

Contributors	ix
Editors	xvi
Preface	xvii

## **PART A. CENTRAL NERVOUS SYSTEM**

### **Section I. Metabolic Diseases**

**Hugo W. Moser, MD**

- |   |    |
|---|----|
| 1. Lysosomal Disorders of the Nervous System    | 1  |
| Steven U. Walkley, DVM, PhD                     |    |
| 2. Neurobiology of Peroxisomal Disorders        | 19 |
| James M. Powers, MD                             |    |
| 3. Creatine Deficiency Syndromes                | 33 |
| Peter W. Schütz, MD, and Sylvia<br>Stöckler, MD |    |
| 4. Leukodystrophies                             | 43 |
| Shoji Tsuji                                     |    |

### **Section II. Neurodegenerative Disorders**

**Gregor K. Wenning, MD, PhD**

- |  |     |
|--|-----|
| 5. Parkinson's Disease   | 51  |
| Néstor Gálvez-Jiménez, MD, MSc, MHSA, FACP   |     |
| 6. Alzheimer's Disease   | 69  |
| Kurt A. Jellinger, MD  |     |
| 7. Multiple System Atrophy   | 83  |
| Carlo Colosimo, MD; Felix Geser, MD, PhD;<br>Eduardo E. Benarroch, MD, DSci; and Gregor K.<br>Wenning, MD, PhD |     |
| 8. Olivopontocerebellar Atrophy (OPCA)   | 95  |
| José Berciano  |     |
| 9. Neurobiology of Progressive Supranuclear<br>Palsy   | 105 |
| Pratap Chand, DM, FRCP, and<br>Irene Litvan, MD  |     |

**Section III. Genetic Diseases**  
**Christopher Gomez, MD, PhD**

- |  |     |
|--|-----|
| 10. Protein Aggregation Disorders  | 111 |
| Tiago Fleming Outeiro, PhD; Pamela J. McLean, PhD; and Bradley T. Hyman, MD, PhD |     |
| 11. RNA-Based Disorders of Muscle and Brain                                      | 125 |
| Paul J. Hagerman, MD, PhD  |     |
| 12. Ion Channel Disorders  | 135 |
| Alan L. Goldin, MD, PhD  |     |
| 13. Spinocerebellar Ataxia Type 1  | 149 |
| Harry T. Orr, PhD  |     |
| 14. Mitochondrial Genetic Diseases   | 157 |
| Alice Wong, PhD, and Gino Cortopassi, PhD  |     |

**Section IV. Neuroimmunological Disorders**  
**Anthony T. Reder, MD**

- |   |     |
|---|-----|
| 15. Paraneoplastic Neurological Disorders   | 163 |
| Steven Vernino, MD, PhD, and Josep Dalmau, MD, PhD  |     |
| 16. Systemic Lupus Erythematosus: Descriptive Past and Mechanistic Future                             | 171 |
| Czeslawa Kowal, PhD; Cynthia Aranow, MD; Meggan Mackay, MD; Betty Diamond, MD; and Bruce T. Volpe, MD |     |
| 17. Progressive Multifocal Leukoencephalopathy  | 185 |
| Benjamin Brooks, MD   |     |
| 18. Immunopathogenesis of Multiple Sclerosis  | 197 |
| Bernhard Hemmer, MD; Nicole Töpfner; and Hans-Peter Hartung, MD                                       |     |
| 19. Immune-Mediated Neuropathies  | 205 |
| Michael Schroeter, MD; Bernd C. Kieseier, MD; Hubertus Köller, MD; and Hans-Peter Hartung, MD         |     |
| 20. Hashimoto Encephalopathy  | 217 |
| Ji Y. Chong, MD   |     |

