This volume deals with nervous system injuries, repair and therapeutic approaches, and some neurodegenerative diseases not covered in other volumes of the Handbook. How current research changed our understanding of the epidemiology, pathophysiological mechanisms, cell demise leading to loss of function, whether in traumatic brain injury (TBI), spinal cord injury (SCI), or neurodegenerative diseases, and therapeutic approaches to ameliorate dysfunction of these devastating conditions are emphasized. Central nervous system (CNS) trauma (TBI and SCI combined) is one of the major causes of death in the United States and is one of the main killers (perhaps number one) of the young people below the mid-thirties. While TBI kills the majority of these victims, SCI, depending on the severity, leads to lifelong disability and despair at the time of their highest productivity. One of the most important areas in medicine now is the repair of the damaged tissue of injured brain and spinal cord so the function may be improved or restored. The major problem facing clinicians and researchers is the failure of brain and spinal cord to repair or regenerate the damaged areas, perhaps because these organs are so overly complex, functionally and structurally, containing different cell types, fiber pathways, messengers (neurochemicals), and other elements. In addition, damage to tissue in trauma is caused by not one, but many multi-destructive pathways.

In spite of this complexity, neuroscience has made significant advances in understanding of the delayed injury process (i.e. secondary damage), providing opportunities for target-based therapeutic intervention, improved imaging, blood vessel growth, regeneration, and tissue transplantation, including stem cell application. During the last two decades of vigorous research, scientists have identified several secondary injury factors, although many still remain unknown, that damage or destroy injured brain and spinal cord. They are trying to understand how these factors, including increased calcium and calcium-mediated events (namely lipases and proteases), free radicals, excitotoxicity, alterations in structural integrity of cell membrane, axonal damage in white matter, and reduction in blood flow, lead to apoptosis and necrosis of neurons and myelinating oligodendrocytes and ultimately destruction of tissue following injury. Although better imaging and pharmacological therapy using methylprednisolone and surgical manipulation, particularly in SCI, have slightly improved the clinical management of patients, we are still nowhere near acknowledging any real recovery of function. Yes, advances have been made over the years. Yet, we know little and much needs to be learned about how to reduce disability and restore function in TBI and SCI. Therefore, vigorous research is needed in other areas, including regeneration, protection of cells and preservation of axons, imaging by distension tensor imaging (DTI) and restoring blood supply that may help further improve function following TBI and SCI. Some of these detrimental pathways may be common to neurodegenerative disease such as Alzheimer’s disease (AD), Parkinson’s disease (PD), multiple sclerosis (MS), and amyotrophic lateral sclerosis (ALS), which will also benefit from this research attenuating dysfunction.

The chapters included in this volume clearly demonstrate the progress made in understanding the destructive mechanisms involved not only in TBI and SCI, but also in other neurodegenerative and neoplastic diseases. The work on enzymes (proteases and lipases), lipids, proteins, free radicals, and others have established roles as significant mediators of cell damage and disintegration of membrane architecture in diseases and injuries. We can learn more about how the blood-brain barrier (BBB) or spinal cord-blood barrier are maintained so that foreign elements can not enter and provide protection, how elements enter the CNS through the barrier that has been compromised in injury and inflammatory diseases (e.g. MS, AD, PD), and how to kill brain tumor cells by increasing the permeability. The contributors in this volume discussed the importance of microcirculation in terms of blood flow through microvessel growth following...
injury or in ischemic conditions, controlling angiogenesis in CNS tumor, and maintaining the BBB function. Other chapters have described cell death and degenerative processes in macular degeneration and diabetic retinopathy as well as in autoimmune diseases like optic neuritis and experimental allergic encephalomyelitis (EAE), which is the animal model of MS. Several chapters have elaborated on diseases, including adrenoleukodystrophy (a secondary demyelinating disease), peripheral neuropathy, and hyperammonemia. At the cellular level, white matter degeneration, including axon and cell death in CNS injuries as well as in neurodegenerative disease, has been emphasized. Although there is little or no CNS repair or regeneration in the brain, a chapter has been devoted to elucidate the potential therapeutic aspects of utilizing stem cell transplantation. Finally, chapters have been included on the rehabilitation of SCI patients and current management and ongoing clinical trials for treatment. The studies described in these chapters have also emphasized the importance of therapeutic strategies to combat dysfunction in injuries and diseases.

