

Responsible Editor: PANG Zaitang

Copyright 2003 by Science Press
Published by Science Press
16 Donghuangchenggen North Street
Beijing 100717, China

[http:// www lifescience .com .cn](http://www.lifescience.com.cn)

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, electronic, mechanical, photocopying, recording or otherwise, without the prior written permission of the copyright owner .

ISBN 7-03-011692-5

List of Contributing Authors

Lars Arendt-Nielsen MD, PhD
Professor and Chairman
Center for Sensory-Motor Interaction (SMI)
Laboratory for Experimental Pain Research
Aalborg University
Fredrik Bajers Vej 7, Aalborg 9220
Denmark
LAN@smi.auc.dk

Jean-Marie Besson PharmD, DSc
Professor and past IASP President
INSERM, UNITE 161 and EPHE
2 rue d'Alésia, Paris 75014 63:569 - 611 .
France
besson@broca.inserm.fr

Andrew CN Chen MD, PhD
Professor
Human Brain Mapping and Cortical Imaging Laboratory
The International Doctoral School in Biomedical Science and Engineering
Center for Sensory-Motor Interaction (SMI)
Aalborg University
Fredrik Bajers Vej 7, Aalborg 9220
Denmark
ac@smi.auc.dk

Jun Chen MD, PhD
Professor and Chief
Pain Research Center (PRC)
Department of Neurobiology & Institute of Neuroscience
The Fourth Military Medical University
17 West Chang-le Road, Xi an 710032
PR China
junchen@fmmu.edu.cn

Andy Dray PhD
AstraZeneca Research & Development Montreal
7171 Frederick Banting St ., Montreal H4S 1Z9
Canada
andy .dray@astrazeneca .com

Xiu Gao
State Key Laboratory of Medical Neurobiology
Fudan University
138 Yi Xue Yuan Road, Shanghai 200032
PR China

Ji-Sheng Han MD, ACAS
Professor and Chairman
Neuroscience Research Institute
Peking University
38 Xueyuan Road, Beijing 100083
PR China
hanjisheng@263 .net

Yoko Hoshi MD, PhD
Professor and Head
Department of Integrated Neuroscience
Tokyo Institute of Psychiatry
2-1-8 Kamikitazawa, Setagaya-ku, Tokyo 156-8585
Japan
Tel: 81-3-3304-5701(555)
Fax: 81-3-3329-8035
yhoshi@prit .go .jp

San-Jue Hu
Professor
Department of Neurobiology & Institute of Neuroscience
The Fourth Military Medical University
17 West Chang-le Road, Xi an 710032
PR China
sjhu@ fmmu .edu .cn

Ya-Lin Huang
State Key Laboratory of Medical Neurobiology

Fudan University
138 Yi Xue Yuan Road, Shanghai 200032
PR China

Lisbeth Illum MSC, PhD, DSc
West Pharmaceutical Services
Drug Delivery & Clinical Research Centre Ltd
Albert Einstein Centre
Nottingham Science & Technology Park
Nottingham NG7 2TN
UK
lisbeth.illum@westpharma.com

Martin Ingvar MD, PhD
Professor and Chairman
Cognitive Neurophysiology
Karolinska Hospital
171 76 Stockholm
Sweden
martin.ingvar@knv.ki.se

Guang-Chen Ji
State Key Laboratory of Medical Neurobiology
Fudan University
138 Yi Xue Yuan Road, Shanghai 200032
PR China

Zhong Jian
Department of Physics
School of Biomedical Electronic Engineering
The Fourth Military Medical University
17 West Chang-le Road, Xi an 710032
PR China
jz68720@263.net

Thomas R. Knosche PhD
ANT Software BV
Netherlands
knosche@ant-software.nl

William R . Lariviere PhD
Post-doc fellow
Department of Psychology and Neuroscience Program
University of Illinois at Urbana-Champaign
Illinois, USA
william.lariviere@uiuc.edu

Jon D . Levine MD, PhD
Professor and Chairman
NIH Pain Center
University of California
Box # 0440, 521 Parnassus Avenue, San Francisco 94143-0440
CA, USA
levine@itsa.ucsf.edu

Zhen Li
PhD student
Pain Research Center (PRC)
Department of Neurobiology & Institute of Neuroscience
The Fourth Military Medical University
17 West Chang-le Road, Xi an 710032
PR China
painlab@fmmu.edu.cn

Qing Lin MD, PhD
Assistant Professor
Department of Anatomy & Neurosciences
The University of Texas Medical Branch
Galveston, Texas, 77555-1069
USA
qilin@utmb.edu