## **Section V. Cerebrovascular Diseases**

**Lewis B. Morgenstern, MD**

- |  |     |
|--|-----|
| 21. Vascular Cognitive Impairment<br>Velandai Srikanth, PhD; Michael M. Saling, PhD;<br>and Amanda G. Thrift, PhD                                      | 223 |
| 22. Cardioembolism<br>Karen Furie, MD, MPH   | 235 |
| 23. Clinical and Neurobiological Aspects of Stroke<br>Recovery<br>Bruce T. Volpe, MD, and Rajiv R.<br>Ratan, MD, PhD                                   | 241 |
| 24. Nonatherosclerotic Cerebral<br>Vasculopathies<br>Rima M. Dafer, MD, MPH, and<br>Jose Biller, MD  | 255 |
| 25. Subarachnoid Hemorrhage<br>David Palestrant, MD, and E. Sander<br>Connolly, Jr., MD  | 265 |
| 26. Cerebral Ischemia: Molecular Mechanisms<br>and Protective Therapies<br>Kenneth R. Wagner, PhD  | 271 |
| 27. Intracerebral Hemorrhage and Intraventricular<br>Hemorrhage–Induced Brain Injury<br>Richard F. Keep, PhD; Guohua Xi, MD; and<br>Julian T. Hoff, MD | 281 |

## **Section VI. Paroxysmal Disorders**

**Timothy A. Pedley, MD**

- |   |     |
|---|-----|
| 28. Idiopathic Generalized Epilepsy<br>Jose-Luis Perez-Velasquez, PhD; Edward H.<br>Bertram, III, MD; and O. Carter Snead, III, MD                    | 289 |
| 29. Paroxysmal Dyskinesia<br>Laurent Vercueil, MD, PhD; Anne de Saint<br>Martin, MD; and Edouard Hirsch, MD   | 297 |
| 30. Myoclonus<br>Pietro Mazzoni, MD, PhD, and<br>Samay Jain, MD   | 305 |
| 31. Channelopathies of the Nervous System<br>James C. Cleland, MBChB, and Robert C.<br>Griggs, MD   | 319 |
| 32. Migraine as a Cerebral Ionopathy with<br>Abnormal Central Sensory Processing<br>Michel D. Ferrari, MD, PhD, and Peter J.<br>Goadsby, MD, PhD, DSc | 333 |
| 33. Temporal Lobe Epilepsy<br>Helen E. Scharfman, PhD, and Timothy A.<br>Pedley, MD   | 349 |

## **Section VII. Neoplastic Diseases**

**John J. Laterra, MD, PhD**

- |   |     |
|---|-----|
| 34. Central Nervous System Metastases<br>Robert J. Weil, MD, FCAS | 371 |
|---|-----|

- |   |     |
|---|-----|
| 35. Meningioma  | 381 |
| Katrin Lamszus, MD; Christian Hagel, MD;<br>and Manfred Westphal, MD                          |     |
| 36. Primary Central Nervous System<br>Lymphoma  | 395 |
| Maciej Mrugala, MD, PhD, MPH; Anne<br>Newcomer; and Tracy Batchelor, MD, MPH                  |     |
| 37. Neurofibromatosis 1   | 413 |
| Linda Piersall, MS, and David H. Gutmann,<br>MD, PhD  |     |
| 38. Medulloblastoma and Primitive<br>Neuroectodermal Tumors                                   | 425 |
| Said Elshihabi, MD, and James T.<br>Rutka, MD, PhD  |     |
| 39. Glioma  | 433 |
| Anders I. Persson, PhD; QiWen Fan, PhD;<br>Joanna J. Phillips, PhD; and William A. Weiss, PhD |     |

### **Section VIII. Infectious Diseases**

**Richard T. Johnson, MD, FRCP**

- |  |     |
|--|-----|
| 40. Bacterial and Fungal Infections of the<br>Nervous System   | 445 |
| Thomas P. Bleck, MD, FCCM  |     |
| 41. Parasitic Infections   | 453 |
| Ana-Claire Meyer, MD, and Gretchen L.<br>Birbeck, MD, MPH  |     |
| 42. Prion Diseases   | 473 |
| Adriano Aguzzi, MD, PhD, DVM, hc, FRCP,<br>FRCPATH; Frank L. Heppner, MD; Ingo M.<br>Westner, MD; and Markus Glatzel, MD |     |
| 43. Central Nervous System Viral Infections:<br>Clinical Aspects and Pathogenic<br>Mechanisms                            | 485 |
| Christopher Power, MD, FRCP (C), and Farshid<br>Noorbakhsh, MD, PhD  |     |

