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Parkinson's disease: Novel thoughts

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Parkinson's disease (PD) is a neurodegenerative disorder characterized by progressive loss of dopaminergic neurons in the substantia nigra pars compacta. The incidence is increasing with the aging population. Epidemiological studies imply that environmental and genetic factors are important in the development of Parkinson's disease. Although the pathogenesis of the disease is not fully understood, mechanisms related to free radical stress, mitochondrial dysfunction, neuroinflammation, apoptosis, and protein aggregation are the major factors in the degeneration of dopaminergic neurons. The clinical features of the disease are non-motor symptoms such as hyposmia, sleep disorder, and depression and motor symptoms such as tremor, rigidity, and imbalance that appear as the disease progresses. The available treatment of Parkinson's disease is so that novel neuroprotective or neurorestorative treatments are needed. Therefore, understanding the molecular mechanisms of Parkinson's disease pathogenesis is crucial in the development of the novel therapies for Parkinson's disease. Increasing number of studies indicate the important role of epigenetic mechanisms in Parkinson's disease pathogenesis and histone deacetylase inhibitors have been implicated in the treatment of neurodegenerative disorders. Promising studies show that histone deacetylase inhibitors increase the acetylation levels in the brain and provide neuroprotection via affecting many genes involved in cell cycle regulation, apoptosis, and DNA repair process. In the studies conducted in our laboratory, the anticonvulsant drug valproic acid has been found to be effective by producing antioxidant and antiapoptotic effects. Epigenetic modulation was also effective. In an animal model of Parkinson's disease developed in rats, stereotaxic injection of 6-OHDA (8 g/2 L) to the right substantia nigra pars compacta was conducted. The following coordinates of substantia nigra pars compacta were used: (AP) = -4.8mm, (ML) = -1.8mm and (DV) = -8.2mm. Only the rats showing pronounced rotational behavior (more than 5 contralateral turns) were included in the study after apomorphine (0.5mg/kg sc) test. The effects of valproic acid were compared with levodopa.

Biography

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