Towards a unified vision of copper involvement in Alzheimer's disease: a review connecting basic, experimental, and clinical research.

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Abstract
Copper is an essential micronutrient for physiological cell functioning and central nervous system (CNS) development. Indeed, it is a cofactor of many proteins and enzymes in a number of molecular pathways, including energy generation, oxygen transportation, hematopoiesis, cellular growth and metabolism, and signal transduction. This is because it serves as a catalyst of reduction-oxidation (redox) reactions in these processes. When copper is kept under control, bound to special proteins, it yields key properties. However, when it spirals out of control, it is exchanged among small compounds (it is loosely bound to them), and its redox activity makes it dangerous for cell viability, promoting oxidative stress. Copper homeostasis in the CNS is securely synchronized, and perturbations in brain copper levels are known to underlie the pathoetiology of wide spectrum of common neurodegenerative disorders, including Alzheimer's disease. The main objective of this review is to provide some of the most relevant evidence gleaned from recent studies conducted on animal models and humans, and to discuss the evidence as it pertains to a new concept: Aberrant copper metabolism, which appears to have a genetic basis, is a modifiable risk factor accelerating Alzheimer's disease and initiation/progression of cognitive deficits in a percentage of susceptible persons.

KEYWORDS: Alzheimer's disease; ceruloplasmin; copper; metal; subtype

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