Are Dopamine Oxidation Metabolites Involved in the Loss of Dopaminergic Neurons in the Nigrostriatal System in Parkinson's Disease?

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 In 1967, L-dopa was introduced as part of the pharmacological therapy of Parkinson's disease (PD) and, in spite of extensive research, no additional effective drugs have been discovered to treat PD. This brings forward the question: why have no new drugs been developed? We consider that one of the problems preventing the discovery of new drugs is that we still have no information on the pathophysiology of the neurodegeneration of the neuromelanin-containing nigrostriatal dopaminergic neurons. Currently, it is widely accepted that the degeneration of dopaminergic neurons, i.e., in the substantia nigra pars compacta, involves mitochondrial dysfunction, the formation of neurotoxic oligomers of alpha-synuclein, the dysfunction of protein degradation systems, neuroinflammation, and oxidative and endoplasmic reticulum stress. However, the initial trigger of these mechanisms in the nigrostriatal system is still unknown. It has been reported that aminochrome i