Our knowledge of the pathophysiology of CNS injuries and diseases has increased over the years only due to the tremendous advances that have been made in many areas of basic neuroscience research. The exciting findings of all contributors to this volume emphasize one most important aspect – applying basic neuroscience to the understanding of clinical problems of patients with diseases and injuries. Needless to say, although we have made substantial progress in some areas, further research is vital in areas such as regeneration/repair, axonal guidance, preservation and protection of cells and their processes, genetic regulation, growth factors, transplantation, and stem cell biology for attenuation of dysfunction through development of new therapeutic strategies. The advances made thus far on scientific research give us, the researchers, hope that further progress will help restore function and cure CNS diseases in the future.

We thank our authors for their excellent contributions to this volume. We also thank Ms. Denise Matzelle and Ms. Kristine Immediato for their patience and efforts in making this volume into its final form.

Naren L. Banik and Swapan K. Ray
# Table of Contents

<table>
<thead>
<tr>
<th>Chapter</th>
<th>Title</th>
<th>Authors</th>
</tr>
</thead>
<tbody>
<tr>
<td>Preface</td>
<td></td>
<td>v</td>
</tr>
<tr>
<td>xi</td>
<td>Contributors</td>
<td></td>
</tr>
<tr>
<td>1</td>
<td>Brain Tumor Angiogenesis</td>
<td>S. Lakka · J. S. Rao</td>
</tr>
<tr>
<td>13</td>
<td>Adrenoleukodystrophy: Molecular, Metabolic, Pathologic, and Therapeutic Aspects</td>
<td>M. A. Contreras · I. Singh</td>
</tr>
<tr>
<td>43</td>
<td>Hyperammonemia</td>
<td>V. Felipo</td>
</tr>
<tr>
<td>71</td>
<td>Glutamate and Cytokine-Mediated Alterations of Phospholipids in Head Injury and Spinal Cord Trauma</td>
<td>A. A. Farooqui · L. A. Horrocks</td>
</tr>
<tr>
<td>91</td>
<td>Kynurenines in the Brain: Preclinical and Clinical Studies, Therapeutic Considerations</td>
<td>C. Kiss · L. Vecsei</td>
</tr>
<tr>
<td>107</td>
<td>Neurofibromatosis Type I: From Genetic Mutation to Tumor Formation</td>
<td>S. L. Thomas · G. H. De Vries</td>
</tr>
<tr>
<td>131</td>
<td>Amyloid and Neurodegeneration: Alzheimer's Disease and Retinal Degeneration</td>
<td>A. Prakasam · C. Venugopal · A. Suram · J. Pacheco-Quinto · Y. Zhou · M. A. Pappolla · K. A. Sharpe · D. K. Lahiri · N. H. Greig · B. Rohrer · K. Sambamurti</td>
</tr>
<tr>
<td>165</td>
<td>Diabetic Retinopathy</td>
<td>E. Bowie · C. E. Crosson</td>
</tr>
<tr>
<td>179</td>
<td>Neurotransmitters and Electrophysiology in Traumatic Brain Injury</td>
<td>C. E. Dixon · A. E. Kline</td>
</tr>
</tbody>
</table>

© 2009 Springer Science+Business Media, LLC.
10 Free Radicals and Neuroprotection in Traumatic Brain and Spinal Cord Injury .............................................................. 203
   E. D. Hall

11 Neuroimmunology of Paraproteinemic Neuropathies ...................... 229
   A. A. Ilyas

12 Proteolytic Mechanisms of Cell Death in the Central Nervous System ...... 249
   S. F. Larner · R. L. Hayes · K. K. W. Wang

13 Nitric Oxide in Experimental Allergic Encephalomyelitis .................. 281
   S. Brahmachari · K. Pahan

14 The Blood–Brain Barrier—Biology, Development, and Brain Injury .......... 303
   C. L. Keogh · K. R. Francis · V. R. Whitaker · L. Wei

15 Phospholipase A\textsubscript{2} in CNS Disorders: Implication on Traumatic Spinal Cord and Brain Injuries ......................... 321
   N.-K. Liu · W. Titsworth · X.-M. Xu

16 Axonal Damage due to Traumatic Brain Injury ................................ 343
   K. E. Saatman · G. Serbest · M. F. Burkhardt

17 Blood–Central Nervous System Barriers: The Gateway to Neurodegeneration, Neuroprotection and Neuroregeneration .................. 363
   H. S. Sharma

18 Engineered Antibody Fragments as Potential Therapeutics against Misfolded Proteins in Neurodegenerative Diseases .................. 459
   E. Kvam · A. Messer

19 Pathogenesis and Treatment of HIV-associated Dementia: Recent Studies in a SCID Mouse Model ........................................... 471
   W. R. Tyor

20 Stem Cell Transplantation Therapy for Neurological Diseases ................ 491
   X.-Y. Hu · J.-A. Wang · K. Francis · M. E. Ogle · L. Wei · S. P. Yu

