

Oxidative stress as a cause of nigral cell death in Parkinson's disease and incidental Lewy body disease. The Royal Kings and Queens Parkinson's Disease Research Group.

Ann Neurol. 1992;32 Suppl:S82-7.

Jenner P, Dexter DT, Sian J, Schapira AH, Marsden CD.

Parkinson's Disease Society Experimental Research Laboratories, King's College London, UK.

We examine the evidence for free radical involvement and oxidative stress in the pathological process underlying Parkinson's disease, from postmortem brain tissue. The concept of free radical involvement is supported by enhanced basal lipid peroxidation in substantia nigra in patients with Parkinson's disease, demonstrated by increased levels of malondialdehyde and lipid hydroperoxides. The activity of many of the protective mechanisms against oxidative stress does not seem to be significantly altered in the nigra in Parkinson's disease. Thus, activities of catalase and glutathione peroxidase are more or less unchanged, as are concentrations of vitamin C and vitamin E. The activity of mitochondrial superoxide dismutase and the levels of the antioxidant ion zinc are, however, increased, which may reflect oxidative stress in substantia nigra. Levels of reduced glutathione are decreased in nigra in Parkinson's disease; this decrease does not occur in other brain areas or in other neurodegenerative illnesses affecting this brain region (i.e., multiple system atrophy, progressive supranuclear palsy). Altered glutathione metabolism may prevent inactivation of hydrogen peroxide and enhance formation of toxic hydroxyl radicals. In brain material from patients with incidental Lewy body disease (presymptomatic Parkinson's disease), there is no evidence for alterations in iron metabolism and no significant change in mitochondrial complex I function. The levels of reduced glutathione in substantia nigra, however, are reduced to the same extent as in advanced Parkinson's disease. These data suggest that changes in glutathione function are an early component of the pathological process of Parkinson's disease.

