Progress in Inflammation Research

Series Editor

Prof. Dr. Michael J. Parnham
PLIVA
Research Institute
Prilaz baruna Filipovica 25
10000 Zagreb
Croatia

Forthcoming titles:
Mechanisms and Mediators of Neuropathic Pain, A.B. Malmberg, S.R. Chaplan (Editors), 2002
The Hereditary Basis of Allergic Disorders, J. Holloway, S. Holgate (Editors), 2002
Bone Morphogenetic Proteins: From Laboratory to Clinical Practice, S. Vukicevic, K.T. Sampath (Editors), 2002

(Already published titles see last page.)

Migraine: A Neuroinflammatory Disease?

Egilius L. H. Spierings
Margarita Sánchez del Río

Editors

Springer Basel AG

Editors

Egilius L.H. Spierings
Brigham and Women's Hospital
Harvard Medical School
75 Francis Street
Boston, MA 02115
USA

Margarita Sánchez del Río
Headache Unit
Department of Neurology
Fundación Hospital Alcorcón
Juan Carlos I University
Madrid
Spain

A CIP catalogue record for this book is available from the Library of Congress, Washington D.C., USA

Deutsche Bibliothek Cataloging-in-Publication Data
Migraine: a neuroinflammatory disease? / Egilius L. H. Spierings ; Margarita Sanchez del Rio, ed.. - Basel ; Boston ; Berlin : Birkhäuser, 2002
(Progress in inflammation research)
ISBN 978-3-0348-9449-4 ISBN 978-3-0348-8131-9 (eBook)
DOI 10.1007/978-3-0348-8131-9

Originally published by Birkhäuser Verlag, Basel, Switzerland in 2002

Member of the BertelsmannSpringer Publishing Group
Printed on acid-free paper produced from chlorine-free pulp. TCF ∞
Cover design: Markus Etterich, Basel
Cover illustration: Photomicrograph of a dura perivascular mast cell examined with electron microscopy (see p. 116)

ISBN 3-7643-6231-6

9 8 7 6 5 4 3 2 1 www.birkhauser.ch

Contents

List of contributors

Guy Arnold, Humboldt Universität zu Berlin, Charité, Neurologische Klinik und Poliklinik, Schumannstrasse 20–21, 10098 Berlin, Germany;
e-mail: guy.arnold@charite.de

David W. Dodick, Mayo Clinic, Department of Neurology, 13400 East Shea Boulevard, Scottsdale, AZ 85259, USA; e-mail: dodick.david@mayo.edu

Kristiana Kandere, Tufts University School of Medicine, New England Medical Center, 136 Harrison Avenue, Boston, MA 02111, USA

Richard B. Lipton, IMR, 1200 High Ridge Road, Stamford, CT 06905, USA;
e-mail: rlipton@imrinc.com

Elizabeth W. Loder, Spaulding Rehabilitation Hospital, Pain Inpatient Unit, 125 Nashua Street, Boston, MA 02114-1198, USA; e-mail: eloder@partners.org

Dimos D. Mitsikostas, Athens Naval Hospital, Headache Clinic, 70 Dinokratous Street, 11521 Athens, Greece; e-mail: dmitsikostas@ath.forthnet.gr

Uwe Reuter, Humboldt Universität zu Berlin, Charité, Neurologische Klinik und Poliklinik, Schumannstrasse 20–21, 10098 Berlin, Germany;
e-mail: uwe.reuter@charite.de

Margarita Sánchez del Río, Headache Unit, Department of Neurology, Fundación Hospital Alcorcón, Juan Carlos I University, Madrid, Spain;
e-mail: msanchezdelrio@hotmail.com

Ann I. Scher, National Institutes of Health, Neuroepidemiology Branch/NINDS, 10 Center Drive, 55220, Bethesda, MD 20892, USA; e-mail: schera@ninds.nih.gov

Egilius L.H. Spierings, Brigham and Women's Hospital, Harvard Medical School, 75 Francis Street, Boston, MA 02115, USA; e-mail: spierings@mediaone.net

Walter F. Stewart, Department of Epidemiology, Johns Hopkins School of Public Health, 615 North Wolfe Street, Baltimore, MD 21205, USA;
e-mail: wstewart@jhsph.edu

Theoharis C. Theoharides, Tufts University School of Medicine, New England Medical Center, 136 Harrison Avenue, Boston, MA 02111, USA;
e-mail: theoharis.theoharides@tufts.edu

Preface

This book contains reviews by a renowned group of clinicians and scientists, which consider in great depth the potential involvement of neurogenic inflammation in the pathogenesis of migraine and inhibition of this putative mechanism as a possible mode of action of antimigraine medications. The authors carefully consider current and future potential therapeutic approaches for the abortive as well as preventive treatment of migraine.

The pioneering work by Professor Michael A. Moskowitz's group at Harvard gave rise to the "neurogenic hypothesis" of migraine pathogenesis and to an intellectual framework for many aspects of migraine research through a detailed pharmacological characterization of the trigeminovascular system. This knowledge then spurred detailed research worldwide into the roles of the dural vasculature, trigeminal nerve fibers, and sensory neuropeptides, such as substance P and calcitonin gene-related peptide, in migraine. Similar in-depth investigations have not been made of the role of the seventh cranial parasympathetic nerves but this area warrants further study because of its potential for interactions with the trigeminovascular system and its clear involvement in cluster headache.

Clinical studies have systematically tested many of the hypotheses arising from the experimental characterization of the trigeminovascular system but, so far, only compounds that have vasoconstrictor as well as trigeminal inhibitory properties, such as the ergots and triptans, seem to show unequivocal activity in the abortive treatment of migraine. Approaches targeting only one of these processes or pain signal mediators have generally failed or still require more proof of concept after promising preliminary studies. Perhaps the most important hypothesis that remains to be tested is the role of vasodilation induced by calcitonin gene-related peptide in migraine headache but this awaits a suitable compound for clinical trials.

There is undoubtedly a large reserve built into the pain signaling process to ensure adequate activation of a response that is part of a primary survival mechanism. It is, therefore, interesting to speculate that approaches that simultaneously inhibit a broad spectrum of pain-signaling molecules may have the greatest chance of efficacy against migraine because a single target approach leaves other transmit-

ter systems free to execute the pain response. This can be achieved by prejunctional inhibition of transmitter release more readily than by a polypharmacological approach to achieve postjunctional blockade of multiple mediators. Research for specific trigeminal terminal receptors that could be suitable medication targets, thus, remains intense.

Research into migraine pathogenesis has benefited enormously from true synergy between astute clinical observations and investigations and the development of antimigraine medications with highly specific and well-defined pharmacology. The main challenges that now face the field are the discovery of the underlying factors that predispose migraineurs to the migraine trigger factors and the relationship between neural central nervous system dysfunction and the activation of pain-producing trigeminovascular structures. Such understanding may lead to new approaches that improve the success rate of current migraine preventive strategies and these are clearly needed.

Richard J. Hargreaves, Ph.D.
Senior Director, Pharmacology and Imaging Research
Merck Research Laboratories, West Point, Pennsylvania

Acknowledgement
The editors would like to thank Richard J. Hargreaves, Ph.D., and the series editor, Michael J. Parnham, Ph.D., for critically reviewing the manuscripts.