### **Section IX. Motor Neuron Diseases**

**Eva L. Feldman, MD, PhD**

- |  |     |
|--|-----|
| 44. Spinal Muscular Atrophy  | 501 |
| Charlotte J. Sumner, MD, and Kenneth H.<br>Fischbeck, MD                       |     |
| 45. Amyotrophic Lateral Sclerosis–Like Syndromes<br>Associated with Malignancy | 513 |
| Zachary Simmons, MD  |     |
| 46. Amyotrophic Lateral Sclerosis: Idiopathic<br>and Inherited                 | 521 |
| Nicholas J. Maragakis, MD, and Jeffrey D.<br>Rothstein, MD, PhD                |     |
| 47. Hereditary Spastic Paraplegia and Primary<br>Lateral Sclerosis             | 537 |
| Philip A. Wilkinson, BSc, MBBS, MRCP, and<br>Michael Swash, MD, FRCP, FRCPATH  |     |

48. Poliomyelitis 545  
Eric J. Sorenson, MD
49. Spinobulbar Muscular Atrophy (Kennedy's Disease) 553  
Jeffrey D. Zajac, MBBS, PhD, FRACP, and Karen J. Greenland, BSc, (Hons) PhD

## **Section X. Malformations and Developmental Disorders**

**Michael V. Johnston, MD**

50. Neurobiology of Genetic Mental Retardation 563  
Walter E. Kaufmann, MD; John C. Carter; Irena Bukelis; and David N. Lieberman, MD, PhD
51. Cerebral Palsy 575  
Alexander H. Hoon, Jr., MD, MPH
52. Autism 581  
Martha R. Herbert, MD, PhD
53. Neurobiology of Dyslexia 593  
Sheryl L. Rimrodt, MD, and Laurie E. Cutting, PhD
54. Neonatal Brain Injuries 599  
Steven P. Miller, MD, MAS, and Donna M. Ferriero, MD, MS
55. Spina Bifida 611  
Stephen L. Kinsman, MD
56. Circuits to Synapses: The Pathophysiology of Tourette Syndrome 619  
Harvey S. Singer, MD, and Kendra Harris, MSc
57. Attention-Deficit Hyperactivity Disorder 631  
Paul H. Lipkin, MD, and Stewart Mostofsky, MD
58. Congenital Hydrocephalus 641  
Stephen L. Kinsman, MD

## **Section XI. Neurologic Manifestations of Medical Diseases**

**John J. Caronna, MD**

59. Neurological Manifestations of Hematological Disease 649  
Babette B. Weksler, MD
60. Neurological Manifestations of Renal Disease 659  
Ajay K. Singh, MB, MRCP, and Radhika Bhatia, MD
61. Diabetes and Endocrine Disorders 669  
Rodica Pop-Busui, MD, PhD; Zachary London, MD; and Aaron Kellogg, BS
62. Mechanisms and Consequences of Central Nervous System Hypoxia 681  
Meredith L. Turetz, MD, and Ronald G. Crystal, MD

63. Neurological Manifestations of  
Gastrointestinal and Hepatic Diseases 689  
Brain P. Bosworth, MD, and Brian R.  
Landzberg, MD
64. Neurosarcoidosis 703  
John J. Caronna, MD

**Section XII. Sleep Disorders**  
**Emmanuel Mignot, MD, PhD**

65. REM Sleep Behavior Disorder 709  
Carlos H. Schenck, MD, and Mark W.  
Mahowald, MD
66. Neurobiology of Narcolepsy and  
Hypersomnia 715  
Emmanuel Mignot, MD, PhD, and Jamie M.  
Zeitzer, PhD
67. Restless Legs Syndrome and Periodic Limb  
Movements in Sleep 723  
Richard P. Allen, PhD
68. Neurobiology of Insomnia 735  
Michael L. Perlis, PhD; Wilfred R.  
Pigeon, PhD; and Sean Patrick Andrews  
Drummond, PhD

