The relevance of iron in the pathogenesis of Parkinson's disease.

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Source

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Abstract

Alterations of iron levels in the brain has been observed and documented in a number of neurodegenerative disorders including Parkinson's disease (PD). The elevated nigral iron levels observed in PD may reflect a dysfunction of brain iron homeostasis. Under normal physiological conditions excess iron can be sequestrated in ferritin and neuromelanin. Alternatively, the excess iron may represent a component of brain iron deposition associated with ageing. The aetiology of idiopathic PD largely remains an enigma. However, intensive investigations have provided a host of putative mechanisms that might contribute to the pathogenesis underlying the characteristic degeneration of the dopaminergic neurons in the substantia nigra (SN). The mechanisms proposed include oxidative (and nitrative) stress, inflammation, excitotoxicity, mitochondrial dysfunction, altered proteolysis and finally apoptotic induced cell death. Iron-mediated cellular destruction is mediated primarily via reactive oxygen or/and nitrogen species induced oxidative stress. Furthermore, these pathogenic mechanisms appear to be closely interlinked to the cascade of events leading to cellular death. There are conflicting reports about the stage during disease progression at which nigral iron change occurs in PD. Some have found that there are no changes in iron content SN in asymptomatic incidental Lewy body disease, suggesting it may represent a secondary event in the cascade of neuronal degeneration. In contrast, others have found an elevation of iron in SN in pre-clinical stages. These discrepancies may be attributed to the occurrence of different sub-groups of the disease. This concurs with the notion that PD represents a group of related diseases with a number of potential pathogenic pathways.

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