Documentation of a Striatal Glutathione Deficit *In Vivo* in Parkinson's Disease Directly Implicates Oxidative Stress in Disorder Pathophysiology

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Background*: Postmortem* studies of Parkinson's disease (PD) brain have consistently reported deficits of nigrostriatal glutathione (GSH) – the primary living tissue antioxidant– of up to 40% compared to normal brain, strongly implicating oxidative stress in the pathophysiology of PD. However, direct evidence corroborating a striatal GSH deficit in PD brain *in vivo* is currently lacking. This study assessed whether there is a GSH deficit in living PD brain by directly measuring cortical levels of the antioxidant *in vivo* with MRS. Methods: For this pilot study, 22 patients diagnosed with idiopathic PD per the United Kingdom Parkinson's Disease Society Brain Bank criteria, and 27 medically healthy volunteers (HV) were recruited. *In vivo* spectra of GSH were measured in 15 min with proton MRS on a 3T GE MRI system from voxels of interest in the left striatum and the occipital cortex (OCC). Results: In the striatum, the region of primary interest, GSH in PD patients was 15% lower ($p=0.04$) than in the HV group. In the OCC, a region not directly implicated in PD, there was a trend-level lower GSH ($p=0.08$) in PD patients than in the HV group. Conclusion: This study has obtained what may be the first *in vivo* evidence of a nigrostriatal GSH deficit in PD compared to healthy subjects, a finding that corroborates *postmortem* PD brain results that have consistently shown striatal GSH deficits and are the basis for a pathophysiological model of PD that places oxidative stress centrally in disorder pathogenesis.