



Metal Ions and Neurodegenerative Disorders

Editor

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Preface

Many metal ions are as essential to life (Williams and Fausto da Silva, 1996) as other constitutive elements within living matter, such as fats, carbohydrates, and proteins. Today, research into the role of metal ions is of particular interest to nutritional sciences, which have discovered that a wide range of common pathologies are caused by a lack of metalloions.

Physiologists maintain that the constitutive and functional roles of some metal ions (such as Na, K, Ca, Mg, Fe, Co, Mn, Cu, and Zn) are vital to the smooth functioning of cells, as well as various organs and tissues. Toxicologists have performed indepth research into the harmful properties of some metal ions (such as Al, Cd, Hg, and Pb), and environmental disasters, such as Camelot and Minamata, have enabled them to be studied on a vast scale. However, until recently, little attention had been paid to the role of metal ions as etiopathogenic agents for some neurodegenerative diseases such as Alzheimer's, Parkinson's, and Lateral Amyotrophic Sclerosis, to name but three.

Today, a new field, *metalloneurochemistry*, is breaking fresh ground on account of the burgeoning number of studies which show the importance of metal ions as etiopathogenic factors or co-factors (Bush, 2000; Zatta, 2001). From this point of view, the concept of *metallochaperones* is comparatively new in that molecules that could be used for this function were only discovered in the mid-1990s (Halloran and Culotta, 2000).

Theories that suggest metal ions are vital etiological agents in neurodegenerative diseases are finding it hard to break into mainstream thought not only on account of the technical and conceptual difficulties, but also of the financial complexities of investing in both basic and applied research in order to discover more about the molecular mechanisms that account for the physiopathological action of metalloions.

Chelation therapy is still in the early days of its research into new products that could revolutionize treatment. Two international conferences, *Metals and the Brain: From Neurochemistry to Neurodegeneration* (University of Padova, Italy, 2000 and University of Fez, Morocco, 2002;

see also Zatta, 2001), were held on metals and their role in physiopathology as a sign of their importance.

This book follows the same train of thought as these conferences in order to highlight the unquestionable importance of metal ions to research into the neurochemistry of neurodegenerative diseases. The excellent reputation of the scientists who have contributed to this project bears testimony to the quality of these studies, which we hope can be developed further with a whole host of new research within this field; one which is still in its infancy.

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REFERENCES

- Bush AI. Metals and neuroscience. *Curr Op Chem Biol* 2000; **4**:184–191.
- Halloran TV, Culotta VC. Metallochaperones: An intracellular shuttle service for metal ions. *J Biol Chem* 2000; **275**:25047–25060.
- William RJP, Frausto da Silva JJR. *The Natural Selection of the Chemical Elements*. Oxford: Clarendon Press, 1996.
- Zatta P, editor. Metals and the brain. A special issue. *Brain Res Bull* 2001; **55**:123–325.

Contents

<i>Preface</i>	v
<i>List of Contributors</i>	xi
Chapter 1. Metal-Catalyzed Redox Activity in Neurodegenerative Disease <i>Marta A Taddeo, Mark A Smith, Quan Liu, Craig S Atwood, Lawrence M Sayre, George Perry</i>	1
Chapter 2. Metals Distribution and Regionalization in the Brain <i>Margherita Speziali, Edoardo Orvini</i>	15
Chapter 3. The Olfactory Pathway as a Route of Entry of Metals into the Brain <i>Hans Tjälve, Jonas Tallkvist</i>	67
Chapter 4. Aluminum in Neurological Disorders and Systemic Chelation Therapy <i>Theo P Kruck, Walter J Lukiw</i>	99
Chapter 5. Aluminum and Central Nervous System Morphology in Hemodialysis <i>Erich Reusche</i>	117
Chapter 6. Zinc, Brain, and Aging <i>Eugenio Mocchegiani, Mario Muzzioli, Robertina Giacconi, Tiziana Casoli, Giuseppina DiStefano, Patrizia Fattoretti</i>	139
Chapter 7. Transition Metals, Oxidation, Lipoproteins, and Amyloid- β : Major Players in Alzheimer's Disease <i>Anatol Kontush</i>	183
Chapter 8. Molecular Basis of Copper Transport: Cellular and Physiological Functions of Menkes and Wilson Disease Proteins (ATP7A and ATP7B). <i>David R Kramer, Roxana M Llanos, Julian F B Mercer</i>	207

- Chapter 9. Importance of Copper and Zinc in Alzheimer's Disease and the Biology of Amyloid- β Protein and Amyloid- β Protein Precursor 245
Avi L Friedlich, Xudong Huang, Seiichi Nagano, Jack T Rogers, Lee E Goldstein, Ashley I Bush, Gerd Multhaup, Konrad Beyreuther, Wolfgang Stremmel, Thomas Bayer
- Chapter 10. Copper-Zinc Superoxide Dismutase and Familial Amyotrophic Lateral Sclerosis 263
Moon B Yim, P Boon Chock, Earl R Stadtman
- Chapter 11. Copper and Prion Disease 279
Judyth Sasson, David R Brown
- Chapter 12. Metallothioneins in Neurodegeneration 307
Michael Aschner, William F Silverman, Israel Sekler, Paolo Zatta
- Chapter 13. Iron and Neurodegeneration 323
Stacey L Grab, James R Connor
- Chapter 14. Iron, Neuromelanin, and α -Synuclein in Neuropathogenesis of Parkinson's Disease 343
Kay L Double, Kurt Jellinger, Luigi Zecca, Moussa B H Youdim, Peter Riederer, Manfred Gerlach
- Chapter 15. Iron and Epilepsy 365
Wie-Yi Ong, Benjamin Kian-Chung Ong, Akhlaq A Farooqui, Chuang-Chin Chiueh, James R Connor
- Chapter 16. Role of Iron Metabolism in Multiple Sclerosis 399
Maritha J Kotze, J Nico P De Villiers, Monique G Zaahl, Kathryn J H Robson
- Chapter 17. Manganese Toxicity: A Critical Reappraisal 415
Patrizia Vernole, Maria Morello, Giuseppe Sancesario, Alessandro Martorana, Giorgio Bernardi, Antonella Canini, Palma Mattioli

Chapter 18. Cupric and Mercuric Ions Affect the Structure and Functions of Cell Membranes	427
<i>Mario Suwalsky, Fernando Villena, Hernan Cárdenas, Beryl Norris, Carlos Patricio Sotomayor, Paolo Zatta</i>	
Chapter 19. Influence of Lead Exposure on Brainstem Functions	441
<i>Ombretta Mameli, Marcello Alessandro Caria</i>	
Chapter 20. Neuroprotective Effects of Lithium	467
<i>Sophie Ermidiou-Pollet, Serge Pollet</i>	
Chapter 21. Histopathological Changes in Brain of Uremic Patients on Chronic Hemodialysis	483
<i>Pamela Zambenedetti, Mario Andriani, Maurizio Nordio, Paolo Zatta</i>	
Chapter 22. Clinical Neurotoxicity of Metals and Neurodegenerative Disorders	495
<i>Marcello Lotti</i>	
<i>Index</i>	509