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.