

Foreword

Metals in Alzheimer's Disease

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One hundred years since the description of the first case of Alzheimer's disease (AD), we are still spectators of the devastating blow of this disease paralleling the rapid growth of the aged population. Since for at least 95% of all AD cases there is no clear pattern of inheritance, it is generally believed that interactions of genetic and environmental factors contribute to the etiology of AD.

The hypothetical involvement of some heavy metals, both physiological (Fe, Cu, Zn), and toxic (Al, Mn), in the etiology and pathogenesis of AD has been suggested decades ago. The interest in this hypothesis survived many controversies that have sometimes surrounded circumstantial evidence, and it has grown stronger in recent years, with the advent of modern cellular and molecular techniques and their expanding use in neuroscience. While the possible involvement of aluminum in AD was first suggested in experimental animal studies of neurofibrillary degeneration and was further accredited by the pioneering studies showing the accumulation of aluminum in neurofibrillary tangle-bearing neurons from AD brains, other metals have been linked to AD through their relationship with oxidative stress, by metal-protein associations leading to pathogenetic protein aggregation and metal-catalyzed protein oxidation resulting in protein damage.

This special issue puts forward a set of articles by an international group of metallobiologists. The order of the articles should reflect what we viewed as six categories of papers: comprehensive reviews with a historical flavor (Drs. Savory, Herman, and Ghribi; Drs. Adlard and Bush; Dr. Campbell; Dr. Exley; and Drs. Miu and Benga), methodological

perspectives (Dr. Platt and Drs. Collingwood and Dobson), topical review (Dr. Yokel), integrative genetic and epigenetic reviews and reports (Dr. Atamna; Drs. Connor and Lee; Dr. Dewji; Drs. Dolev and Michaelson), review focused on risk factors (Dr. Solfrizzi et al.), and last, but not least, "benchmark to clinical" review (Dr. Domingo). When we considered the idea of editing this special issue, we thought that it was important to invite contributions from scientists who have emphasized in their work the interactions of aging with both genetic and environmental factors in the etiology and pathogenesis of AD. We are grateful to the authors who accepted our challenge and who have shown in the following articles that metallobiologists working in AD research have been less fascinated with describing end-stage pathognomonic lesions, and more concerned with identifying risk and aggravating factors that might help us better predict, diagnose and hopefully prevent AD in the future.

Like any other special issue, this is only a sample of research from a group of scientists working in an enormous field of study covered by an expanding community of multidisciplinary researchers. We think that the following sample of studies is representative, for their authors are all leaders in this field. However, we also refer the readers to a previous special issue of JAD on a similar theme (vol. 8, no. 2, 2005, edited by P. Zatta).

We thank the scientists who contributed to the final result of this issue as reviewers of the manuscripts. We are particularly grateful to Christopher Exley for encouragement, and George Perry who trusted us with this special issue.