Ceng Luo PhD
Lecturer and Research Fellow
Pain Research Center (PRC)
Department of Neurobiology & Institute of Neuroscience
The Fourth Military Medical University
17 West Chang-le Road, Xi an 710032
PR China
painlab@fmmu.edu.cn

Jeffrey S . Mogil PhD
Professor
Department of Psychology
McGill University
Montreal, Quebec
Canada
jeff@hebb.psych.mcgill.ca

Koichi Noguchi MD, PhD
Professor and Chairman
Department of Anatomy
Hyogo College of Medicine
Japan
noguchi@hyo-med.ac.jp

Dejan B . Popovic PhD
Professor
Center for Sensory Motor Interaction (SMI)
Aalborg University
Fredrik Bajers Vej 7, Aalborg 9220
Denmark
dbp@smi.auc.dk

Mirjana B . Popovic PhD
Center for Sensory Motor Interaction (SMI)
Aalborg University
Fredrik Bajers Vej 7, Aalborg 9220
Denmark

Barry J . Sessle BDS, BSc, MDS, PhD, FRSC
Professor & immediate past IASP President
Department of Physiology
Faculty of Dentistry, University of Toronto
Canada
barry.sessle@utoronto.ca

Thomas Sinkj r PhD
Professor and Chairman
Center for Sensory Motor Interaction (SMI)

Aalborg University
Fredrik Bajers Vej 7, Aalborg 9220
Denmark
ts@miba.auc.dk

William D . Willis MD, PhD
Professor and Chairman
Department of Anatomy & Neuroscience
University of Texas Medical Branch
Galveston, Texas, 77555-1069
USA
wdwillis@utmb.edu

Gen-Cheng Wu
Professor
State Key Laboratory of Medical Neurobiology
Fudan University
138 Yi Xue Yuan Road, Shanghai 200032
PR China

Yu-Qiu Zhang PhD
Professor
Institute of Neurobiology
Fudan University
220 Han Dan Road, Shanghai 200433
PR China
yuqzhang@fudan.edu.cn

Zhi-Qi Zhao, PhD
Professor
Institute of Neurobiology
Fudan University
220 Han Dan Road, Shanghai 200433
PR China
zqzhao@fudan.edu.cn

Ji-Hong Zheng
PhD student
Pain Research Center (PRC)
Department of Neurobiology & Institute of Neuroscience

The Fourth Military Medical University
17 West Chang-le Road, Xi an 710032
PR China
painlab@fmmu.edu.cn

Foreword I

This book is based on the proceedings of a Symposium on the “ International Advanced Workshop on Brain/ Pain Research: from Molecules to Mind ” held from April 30 to May 2, 2001 in Xi an, China . The Symposium brought together an international group of renowned basic scientists and clinical investigators actively involved in research of the mechanisms underlying pain .

The Symposium provided an opportunity for Chinese scientists and clinicians to learn from international colleagues, as well as the participants from overseas to gain first-hand insights into the many recent scientific, and social advances in the People s Republic of China . Oral presentations reviewed recent advances in the field, while poster presentations dealt with the latest specific research results . Thus, the papers in this book will help readers to obtain an overview of our current understanding of pain, with an emphasis on recent advances and future research directions . The Symposium and this book are indeed very much in accordance with the guiding principles of the International Association for the Study of Pain, which are principally to foster pain research, management, education and communication . The Symposium indeed was co-sponsored by the China Chapter of IASP, and as President of IASP, I had the pleasure of being one of the participants .

While the book gives in-depth coverage of the topics presented at the Symposium, it cannot adequately convey the social and cultural activities and insights that the Symposium provided for the participants . The scientific programme allowed for much fruitful interaction, but the organizers also arranged a wonderful social and touristisc programme giving many memorable experiences as well as opportunities for participants from the People s Republic of China and the international speakers to interact less formally and learn from each other . Drs . Jun Chen and Andrew Chen are to be congratulated for organizing such a successful Symposium and book .

I hope that the readers of this book will enjoy and learn from its contents as much as I enjoyed participating in and learning from this important Symposium .

Barry J . Sessle BDS, BSc, MDS, PhD, FRSC, DSc
President of
International Association for the Study of Pain (IASP)
Professor and Research Chair
Faculty of Dentistry
University of Toronto
Canada

Foreword II

The opening of the International Advanced Workshop on Brain/ Pain Research and the International Workshop on Brain Mapping and Neuro-modulation in Xi an in the April of 2001 was a great event of pain and brain research in the beginning of the new century in China . Since 1989, the China Chapter of the International Association for the Study of Pain (CASP) has set up a serial international pain meetings entitled “ East and West Pain Conference ” to be held every 3-4 years, devoting to the exchange of information on pain research and pain management between China and Asian countries and the rest of the world, with the latest (the 4th) one being held in Beijing in 2000 . I am happy that in between the 4th and the 5th East and West Pain Conference, we are able to sponsor another pain meeting with more emphasis on theoretical aspects, especially on brain mapping and cognitive sciences, which are certainly very important aspects in pain research today . In fact some of the presentations are dealing with brain functions other than pain, which is also very welcome by the pain researchers who are eager to learn from colleagues of other disciplines . The formal publication of the contents of the presentations will certainly benefit not only members of the CASP, but also pain researchers as well as neuroscientists in China .

