Iron mediates neuritic tree collapse in mesencephalic neurons treated with 1-methyl-4-phenylpyridinium (MPP+).

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Studies in post-mortem tissues of patients with Parkinson's disease (PD) and in mice treated with 6-hydroxydopamine have shown a decrease in the length of axon and dendrites of striatal neurons. However, the etiology of the morphological changes and their relationship to inhibition of mitochondrial complex I and the cellular levels of iron and glutathione (GSH) have not been described. In this study, we characterized the effect of MPP+, an inhibitor of mitochondria complex I, on the integrity of the neuritic tree of midbrain dopaminergic neurons, and determined the influence of iron and cellular levels of GSH on this degeneration. Sub-maximal concentrations of MPP+ induced a drastic dose-dependent reduction of neurites, without modification of the soma or apparent cell death. Concurrent treatment with MPP+ and non-toxic concentrations of iron accelerated the process of degeneration, whereas neurons grown on a medium low in iron showed enhanced resistance to MPP+ treatment. MPP+-induced