Abstract
The goal of this review was to examine whether chronic Mn exposure produces dopamine neuron degeneration and PD or whether it has a distinct neuropathology and clinical presentation. I reviewed available clinical, neuroimaging, and neuropathological studies in humans and nonhuman primates exposed to Mn or other human conditions that result in elevated brain Mn concentrations. Human and nonhuman primate literature was examined to compare clinical, neuroimaging, and neuropathological changes associated with Mn-induced parkinsonism. Clinical, neuroimaging, and neuropathological evidence was used to examine whether Mn-induced parkinsonism involves degeneration of the nigrostriatal dopaminergic system as is the case in PD. The overwhelming evidence shows that Mn-induced parkinsonism does not involve degeneration of midbrain dopamine neurons and that l-dopa is not an effective therapy. New evidence is presented on a putative mechanism by which Mn may produce movement abnormalities. Confirmation of this hypothesis in humans is essential to make rational decisions about treatment, devise effective therapeutic strategies, and set regulatory guidelines.

Keywords
Basal ganglia, Dopamine, Humans, Manganese, Movement disorder, Neuroimaging, Neurotoxicity, Nonhuman primates, Parkinson's disease, Striatum.