Hiroyuki Kinouchi, M.D., Ph.D. Department of Neurosurgery, Interdisciplinary Graduate School of Medicine and Engineering, University of Yamanashi, Yamanashi, Japan

Rehana K. Leak, Ph.D. Division of Pharmaceutical Sciences, Mylan School of Pharmacy, Duquesne University, Pittsburgh, PA, USA

Yang V. Li Department of Biomedical Sciences, Ohio University, Athens, OH, USA

Starlee Lively Genes & Development, Toronto Western Research Institute, University Health Network, Toronto, ON, Canada

Eng H. Lo Neuroprotection Research Laboratory, Departments of Radiology and Neurology, Massachusetts General Hospital/Harvard Medical School, Charlestown, MA, USA

Po H. Lu, Psy.D. Department of Neurology, The David Geffen School of Medicine at UCLA, Los Angeles, CA, USA

Maria Ly Department of Psychological and Brain Sciences, Johns Hopkins University, Baltimore, MD, USA

Takakuni Maki Neuroprotection Research Laboratory, Departments of Radiology and Neurology, Massachusetts General Hospital/Harvard Medical School, Charlestown, MA, USA

Gian Marco De Marchis, M.D. Division of Neurocritical Care, Department of Neurology, New York Presbyterian Hospital/Columbia University Medical Center, New York, NY, USA

Carlos Matute Departamento de Neurociencias, Achucarro Basque Center for Neuroscience, Universidad del País Vasco (UPV/EHU), Leioa, Spain

Centro de Investigación Biomédica en Red en Enfermedades Neurodegenerativas (CIBERNED), Leioa, Spain