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Beta-amyloidolysis and glutathione in Alzheimer's disease

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Abstract

In this review, we hypothesized the importance of the interaction between the brain glutathione (GSH) system, the proteolytic tissue plasminogen activator (t-PA)/plasminogen/ plasmin system, regulated by plasminogen activator inhibitor (PAI-1), and neuroserpin in the pathogenesis of Alzheimer's disease. The histopathological characteristic hallmark that gives personality to the diagnosis of Alzheimer's disease is the accumulation of neurofibroid tangles located intracellularly in the brain, such as the protein tau and extracellular senile plaques made primarily of amyloidal substance. These formations of complex etiology are intimately related to GSH, brain protective antioxidants, and the proteolytic system, in which t-PA plays a key role. There is scientific evidence that suggests a relationship between aging, a number of neurodegenerative disorders, and the excessive production of reactive oxygen species and accompanying decreased brain proteolysis. The plasminogen system in the brain is an essential proteolytic mechanism that effectively degrades amyloid peptides ("beta-amyloidolysis") through action of the plasmin, and this physiologic process may be considered to be a means of prevention of neurodegenerative disorders. In parallel to the decrease in GSH levels seen in aging, there is also a decrease in plasmin brain activity and a progressive decrease of t-PA activity, caused by a decrease in the expression of the t-PA together with an increase of the PAI-1 levels, which rise to an increment in the production of amyloid peptides and a lesser clearance of them. Better knowledge of the GSH mechanism and cerebral proteolysis will allow us to hypothesize about therapeutic practices.

Keywords: Alzheimer's disease; PAI-1; glutathione; plasminogen; t-PA.

Figures

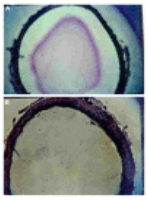

Figure 1 Inhibition of fibrinolytic activity by...

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