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Neurodegenerative Diseases

Molecular and Cellular Mechanisms
and Therapeutic Advances

Edited by

Gary Fiskum

The George Washington University Medical Center
Washington, D.C.



Springer Science+Business Media, LLC

Library of Congress Cataloging in Publication Data

Neurodegenerative diseases: molecular and cellular mechanisms and therapeutic advances / edited by Gary Fiskum.

p. cm.—(GWUMC Department of Biochemistry and molecular biology annual spring symposia)

“Proceedings of the Fifteenth Washington International Spring Symposium at The George Washington University, held May 15–17, 1995, in Washington, D.C.”—Tp. verso.

Includes bibliographical references and index.

ISBN 978-1-4899-0211-5

1. Nervous system—Degeneration—Molecular aspects—Congresses. 2. Pathology, Cellular—Congresses. 3. Neurogenetics—Congresses. 4. Neurons—Congresses. 5. Nervous system—Metabolism—Congresses. 6. Amyloid—Congresses. I. Fiskum, Gary. II. International Spring Symposium on Health Sciences (15th: 1995: Washington, D.C.) III. Series.

RC365.N476 1996

96-5688

616.8'047—dc20

CIP

Proceedings of the Fifteenth Washington International Spring Symposium at The George Washington University, held May 15 – 17, 1995, in Washington, D.C.

ISBN 978-1-4899-0211-5

ISBN 978-1-4899-0209-2 (eBook)

DOI 10.1007/978-1-4899-0209-2

© 1996 Springer Science+Business Media New York
Originally published by Plenum Press, New York in 1996
Softcover reprint of the hardcover 1st edition 1996

10 9 8 7 6 5 4 3 2 1

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PREFACE

This book presents much of the exciting new information on mechanisms of neurodegenerative disorders that was presented at the XVth International Spring Symposium on Health Sciences at George Washington University in Washington, D.C. The organization of the symposium as well as the chapters within this book were based upon fundamental molecular and cellular mechanisms of neurodegeneration rather than upon different clinically defined disorders, in order to emphasize the commonality of cause rather than effect.

The first part of the book is devoted to the relationships between selective vulnerability of different neuronal cell types to injury and their functional characteristics related to the transport, binding, and responses for excitatory amino acids, e.g., glutamate, as well as other neurotransmitters involved in toxicity. These relationships are studied in the context of neurodegeneration associated with several disorders including Parkinson's disease, amyotrophic lateral sclerosis (ALS), cerebral ischemia, and AIDS dementia.

Part II emphasizes the role of amyloid proteins in neurodegeneration but also covers other molecular and genetic risk factors, e.g., expression of different apolipoprotein isoforms and the involvement of abnormal superoxide dismutase in neuropathology. These topics are applied primarily to the aging brain, Alzheimer's disease, and ALS.

The third part, Cellular Metabolism, provides an overview of how altered cerebral energy and amino acid metabolism and protein synthesis predispose the CNS to injury caused by other closely associated mechanisms, including oxidative stress and excitotoxicity. This concept is applied to a broad range of neurodegenerative disorders including Alzheimer's and Huntington's diseases as well as those caused by neurotoxins, poor nutrition, cerebral ischemia, and inborn errors of metabolism.

The fourth part of the book concentrates on the rapidly growing field of research addressing the roles that free radicals and oxidative stress play in cellular injury and death associated with neurological disorders, e.g., stroke, ALS, Alzheimer's and Parkinson's diseases, and meningitis. Important new information on the actions of nitric oxide in the nervous system is also covered in this section.

Part V elaborates on how calcium transport and calcium-dependent enzymes and regulatory proteins provide either protection against, or exacerbation of, the cascade of events leading to irreversible neuronal injury. In addition to the application of this information to mechanisms of neurodegeneration in Alzheimer's, ischemia, trauma, and AIDS dementia, this section of the book covers many of the pharmacological interventions being tested for therapeutic efficacy toward these disorders.

The final section of the book deals with the extremely important topics of neuronal growth regulation and apoptotic cell death. As these issues are considered to be of fundamental importance with regard to cellular mechanisms of neurodegeneration, it is not surprising that the chapters within this section touch upon many of the basic molecular mechanisms of neuronal injury covered in previous sections, including metabolic failure, excitotoxicity, and oxidative stress.

