





The 8th International Winter Conference on Neurodegeneration (IWCN) had been dedicated to Prof. Dr. Dr. hc. Moussa B. H. Youdim, at the occasion of his 60th anniversary

P. Riederer,  
D. B. Calne, R. Horowski, Y. Mizuno,  
C. W. Olanow, W. Poewe, M. B. H. Youdim (eds.)

Advances in Research on Neurodegeneration

Volume 8

Springer-Verlag Wien GmbH

Prof. Dr. P. Riederer  
Department of Psychiatry, University of Würzburg, Federal Republic of Germany

Prof. Dr. D. B. Calne  
Neurodegenerative Disorders Centre, Faculty of Medicine, University Hospital,  
Vancouver, B.C., Canada

Dr. R. Horowski  
Schering AG Berlin, Berlin, Federal Republic of Germany

Prof. Dr. Y. Mizuno  
Department of Neurology, Juntendo University, Tokyo, Japan

Prof. Dr. C. W. Olanow  
Department of Neurology, Mount Sinai Medical Center, New York, U.S.A.

Prof. Dr. W. Poewe  
Department of Neurology, University of Innsbruck, Austria

Prof. Dr. M. B. H. Youdim  
Department of Pharmacology, Faculty of Medicine, Technion, Haifa, Israel

This work is subject to copyright.

All rights are reserved, whether the whole or part of the material is concerned, specifically those of translation, reprinting, re-use of illustrations, broadcasting, reproduction by photocopying machines or similar means, and storage in data banks.

Product Liability: The publisher can give no guarantee for all the information contained in this book. This does also refer to information about drug dosage and application thereof. In every individual case the respective user must check its accuracy by consulting other pharmaceutical literature. The use of registered names, trademarks, etc. in this publication does not imply, even in the absence of specific statement, that such names are exempt from the relevant protective laws and regulations and therefore free for general use.

© 2000 Springer-Verlag Wien  
Originally published by Springer-Verlag Wien New York in 2000  
Softcover reprint of the hardcover 1st edition 2000

Typesetting: Best-Set Typesetter Ltd., Hong Kong

Graphic design: Ecke Bonk

Printed on acid-free and chlorine-free bleached paper  
SPIN: 10774512

With 65 (partly coloured) Figures

ISBN 978-3-211-83537-1  
DOI 10.1007/978-3-7091-6301-6

ISBN 978-3-7091-6301-6 (eBook)

## Preface

The 8th International Winter Conference on Neurodegeneration from February 9 to 13, 2000 took place in Tegernsee, Bavaria, Germany. The interest shown in this symposium, which was carried by invited speakers only, was striking. 28 lectures in 5 sessions dealt with themes on basic science and therapy strategies for neurodegenerative illness. This time especially basic mechanism of cell death and resulting causal treatment possibilities were centre themes of the lectures and lively discussions. In accordance with tradition 5 lectures on Multiple Sclerosis finished the convention. 60 scientists from 13 countries discussed current questions to these themes.

The Symposium started with a lecture on the history of the development of modern-L-DOPA-therapy. Lectures on cell death of dopaminergic nerve cells, new valuation regarding assembly, built up and function of neuromelanin of Substantia nigra and with this, the question of the physiologic and pathobiochemical role of dopamine and neuromelanin built the first block of themes which consequently extended to molecular and genetic aspects of cell death. Highlights of the symposium were neuroprotective and neuroregenerative future therapy strategies together with discussions on the difficulties of clinical neuroprotection.

Developmental biological aspects on nerve cells, reorganisation and neurodegeneration showed a stimulating point of view of momentary and future development possibilities of new and more causal forms of therapy of neurodegenerative illness.

The part of glia subtypes for degenerative processes and Multiple Sclerosis in particular brought important leading findings into the lectures and discussions on diagnosis, progression and molecular reasons. Clinical and pathological aspects on comorbidity of Parkinson-illness, dementive processes and depression showed connections and frequency accumulation on a molecular basis.

This before hand issue reflects the state of knowledge on neurodegenerative illness timely to the symposium.

These proceedings are also seen as a tribute to the excellent and stimulating scientific work carried out by our colleague, cooperative partner and friend Prof. Dr. Moussa B. H. Youdim, who jointly celebrated his 60th birthday with all of us at this lovely place, the "Hotel Bayern" at Tegernsee.

We would like to thank the sponsors of this symposium, traditionally Schering AG, Berlin as well as this time Merz + Co GmbH and Co, Frankfurt, SmithKline Beecham Pharma GmbH and Boehringer Ingelheim Pharma KG. These proceedings were accomplished by the "National Parkinson Founda-

tion Center of Excellence Research Laboratories” at the Clinic and Policlinic for Psychiatry and Psychotherapy of the University of Wuerzburg, Germany. The Editors also acknowledge Springer Verlag, Vienna, for their usual extraordinary setting of the proceedings.