21 Ubiquitin/Proteasome and Autophagy/Lysosome Pathways: Comparison and Role in Neurodegeneration .................................. 513
   N. Myeku · M. E. Figueiredo-Pereira

22 Experimental Autoimmune Encephalomyelitis in the Pathogenesis of Optic Neuritis: Is Calpain Involved? ................................. 525
   M. K. Guyton · A. W. Smith · S. K. Ray · N. L. Banik

23 Protein Carbonylation in Neurodegenerative and Demyelinating CNS Diseases .......................................................... 543
   O. A. Bizzozero
| 24 | Clinical Considerations in Translational Research with Chronic Spinal Cord Injury: Intervention Readiness and Intervention Impact | 563 |
|    | J. S. Krause · S. D. Newman · S. S. Brotherton |
| 25 | Estrogen as a Promising Multi-Active Agent for the Treatment of Spinal Cord Injury | 581 |
|    | E. A. Sribnick · D. D. Matzelle · S. K. Ray · N. L. Banik |
| 26 | Immunotherapy Strategies for Lewy Body and Parkinson’s Diseases | 599 |
|    | L. Crews · B. Spencer · E. Masliah |
| 27 | Clinical Outcomes After Spinal Cord Injury | 615 |
|    | J. S. Krause · S. D. Newman |
| 28 | Spinal Cord Injury – A Clinical Perspective | 633 |
|    | A. Varma |
| 29 | Cubing the Brain: Mapping Expression Patterns Genome-Wide | 649 |
|    | M. H. Chin · D. J. Smith |

Index | 657
Contributors

N. L. Banik
Department of Neurosciences
Division of Neurology
Medical University of South Carolina,
96 Jonathan Lucas Street, Suite 309
Charleston, SC 29425, USA
E-mail: baniknl@musc.edu

O. A. Bizzozero
Department of Cell Biology and Physiology,
University of New Mexico School of Medicine,
1 University of New Mexico, MSC08 4750,
Albuquerque, NM 87131, USA
E-mail: obizzozero@salud.unm.edu

E. Bowie
Department of Ophthalmology,
Storm Eye Institute,
Medical University of South Carolina,
Charleston, SC, USA

S. Brahmachari
Department of Neurological Sciences,
Rush University Medical Center, Chicago,
Illinois 60612, USA

S. S. Brotherton
Spinal Cord Injury Outcomes Research Group,
Medical University of South Carolina,
Charleston, SC, USA

M. F. Burkhardt
Spinal Cord and Brain Injury Research Center,
Department of Physiology, University of Kentucky,
Lexington, KY 40536, USA

M. H. Chin
Department of Human Genetics,
David Geffen School of Medicine at UCLA,
Los Angeles, CA 90095, USA

M. A. Contreras
Charles Darby Children’s Research Institute,
Department of Pediatrics,
Medical University of South Carolina,
Charleston, SC 29425, USA

L. Crews
Department of Pathology
University of California San Diego, La Jolla,
CA 92093-0624, USA

C. E. Crosson
MUSC – Storm Eye Institute, 167 Ashley Ave. Room 511,
Charleston, SC 29425, USA
E-mail: crossonc@musc.edu

G. H. De Vries
Research Service, Edward Hines Jr. V.A. Hospital,
5th Avenue and Roosevelt Road,
Hines, IL 60141, USA
E-mail: George.Devries@med.va.gov

C. E. Dixon
Department of Neurosurgery,
University of Pittsburgh, Safar Center,
201 Hill Building, 3434 Fifth Avenue,
Pittsburgh, PA 15260, USA
E-mail: dixonec@upmc.edu

A. A. Farooqui
Department of Molecular and Cellular
Biochemistry, 1645 Neil Avenue,
The Ohio State University,
Columbus, Ohio 43210-1218, USA
E-mail: farooqui.1@osu.edu

V. Felipo
Laboratory of Neurobiology,
Centro de Investigación Príncipe,
Avda del Saler, 16, 46013 Valencia, Spain
E-mail: vfelipo@ochoa.fib.es

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X.-M. Xu
James R Petersdorf Professor,
Department of Neurological Surgery,
University of Louisville School of Medicine,
511 S. Floyd Street, MDR 616, Louisville,
KY 40292, USA
E-mail: xmxu0001@louisville.edu

S. P. Yu
Department of Pharmaceutical and Biological Sciences,
280 Calhoun Street,
Medical University of South Carolina,
Charleston, SC 29464, USA
E-mail: yusp@musc.edu

Y. Zhou
MUSC, Neurosciences,
173 Ashley Avenue, BSB 403, Charleston,
SC 29425, USA