Gary Fiskum

CONTENTS

PART I - EXCITOTOXICITY AND SELECTIVE NEURONAL VULNERABILITY

1. Intracellular Signalling in Glutamate Excitotoxicity1
Ian J. Reynolds, Kari R. Hoyt, R. James White, and Amy K. Stout
2. Long-Term Expression of Proenkephalin and Prodynorphin in the Rat Brain after Systemic Administration of Kainic Acid - an *in Situ* Hybridization Study9
Guoying Bing, Belinda Wilson, Michael McMillian, Zhehui Feng, Qiping Qi, Hyoung-Chum Kim, Wen Wang, Karl Jensen, and Jau-Shyong Hong
3. Modulation of Vesicular Glutamate Release during Anoxia19
Norman Hershkowitz and Alexander N. Katchman
4. A Model for the Expression of Different Glutamate Transporter Proteins from a Rat Astrocyte-Type Glutamate Transporter Gene29
Raymond S. Roginski
5. Glutamate Transporters: Molecular Mechanisms of Functional Alteration and Role in the Development of Excitotoxic Neuronal Injury33
Davide Trotti, Niels C. Danbolt, Barbara Lodi Rizzini, Paola Bezzi, Daniela Rossi, Giorgio Racagni, and Andrea Volterra
6. Neurodegenerative Disease and Oxidative Stress: Insights from an Animal Model of Parkinsonism37
Teresa G. Hastings and Michael J. Zigmond
7. A Progressive Ballooning of Myelinated, TH-Positive Axons Is Produced by MPTP in the Dog47
James S. Wilson, Blair H. Turner, and James H. Baker
8. HIV-1 Coat Protein GP120 Induces Neuronal Injury to Cultured Dopamine Cells55
Barbara A. Bennett, Daniel E. Rusyniak, and Charlotte K. Hollingsworth
9. Platelets as Peripheral Model of Glutamate-Related Excitotoxicity in Parkinson's Disease63
Carlo Ferrarese, Graziella Bianchi, Marianna Bugiani, Tiziana Cogliati, Maura Frigo, Davide Passoni, Nicoletta Pecora, Roberto Piolti, Clara Pozzi, Rachele Tortorella, and Lodovico Frattola

10. Brainstem Motoneuron Cell Groups that Die in Amyotrophic Lateral Sclerosis Are Rich in the GLT-1 Glutamate Transporter69
Loreta Medina, Griselle Figueredo-Cardenas, J.D. Rothstein, and Anton Reiner
11. Progressive Neurodegeneration in Rat Brain after Chronic 3-VO or 2-VO77
J.C. de la Torre, B.A. Pappas, T. Fortin, M. Keyes, and C. Davidson

PART II - MOLECULAR AND GENETIC RISK FACTORS

12. *In Vivo* Biology of APP and Its Homologues85
Sangram S. Sisodia, Gopal Thinakaran, Cornelia S. von Koch, Hilda H. Slunt, A. Jane I. Roskams, Cheryl A. Kitt, Eliezer Masliah, Vassilis E. Koliatsos, Peter R. Mouton, Lee J. Martin, Randall R. Reed, Gabrielle V. Ronnett, Hui Zheng, Lex H.T. Van der Ploeg, and Donald L. Price
13. Lymphocyte Amyloid Precursor Protein mRNA Isoforms in Normal Aging and Alzheimer's Disease91
Richard P. Ebstein, Lubov Nemanov, Gregory Lubarski, Marina Dano, Teres Trevis, and Amos Korczyn
14. Differential Regulation of APP Secretion by Apolipoprotein E3 and E497
Benjamin Wolozin, Jasna Basaric-Keys, Robert Canter, Yunhua Li, Dudley Strickland, and Trey Sunderland
15. Apolipoprotein E Uptake Is Increased by Beta-Amyloid Peptides and Reduced by Blockade of the LDL Receptor103
Uwe Beffert, Nicole Aumont, Doris Dea, Jean Davignon, and Judes Poirier
16. The Non-Amyloid- β Component of Alzheimer's Disease Plaque Amyloid: Comparative Analysis Suggests a Normal Function as a Synaptic Plasticizer109
Julia M. George and David F. Clayton
17. Mutations of Human Cu Zn Superoxide Dismutase Expressed in Transgenic Mice Cause Motor Neuron Disease113
Mark E. Gurney, Arlene Y. Chiu, Mauro C. Dal Canto, John Q. Trojanowski, and Virginia M.-Y. Lee
18. Effect of the Kennedy Mutation of the Androgen Receptor on Gene Expression in Neuroblastoma Cells123
P.A. Yerramilli-Rao, O. Garofalo, P.N. Leigh, and J.-M. Gallo
19. Glutamate-Promoted Survival in Hippocampal Neurons: A Defect in Mouse Trisomy 16133
Linda L. Bambrick, Paul J. Yarowsky, and Bruce K. Krueger