Wuerzburg, August 2000

**P. Riederer**

## Contents

<b>Foley, P.:</b> The L-DOPA story revisited. Further surprises to be expected? . . . . .	1
<b>Jellinger, K. A., Stadelmann, Ch.:</b> The enigma of cell death in neurodegenerative disorders . . . . .	21
<b>Double, K. L., Gerlach, M., Youdim, M. B. H., Riederer, P.:</b> Impaired iron homeostasis in Parkinson's disease . . . . .	37
<b>Barzilai, A., Zilkha-Falb, R., Daily, D., Stern, N., Offen, D., Ziv, I., Melamed, E., Shirvan, A.:</b> The molecular mechanism of dopamine-induced apoptosis: identification and characterization of genes that mediate dopamine toxicity . . .	59
<b>Tatton, W. G., Chalmers-Redman, R. M. E., Elstner, M., Leesch, W., Jagodzinski, F. B., Stupak, D. P., Sugrue, M. M., Tatton, N. A.:</b> Glyceraldehyde-3-phosphate dehydrogenase in neurodegeneration and apoptosis signaling . . . . .	77
<b>Hattori, N., Shimura, H., Kubo, S., Wang, M., Shimizu, N., Tanaka, K., Mizuno, Y.:</b> Importance of familial Parkinson's disease and parkinsonism to the understanding of nigral degeneration in sporadic Parkinson's disease . . . . .	101
<b>Mandel, S., Grünblatt, E., Youdim, M.:</b> cDNA microarray to study gene expression of dopaminergic neurodegeneration and neuroprotection in MPTP and 6-hydroxydopamine models: implications for idiopathic Parkinson's disease . . .	117
<b>Brooks, D. J.:</b> Monitoring neuroprotection and restorative therapies in Parkinson's disease with PET . . . . .	125
<b>Kitani, K., Minami, C., Maruyama, W., Kanai, S., Ivy, G. O., Carrillo, M.-C.:</b> Common properties for propargylamines of enhancing superoxide dismutase and catalase activities in the dopaminergic system in the rat: implications for the life prolonging effect of (-)deprenyl . . . . .	139
<b>Weinstock, M., Bejar, C., Wang, R-H., Poltyrev, T., Gross, A., Finberg, J. P. M., Youdim, M. B. H.:</b> TV3326, a novel neuroprotective drug with cholinesterase and monoamine oxidase inhibitory activities for the treatment of Alzheimer's disease . . . . .	157
<b>Maruyama, W., Akao, Y., Youdim, M. B. H., Naoi, M.:</b> Neurotoxins induce apoptosis in dopamine neurons: protection bei <i>N</i> -propargylamine-1( <i>R</i> )- and ( <i>S</i> )-aminoindan, rasagiline and TV1022 . . . . .	171
<b>Bleich, S., Degner, D., Javaheripour, K., Kurth, C., Kornhuber, J.:</b> Homocysteine and alcoholism . . . . .	187
<b>Waldmeier, P. C., Boulton, A. A., Cools, A. R., Kato, A. C., Tatton, W. G.:</b> Neurorescuing effects of the GAPDH ligand CGP 3466B . . . . .	197
<b>Andringa, G., Cools, A. R.:</b> The neuroprotective effects of CGP 3466B in the best in vivo model of Parkinson's disease, the bilaterally MPTP-treated rhesus monkey . . . . .	215
<b>Belluardo, N., Mudo, G., Blum, M., Amato, G., Fuxe, K.:</b> Neurotrophic effects of central nicotinic receptor activation . . . . .	227

<b>Götz, R.:</b> Regulation of neuronal cell death and differentiation by NGF and IAP family members .....	247
<b>Zheng, W.-H., Kar, S., Doré, S., Quirion, R.:</b> Insulin-like growth factor-1 (IGF-1): a neuroprotective trophic factor acting via the Akt kinase pathway .....	261
<b>Strelau, J., Böttner, M., Lingor, P., Suter-Crazzolara, C., Galter, D., Jaszai, J., Sullivan, A., Schober, A., Krieglstein, K., Unsicker, K.:</b> GDF-15/MIC-1 a novel member of the TGF- $\beta$ superfamily .....	273
<b>Nagatsu, T., Mogi, M., Ichinose, H., Togari, A.:</b> Changes in cytokines and neurotrophins in Parkinson's disease .....	277
<b>Wolters, E. Ch.:</b> Psychiatric complications in Parkinson's disease .....	291
<b>Ransmayr, G.:</b> Dementia with Lewy bodies: prevalence, clinical spectrum and natural history .....	303
<b>Teuchert-Noodt, G.:</b> Neuronal degeneration and reorganization: a mutual principle in pathological and in healthy interactions of limbic and prefrontal circuits .....	315
<b>Stefanova, N., Seppi, K., Scherfler, C., Puschban, Z., Wenning, G. K.:</b> Depression in alpha-synucleinopathies: prevalence, pathophysiology and treatment .....	335
<b>Mössner, R., Schmitt, A., Syagailo, Y., Gerlach, M., Riederer, P., Lesch, K. P.:</b> The serotonin transporter in Alzheimer's and Parkinson's disease .....	345
<b>Berger, T., Reindl, M.:</b> Immunopathogenic and clinical relevance of antibodies against myelin oligodendrocyte glycoprotein (MOG) in Multiple Sclerosis ....	351
<b>Martin, R., Bielekova, B., Gran, B., McFarland, H. F.:</b> Lessons from studies of antigen-specific T cell responses in Multiple Sclerosis .....	361
<b>Werner, P., Pitt, D., Raine, C. S.:</b> Glutamate excitotoxicity — a mechanism for axonal damage and oligodendrocyte death in Multiple Sclerosis? .....	375
<b>Floyd, R. A., Hensley, K., Bing, G.:</b> Evidence for enhanced neuro-inflammatory processes in neurodegenerative diseases and the action of nitrones as potential therapeutics .....	387
<b>Subject Index</b> .....	415