**Section XIII. Substance Abuse**  
**and Basic Toxicology**  
**John C. M. Brust, MD**

69. Organic Chemicals 745  
John L. O'Donoghue, VMD, PhD, DABT
70. Metals 759  
Luigi Manzo, MD
71. Neurobiology of Drug Addiction 771  
Timothy P. Condon, PhD, and Curtis W.  
Balmer, PhD

**Section XIV. Imaging the Nervous System**  
**John C. Mazziotta, MD, PhD**

72. Assessment of Neurobiological Diseases  
with Magnetic Resonance Spectroscopy 781  
Jeffrey R. Alger, PhD
73. Magnetic Resonance Imaging 793  
John A. Detre, MD
74. Neurovascular Computed Tomography  
Angiography 801  
Stuart R. Pomerantz, MD,  
and Michael H. Lev, MD
75. PET Imaging in Parkinson's Disease and Other  
Neurodegenerative Disorders 821  
Vijay Dhawan, PhD, and David  
Eidelberg, MD

76. Single-Photon Emission Computed Tomography 829  
Joseph C. Masdeu, MD, PhD
77. Functional Magnetic Resonance Imaging 839  
Gereon R. Fink, MD, PhD

## **PART B. PERIPHERAL NERVOUS SYSTEM**

### **Section XV. Peripheral Neuropathies**

**James W. Russell, MD**

78. Impaired Glucose Regulation and Neuropathy 849  
James W. Russell, MD, MS, FRCP;  
A. G. Smith, MD; and J. R. Singleton, MD
79. Acquired Inflammatory Demyelinating and Axonal Neuropathies 859  
James W. Teener, MD, and James W. Albers, MD, PhD
80. Toxic and Drug-Induced Neuropathies 871  
Guido Cavaletti, MD
81. Inherited Peripheral Neuropathies 885  
Angelo Schenone, MD, and Lucilla Nobbio, PhD
82. Neurological Manifestations of Vasculitis 901  
Safwan S. Jaradeh, MD
83. Neuropathies Associated with Infections 913  
Paul Twydell, DO, and David N. Herrmann, MBCh

### **Section XVI. Myopathies and Neuromuscular Junction Disorders**

**Charles A. Thornton, MD**

84. Muscular Dystrophies 925  
Leland E. Lim, MD, PhD; Charles A. Thornton, MD;  
and Thomas A. Rando, MD, PhD

- |   |     |
|---|-----|
| 85. Myasthenia Gravis and Myasthenic Syndromes              | 935 |
| Angela Vincent, MA (MB, BS, MSc Lond.),<br>FRCPATH, FMedSci |     |
| 86. Metabolic Myopathies                                    | 947 |
| Michio Hirano, MD   |     |
| 87. Immunobiology of Autoimmune Inflammatory Myopathies     | 957 |
| Marinos C. Dalakas, MD                                      |     |

## **Section XVII. Autonomic Disorders**

**Phillip A. Low, MD**

- |   |     |
|---|-----|
| 88. Central Autonomic Network   | 969 |
| Peter Novak, MD, PhD  |     |
| 89. Autonomic Neuropathies  | 979 |
| Steven Vernino, MD, PhD, and Phillip A.<br>Low, MD                          |     |
| 90. Thermoregulation and Its Disorders                                      | 987 |
| Robert D. Fealey, MD  |     |
| 91. Control of Blood Pressure—Normal and Abnormal                           | 997 |
| Michael J. Joyner, MD; William G. Schrage,<br>PhD; and John H. Eisenach, MD |     |

## **Section XVIII. Pain**

**Kenneth L. Casey, MD**

- |   |      |
|---|------|
| 92. Neoplasm-Induced Pain                             | 1007 |
| Sebastiano Mercadante, MD                             |      |
| 93. Pain Associated with the Autonomic Nervous System | 1021 |
| Wilfrid Jänig   |      |
| 94. Postherpetic Neuralgia                            | 1031 |
| Misha-Miroslav Backonja, MD                           |      |
| 95. Central Post-Stroke Pain                          | 1039 |
| David Bowsher, MD, ScD, PhD, FRCPEd,<br>FRCPATH       |      |
| Index   | 1047 |