20. RNA Message Levels in Normally Aging and in Alzheimer's Disease (AD)-Affected Human Temporal Lobe Neocortex141
Walter J. Lukiw, Donald R. McLachlan, and Nicholas G. Bazan

PART III - CELLULAR METABOLISM

21. Functional Activation of Energy Metabolism in Nervous Tissue: Where and Why147
Louis Sokoloff and Shinichi Takahashi
22. Bioenergetics in Oxidative Damage in Neurodegenerative Diseases171
M. Flint Beal
23. Is there a Relationship between Conditions Associated with Chronic Hypoxia, the Mitochondria, and Neurodegenerative Diseases, such as Alzheimer's Disease?181
Carl R. Merrill, Steve Zullo, and Hossein Ghanbari
24. α -Ketoglutarate Dehydrogenase in Alzheimer's Disease185
John P. Blass, Kwan-Fu Rex Sheu, and Rudolph E. Tanzi
25. Thiamine Deficiency as Model of Selective Neurodegeneration with Chronic Oxidative Deficits193
Noel Y. Calingasan, Kwan-Fu Rex Sheu, Harriet Baker, Samuel E. Gandy, and Gary E. Gibson
26. Metabolic Failure, Oxidative Stress, and Neurodegeneration following Cerebral Ischemia and Reperfusion203
Gary Fiskum and Robert E. Rosenthal
27. Global Brain Ischemia and Reperfusion: Translation Initiation Factors211
Donald DeGracia, Robert Neumar, Blaine White, and Gary Krause
28. Batten Disease: A Typical Neuronal Storage Disease or a Genetic Neurodegenerative Disorder Characterized by Excitotoxicity?217
Steven U. Walkley, Donald A. Siegel, and Kostantin Dobrenis
29. Endogenous Amino Acid Profile during *in Vitro* Differentiation of Neural Stem Cells225
Eulalia Bazan, Miguel A. López-Toledano, Maria A. Mena, Rafel Martín del Rio, Carlos L. Paíno, and Antonio S. Herranz

PART IV - FREE RADICALS AND OXIDATIVE STRESS

30. The Protective Action of Nitron-Based Free Radical Traps in Neurodegenerative Diseases235
Robert A. Floyd

31.	Nitric Oxide Actions in the Nervous System	247
	<i>Valina L. Dawson and Ted M. Dawson</i>	
32.	An Inflammatory Role for Nitric Oxide during Experimental Meningitis in the Rat	263
	<i>Kathleen M. K. Boje</i>	
33.	Oxidative Stress Plays a Role in the Pathogenesis of Familial Sporadic and Amyotrophic Lateral Sclerosis	275
	<i>Catherine Bergeron, Connie Petrunka, and Luitgard Weyer</i>	
34.	Modulation of the Mitochondrial Anti-Oxygen Radical Defense of Rat Astroglial Cells in Culture	281
	<i>Emmanuel Pinteaux, Jean-Christophe Copin, Marc Ledig, and Georges Tholey</i>	
35.	Oxygen Radical-Mediated Oxidation of Serotonin: Potential Relationship to Neurodegenerative Diseases	285
	<i>Monika Z. Wrona, Zhaoliang Yang, Jolanta Waskiewicz, and Glenn Dryhurst</i>	
36.	Dopamine Covalently Modifies DNA in a Tyrosinase-Enhanced Manner	299
	<i>Alan H. Stokes, Buddy G. Brown, Chin K. Lee, David J. Doolittle, and Kent E. Vrana</i>	
37.	Brain [52FE]-Transferrin Uptake in Patients with Alzheimer's Disease and Healthy Subjects: A Positron Emission Tomography (PET) Study	305
	<i>Angelo Antonini, Albert Wettstein, Regula Schmid, and Klaus L. Leenders</i>	

