Initial Study of Parkinson's Disease at 7T: Can Differences Between Parkinson's Patients and Healthy Controls Be Depicted?

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Introduction: Definitive diagnosis of Parkinson's disease (PD) occurs *post mortem* since it is only through gross morphology that neuronal loss in the substantia nigra (SN) and locus ceruleus can be seen (1). For example, we can use histopathological techniques to stain and quantify striatonigral afferent fibers using calbindinin D_{28k} (2) and tissue iron and ferritin staining to show iron increases in brain regions affected by PD (3). The accumulation of this iron is thought to reflect neuronal degeneration in that it may mediate lipid peroxidative reactions and free radical formation that precede neuronal death (4). Standard field strength MRI has yet to demonstrate significant morphologic differences for PD, e.g., no changes have been seen in the olfactory bulbs (6). However, several studies have linked MRI T2 and T2* changes to increased iron in PD (5, 7). The objective of this preliminary study was to explore if ultrahigh field MRI can visualize and quantify changes in PD.

Methods: Using a 7T MR scanner (Phillips, Achieva, Cleveland, OH) and either a 16-channel SENSE (NOVA) or a volume transmit/receive coil, images were acquired from 5 previously diagnosed PD subjects (60-72 y) and 7 control subjects (26-64 y) using a 3D Inversion Recovery prepared dual turbo gradient echo sequence (IR-dTFE: shot interval/TI: 2850/1450ms; TR/TE1/TE2: 13-14/2.3-2.5/10-10.5ms) with acquired voxel sizes of 0.43×0.53×1.2 - 0.57×0.81×1.6 mm^3. For each subject, ROIs were manually traced for various brain regions: red nucleus (RN), substantia nigra (SN), white matter tract medial to the SN (WMT), putamen, globus pallidus, and caudate. For each ROI, T2* was calculated using an in-house IDL program (ITT Corp., Boulder, CO). R2* (in s^{-1}) was then calculated, and plotted against age (in years) for each subject and each brain region for both groups.

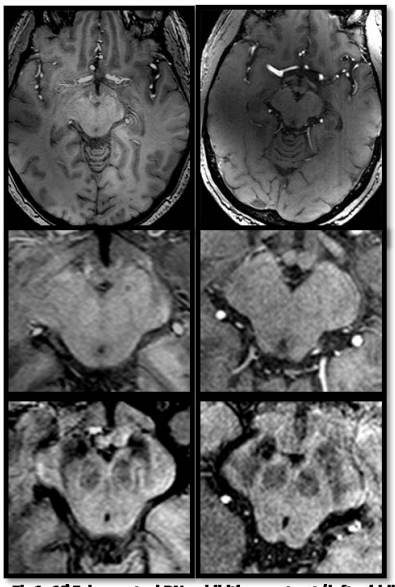

Fig 1: 1st Echo control RN exhibiting contrast (left middle) compared to PD RN exhibiting diminished contrast (right middle). In 2nd Echo both control RN (left bottom) and PD RN (right bottom) have contrast.

Results: Fig 1 shows images of a 63y old control subject (left) and a 66y old PD subject (right). On the 1st echo image (middle), the SN and RN have slightly higher signal than the surrounding white matter. This contrast is diminished on the 1st echo of the PD subject. In all 1st echo control images, the SN and RN were brighter than the adjacent white matter, and was diminished or completely lost in all 1st echo PD images. On the 2nd echo images (bottom), both SN and RN were seen as dark, and this contrast behavior was seen in all subjects in both groups. Fig 2 shows R2* plotted versus age. In all control subjects, R2* increased with age. For all other brain regions except the RN, R2* values were similar for both groups. Only in the RN, did we find that R2* values were smaller in PD (i.e., T2* values were longer for PD than controls).

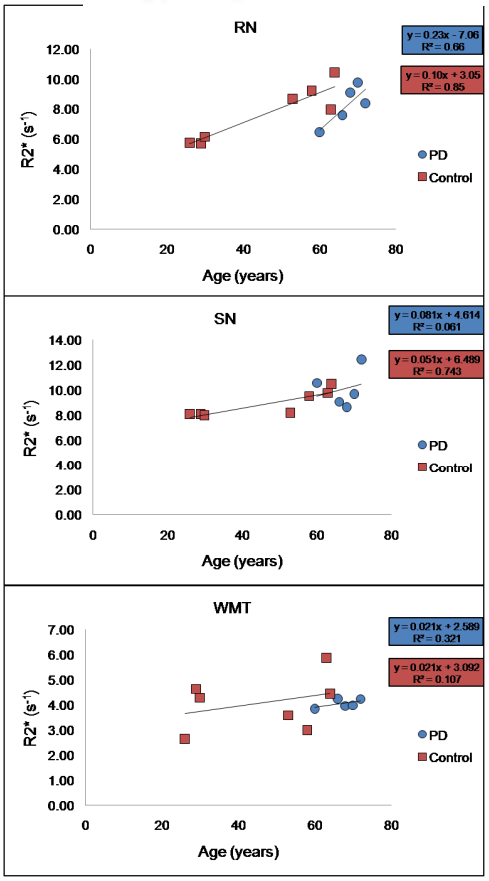

Fig 2 Graphs of R2* in s^{-1} vs. Age (years) For red nucleus (RN-top), substantia nigra (SN-middle), and white matter tract medial to the SN (WMT-bottom.

Discussion: The observed R2* trends between PD subjects and controls seem to be inconsistent with the assumption that R2* reflects iron, and it does not explain the observed loss of contrast in the 1st echo images. Because the 1st echo images are predominantly T1-weighted, contrast changes may be reflective of T1 differences. Furthermore, T2* may represent tissue iron only in part, because the apparent magnetic susceptibility effects may also be due to paramagnetic venous deoxyhemoglobin. Thus, longer T2* in the RN of PD s could be indicative of decreased vasculature. Further studies including improved methodology for T2* measurements, T1 measurements and assessment of T2* contrast mechanism are needed.

References: **1)** Braak, H et al, Neurobiol Aging, 24, 2003:197-211. **2)** Damier, P, et al, Brain, 122, 1999: 1421-36. **3)** Chen, JC et al, Am J of Neurorad, 14, 2, 1993: 275-281. **4)** Gutteridge, JM et al, Ann Neurol, 32, 1992: S16-21. **5)** Stankiewicz, J et al, Neurother, 3, 2007: 371-86. **6)** Mueller, A et al., J Neural Transm, 112, 2005: 1363-1370. **7)** Brass, SD et al, Top Magn Reson Imag, 1, 2006: 31-40.