As president of the CASP, I would like to express my deepest gratitude to Prof . Jun Chen and Prof .Andrew CN Chen, who have put enormous efforts to make this symposium a very successful one, and also to edit the contents in a comprehensive book . I sincerely hope that this will serve as a good sign of the boom of pain research in the “ Decade of Pain Control and Research ” in China .

Ji-Sheng Han MD, ACAS
President of
China Chapter of IASP (CASP)
Professor and Chairman
Neuroscience Research Institute
Peking University
Beijing
PR China

Preface

In the first spring of the new century and millennium, an important international joint scientific meeting associated with brain and pain research was successfully held in Xi an, the ancient capital city of 13 dynasties in China . The meeting was composed of an “ International Advanced Workshop on Brain/ Pain Research: from Molecules to Mind ” (BPR) (April 30 to May 1, 2001) and an “ International Pre-Workshop on Brain Mapping and Neuromodulation ” (BMN) (April 28 - 29, 2001) . The meeting was co-organized by the K .K . Leung Brain Research Center at the FMMU, China and the International Doctoral School in Biomedical Sciences and Engineering, Aalborg University, Denmark .

The theme of the Xi an international meeting was: “ 21st Century: New Era of Brain & Pain Research ” . This will be in conformity with the resolution declaring the decade beginning January 1, 2001 as the “ Decade of Pain Control and Research ” passed by the 106th Congress of the United States (IASP Newsletter, Issue 2, 2001), which just followed the “ Decade of the Brain ” . With the increased media and other attention that such a declaration brings, it represents an important opportunity to bring pain research and management to the forefront of the medical community and to the general public .

We were truly satisfied with what actually happened at the Xi an meeting . The two Xi an Brain/ Pain workshops attracted a total of 270 participants from both western countries and China . It was a grand gathering of neuroscientists, pain researchers, as well as R&D representatives of pharmaceutical industry and medical device makers . The 4-day program of the Xi an meeting was well formed and it included 15 invited lectures at the BPR Workshop and 11 invited lectures at the BMN pre-workshop . Additionally, the meeting also had nearly 40 poster presentations . The program of the BPR Workshop was formed by a 2-day advanced and updated plenary lecture course associated with (1) Functional plasticity of nociceptors, spinal cord and brain, (2) Experimental pharmacology and analgesia, (3) Experimental induction and neuroimaging of human pain, (4) Cellular basis and neuroimaging of acupuncture analgesia, and (5) Open discussion on east-west and perspectives of pain research . The BMN Pre-Workshop mainly introduced two aspects of advanced technologies: (1) EEG/ ERP, MEG/ MEF and optic tomographic imaging systems in recording, mapping, and source analysis of human brain processes in laboratories and clinics, and (2) Neuromodulation in the regulation of brain and bodily function and dysfunction . The program of the two Xi an workshops was highly appreciated by all participants . In particular, each

lecture given by the invited speakers was as long as one hour, which made the program contents and the discussion much more comprehensive and informative .

The successful organization and opening of these two wonderful workshops would have great significance in the history of Chinese brain and pain research and act as a bridge for international scientific and technological cooperations and communications between China and western countries . The two Xi an workshops would also play a role in bridging the gap between Chinese brain/ pain researchers/ clinicians and international world-leading pharmaceutical industry/ medical device makers .

To meet the requirement of Chinese brain/ pain researchers, clinicians and students who are interested in pain research and management, we invited each distinguished speakers and some poster presenters to contribute 22 chapters to form this book: “ *Experimental Pathological Pain: from Molecules to Brain Functions* ” . With formal publication and circulation of this book over the country, the influence of the Xi an international meeting will be further widened .

The book is mostly based on the Xi an workshops and composed of four parts: (1) Part I Neurobiology of pathological pain (chapter 1-11); (2) Part II Neuromodulation of pathological pain and motor dysfunctions (chapter 12-17); and (3) Neuroimaging of experimental human pain (chapter 18-22) .

Finally , we are grateful to the authors for their strong supports and important contributions to the successful formation of this book . We also want to extend our special thanks to Prof . Barry J . Sessle, the president of International Association of Pain (IASP) and Prof . Ji-Sheng Han, the president of China Chapter of the IASP (CASP) , for their wonderful forewords to this book .

