Preface

Alzheimer's disease (AD) has no racial, socioeconomic, or geographic boundaries, since it is the most common cause of dementia in elderly individuals throughout the world.

As people worldwide live to an older age, AD has become a serious ever-growing public health problem. The importance and the scientific challenges of this disease have been well recognized by the neuroscience research community. Approximately 5 % of AD is caused by missense mutations in the gene for either the amyloid β precursor protein (APP) or some of the enzymes (i.e., presenilin-1) involved in its metabolism. However, in its sporadic form, which is the most frequent, the cause(s) remains unknown.

Among different potential mechanisms, the combination of genetic risk factors with abnormal metabolic oxidative reactions in the central nervous system has been consistently implicated in the pathogenesis of the disease, and represents the biological basis for the "oxidative stress hypothesis of AD" which was originally formulated by Markesbery in his article of 1997.

Since then, many studies, ranging from basic research to clinical and epidemiological observations, strongly support what moved from a hypothesis to a certainty: the core role of the slight unbalance between oxidants and antioxidants (redox status) that represents an input for life and, in the meantime, a risk for dysfunction and disease when uncontrolled (oxidative stress). So, after several years from its proposal, it seems appropriate to look and consider all the remarkable advances achieved in understanding the biological complexity and mechanistic relationship between oxidative stress and AD.

In constructing this book, we have tried to draw upon our own experiences and those of our colleagues in order to present the current status of both basic and clinical science research in this specific area.

The authors are expert scientists who are directly involved in the laboratory and clinical research in the field of oxidative metabolism and neurodegenerative diseases with special focus on AD.

The book is divided into three main sections. The first section focuses on new working hypotheses implicating oxidative stress and AD. Its chapters will provide

the reader with insights into the impact that the oxidative stress hypothesis had in neuroscience research (Chap. 1), an overview on the general phenomenon of oxidative stress (Chap. 2), its intricate connection with inflammation (Chap. 3), new experimental evidence involving an old enzyme such as GADPH (Chap. 4), the relationship between mitochondria and Aβ (Chap. 5), and the new role that plasma membrane plays in controlling the cellular redox system (Chap. 6).

The second section reviews some of the cellular and metabolic oxidative mechanisms that have been involved in AD pathogenesis. After focusing on metal dyshomeostasis (Chap. 7) and oxidative posttranslational modification of proteins (Chap. 8), it continues with the analysis of cholesterol oxidative metabolism (Chap. 9), and the provocative theme of brain hypometabolism, oxidative stress, and maternal transmission of AD (Chap. 10), finishing with the role on HPA dysfunction and AD (Chap. 11).

The third section describes the clinical aspects and implications of the oxidative stress hypothesis in the AD neurobiology. In these final chapters the attention is shifted towards the translational aspects of the oxidative stress hypothesis, with the main goal to apply the knowledge accumulated so far into a clinical scenario by looking at preventative as well as therapeutic opportunities derived from it.

The role that diabetes plays in AD pathophysiology will be considered (Chap. 12), and the clinical topics will expand on the current state of the art on peripheral biological measure of oxidative stress in AD (Chap. 13). These two chapters will be followed by the analysis of modifiable environmental risk factors such as nutrition and lifestyle and the risk of AD (Chap. 14), and the intriguing question of the usefulness of nutrients as an important source for antioxidants in preventing cognitive decline (Chap. 15). This section will conclude our editorial effort with an analytical review of the clinical trials that have used antioxidants in mild cognitive impairments and AD (Chap. 16).

No introduction would be complete without a grateful acknowledgement of many friends and colleagues who did the work and wrote the chapters. They are not just experts in their fields but also extraordinary individuals. Thus, without any shadow of doubt this endeavor was enabled by the contributions of many friends, collaborators, and colleagues, without whose enthusiasm and engagement this work could have never been born. An extraordinary link of science and friendship that was really supportive in constructing this book.

While we largely underestimated the devotion and effort necessary on our side at the beginning, we strongly believe that it ultimately yielded an excellent product which fully achieves our original plans. Despite the fact that we confront a continuously evolving topic, where frequent updates would be desirable, if not necessary, we believe in the value of a book like ours that attempts to organize in a snapshot-picture type of work, the enormous amount of literature available in a comprehensive and fulfilling fashion. We are aware of possible gaps, some emerging materials not included, and the ever-rapid evolution of some of the themes highlighted in the book. It is our hope that our colleagues, neurobiologists, neurologists, internists, geriatricians, and other physicians alike will find this compendium a useful guide to this most exciting time in the neurobiology of AD.

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