Neurodegeneration: Metallostatics and Proteostasis
Danilo Milardi and Enrico Rizzarelli (editors)
Copyright Year: 2011
ISBN: 978-1-84973-301-4

Since Alois Alzheimer described the results of his postmortem studies in 1906, significant strides have been made in understanding the pathogenesis of neurodegenerative diseases. The latest advances suggest that deficiencies in protein homeostasis, or proteostasis, may lead to cell dysfunction and disease. This book updates the new key developments in this fast moving field. The traditional views concerning the relationship between the physio-pathological cycles of Copper, Zinc, Iron, Aluminium and the evolution of life, are compared with the new emerging ideas in the neuroscience of metal ions. Topics covered emphasize the importance of metals and oxidation chemistry to neuroscientists as well as providing a wider, multidisciplinary background to chemists who are attracted by these fascinating subjects.

Chapter 9 - The Role of Iron in Neurodegeneration
F. A. Zucca, F. A. Cupaioli and L. Zecca
DOI: 10.1039/9781849733014-00174

Abstract
Iron has a double effect on cells: it is an essential element required for many biological reactions but, on the other hand, its excess could be toxic, resulting in the generation of reactive oxygen species. In this review we discuss how different cell types manage iron homeostasis in order to provide iron where it is needed and avoiding its toxicity. Iron management in the body starts at the level of its absorption through enterocytes, but also involves its utilization in erythroid cells, storage/mobilization in hepatocytes and recycling from macrophages.

The maintenance of appropriate iron homeostasis is also important for brain cells. Here we review more recent hypotheses on mechanisms of brain iron homeostasis under normal conditions: how iron is imported from the blood circulation, redistributed through the brain and stored in neurons and other cells of the central nervous system is described carefully. However, iron accumulation and overload in the brain is commonly associated with neurodegenerative disorders such as Parkinson's (PD) and Alzheimer's diseases (AD): iron accumulates in specific brain regions targeted by these severe diseases, increasing the oxidative-induced neuronal vulnerability. The major risk factor for AD and PD remains brain aging, while genetic components account only for a minor part of these diseases. Iron increases with aging in several brain regions. Mutations in genes encoding proteins involved in iron, leading to iron accumulation, occur in other diseases such as neuroferritinopathy, neurodegeneration with brain iron accumulation, Friedreich's ataxia and aceruloplasminemia. Molecular understanding of iron accumulation in normal, aged and pathological brain may be helpful in identifying new pharmacological targets to improve iron management.
Chapter 8 -
Biological Metals: Metallostasis and Alzheimer's Disease


ISBN: 978-1-84973-301-4
DOI: 10.1039/9781849733014-00152

Abstract

The equilibrium of metal ions is critical for many physiological functions, particularly in the central nervous system, where metals are essential for development and maintenance of enzymatic activities, mitochondrial function, myelination and neurotransmission, as well as learning and memory. Due to their importance, cells have evolved a complex machinery for controlling metal-ion homeostasis. However, disruption of these mechanisms, leading to metallostasis, or absorption of detrimental metals with no known biological function, alters the ionic balance and can result in a disease state, such as those of several neurodegenerative disorders including Alzheimer's disease. Understanding the complex structural and functional interactions of metal ions with the various intracellular and extracellular components of the central nervous system, under normal conditions and during neurodegeneration, is essential for the development of effective therapies. Accordingly, assisting the balance of metal ions back to homeostatic levels has been proposed as a disease-modifying therapeutic strategy for Alzheimer's disease as well as other neurodegenerative diseases.
Title: Neurodegeneration: metallostasis and proteostasis / Danilo Milardi and Enrico Rizzarelli (editors)

Published: [Cambridge] : Royal Society of Chemistry, c2011

Description: xiv, 270 p. : ill. (some col.) ; 24 cm

Series: RSC drug discovery series

Summary: This book covers the latest developments in the understanding the pathogenesis of neurodegenerative diseases

Note: Includes bibliographical references and index

Subject: Nervous system -- Degeneration -- Pathogenesis

Other Name: Milardi, Danilo

OCLC #: 756212712

ISBN: 9781849730501, 1849730504