Editors

Jun Chen MD, PhD

Andrew C . N . Chen PhD

Ji-Sheng Han MD, ACAS

William D . Willis MD, PhD

Acknowledgments

- 1 . National Brain Science Basic Research Program (G1999054004) sponsored by the Ministry of Science and Technology of China (MOST)
- 2 . National Natural Science Foundation of China (NSFC)
- 3 . Chinese Association for the Study of Pain, the IASP Chapter (CASP)
- 4 . Institute of Neuroscience, the Fourth Military Medical University
- 5 . KK Leung Brain Research Centre, the Fourth Military Medical University
- 6 . Center for Sensory-Motor Interaction (SMI), Aalborg University, Denmark
- 7 . Hainan Jizhong Pharmaceutical Group
- 8 . Mermaid Foundation (Denmark)
- 9 . 4-D Neuroimaging (Finland)
- 10 . West Pharmaceutical Services (UK)
- 11 . NeuroScan (USA)
- 12 . CTF Systems Inc . (Canada) and Baima Medical Devices, Ltd . Guangdong
- 13 . ANT Software BV (Netherlands)

Contents

List of Contributing Authors

Foreword I

Foreword II

Preface

Acknowledgments

Part I Neurobiology of Pathological Pain

- 1 . Genetic Basis of Pain Induction and Modulation 3
William R . Lariviere and Jeffrey S . Mogil
- 2 . Gene Expression in Neuropathic Pain Models 16
Koichi Noguchi
- 3 . Peripheral Mechanisms and Modulation in Inflammatory Pain 32
Jon D . Levine
- 4 . A Contribution of Dorsal Root Reflexes to Neurogenic Inflammation and Pain 36
Qing Lin
- 5 . Signal Molecules and Receptors in Primary Afferent Components of Nociceptive Processing and Plastic Changes 57
Zhi-Qi Zhao
- 6 . The Bee Venom Test: A Novel Useful Animal Model for Study of Spinal Coding and Processing of Pathological Pain Information 77
Jun Chen
- 7 . Trigeminal Mechanisms of Orofacial Pain 111
Barry J . Sessle
- 8 . Application of Adult Rat Spinal Slice Patch-clamp Recording Technique in the Study of Nociceptive Transmission and Modulation 124
Ceng Luo, Zhen Li and Jun Chen
- 9 . Temporal Firing Patterns and Responsiveness of Injured Sensory Neurons 141
San-Jue Hu
- 10 . Temporal Decoding of Persistent Pain Signal Processing in the Spinal Cord Dorsal Horn: Application of Non-linear Dynamic Analytical Methods 151

- 11 . Thalamo-Cortical System of Nociception in Animals 165
William D . Willis

Part II Neuromodulation of Pathological Pain and Motor Dysfunctions

- 12 . Physiopharmacological Aspects of Pathological Pain States 199
Jean-Marie Besson
- 13 . Novel Pharmacology for Control of Chronic Pain 207
Andy Dray
- 14 . The Roles of 5-HT_{1A} Receptor in Modulating Spinal Nociceptive Transmission
in Inflammatory Rats 220
*Yu-Qiu Zhang, Xiu Gao, Ya-Lin Huang, Guang-Chen Ji, Gen-Cheng
Wu, Zhi-Qi Zhao*
- 15 . Low- and High-Frequency Electroacupuncture: Difference in Neural Pathways
and Therapeutic Effects 248
Ji-Sheng Han
- 16 . Restitution of Upper-Limb Movement Promoted with Functional Electrical
Therapy (FET) 259
Dejan B . Popovic, Mirjana B . Popovic, Thomas Sinkjaer
- 17 . Intranasal Morphine for Pain Management 285
Lisbeth Illum

Part III Neuroimaging of Experimental Human Pain

- 18 . Experimental Human Pain 301
Lars Arendt-Nielsen
- 19 . EEG/ MEG Brain Mapping of Human Pain 306
Andrew C .N. Chen
- 20 . Principles of Human Pain Imaging with PET 319
Martin Ingvar
- 21 . The Application of Source Modelling to Functional Imaging of the Brain Based
on EEG and MEG 325
Thomas R . Kn sche
- 22 . Near-infrared Optical Imaging of the Human Brain 338
Yoko Hoshi
- Index 349

Part I

Neurobiology of Pathological Pain

From: *Experimental Pathological Pain: from Molecules to Brain Functions*

1

Genetic Basis of Pain Induction and Modulation

William R . Lariviere and Jeffrey S . Mogil

Department of Psychology and Neuroscience Program, University of Illinois at
Urbana-Champaign, Illinois, USA

McGill University, Department of Psychology, Montreal, Quebec, Canada