PART V - CALCIUM TRANSPORT AND REGULATORY PROTEINS

38.	β APP Metabolites, Radicals, Calcium, and Neurodegeneration: Novel Neuroprotective Strategies	309
	<i>Mark P. Mattson, Steven W. Barger, Katsutoshi Furukawa, Robert J. Mark, Virginia L. Smith-Swintosky, L. Creed Pettigrew, and Annadora J. Bruce</i>	
39.	Channel Formation by a Neurotoxic Beta Amyloid Peptide, $A\beta_{25-35}$	331
	<i>Meng-chin Lin, Tajib Mirzabekov, and Bruce Kagan</i>	
40.	Cysteine String Proteins: Presynaptic Function and Dysfunction	337
	<i>Cameron B. Gundersen, Joy A. Umbach, and Alessandro Mastrogiacono</i>	

41.	AIDS Dementia as a Form of Excitotoxicity: Potential Therapy with NMDA Open-Channel Blockers and Redox Congeners of Nitric Oxide	341
	<i>Stuart A. Lipton</i>	
42.	Calcium, AMPA/Kainate Receptors, and Selective Neurodegeneration	357
	<i>John H. Weiss, Hong Z. Yin, Sean G. Carriedo, and You M. Lu</i>	
43.	Diltiazem and MK-801 but not APV Act Synergistically to Protect Rat Hippocampal Slices against Hypoxic Damage	365
	<i>Avital Schurr, Ralphiel S. Payne, and Benjamin M. Rigor</i>	
44.	Intracellular Calcium Stores and Ischemic Neuronal Death	371
	<i>David C. Perry, Huafeng Wei, Wenlin Wei, and Dale E. Bredesen</i>	
45.	Calpain, a Catabolic Mediator in Spinal Cord Trauma	377
	<i>Naren L. Banik, Denise Lobo-Matzelle, Gloria Gantt-Wilford, and Edward L. Hogan</i>	

PART VI - GROWTH REGULATION AND APOPTOSIS

46.	Detection of Single and Double Strand DNA Breaks during Excitotoxic or Apoptotic Neuronal Cell Death	383
	<i>Michel Didier, Sherry Bursztajn, and Stephen A. Berman</i>	
47.	Signalling for Survival: Potential Applications of Signal-Transduction Therapies for Suppression of Apoptosis in the Nervous System	393
	<i>Aviva M. Tolkovsky</i>	
48.	Ciliary Neurotrophic Factor (CNTF): Possible Implications in the Pathogenesis of Amyotrophic Lateral Sclerosis	401
	<i>Richard W. Orrell, Russell J.M. Lane, and Jackie S. de Belleruche</i>	
49.	Neuronal Differentiation of PC12 Cells in the Absence of Extracellular Matrix Adhesion Induces Apoptosis	405
	<i>Herbert W. Harris</i>	
50.	Excitable Membrane-Derived Lipid Mediators: Glutamate Release and Regulation of Gene Expression	409
	<i>Nicolas G. Bazan, Miriam Kolko, and Geoffrey Allan</i>	
51.	Bcl-2 Protection of Mitochondrial Function following Chemical Hypoxia/Aglycemia	427
	<i>Anne N. Murphy, Dale E. Bredesen, and Gary Fiskum</i>	
52.	Biochemical Characteristics of Oxygen-Induced and Low K ⁺ Medium-Induced Apoptotic Neuronal Death	435
	<i>Yasushi Enokido, Takekazu Kubo, Noboru Sato, Yasuo Uchiyama, and Hiroshi Hatanaka</i>	

53.	Mechanisms of Selective Neuronal Vulnerability to 1-Methyl-4-Phenylpyridinium (MPP+) Toxicity	439
	<i>Patricia A. Trimmer, Jeremy B. Tuttle, Jason P. Sheehan, and James P. Bennett, Jr.</i>	
54.	Potential Role of Hyperactivation of Signal Transduction Pathways in Alzheimer's Disease: Protein Kinase C Regulates PHF-like Phosphorylation of Tau within Neuronal Cells	447
	<i>Thomas B. Shea, John J. Boyce, and Corrine M. Cressman</i>	
	Index	469