Quantitative 7T Phase Imaging in Presymptomatic Huntington's Disease

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Introduction: Prior postmortem and *in vivo* MRI studies of Huntington's disease (HD) have demonstrated iron deposition and atrophy within the basal ganglia [1]. Quantitative measurements of local field shift (LFS) derived from phase images are in part related to brain iron concentration [2]. In this work, we exploited the phase sensitivity of ultra-high field 7T MRI to characterize caudate LFS in subjects with genetically confirmed but presymptomatic HD and compared the results to caudate volume, currently the most well accepted imaging marker of disease progression [3].

Methods: Ten subjects with genetically confirmed presymptomatic HD and 8 matched controls were scanned on both 7T and 3T MR scanners (GE Healthcare, Milwaukee, WI) according to a protocol approved by our institutional review board. At 7T, gradient echo images were acquired (GRE; TR/TE=250/12 ms, 20° flip angle, 22 cm FOV, 4 mm slice thickness) along with volumetric T1-weighted images (IRSPGR; TR/TE=11/5 ms, 20° flip angle, 22 cm FOV, 2 mm slice thickness). At 3T, volumetric T1-weighted imaging was performed (IRSPGR; TR/TE=7/3 ms, 15° flip angle, 23 cm FOV, 1 mm slice thickness) for accurate segmentation and morphometry, which was not possible using 7T T1-weighted images due to field inhomogeneity-related variations in image intensity. Phase images were created from the 7T GRE images and used to construct maps of LFS [2] (normalized to the phase of the splenium of the corpus callosum), and caudate regions of interest were automatically delineated from the 3T T1 data using the FIRST tool included in FSL[4]. Using the 3D T1 data from both field strengths as an intermediate, the caudate segmentations were co-registered with the 7T GRE images using FSL. Then the LFS within the right and left caudate nuclei were derived (Figure 1). For comparison, Freesurfer (MGH Martinos Center for Biomedical Imaging) was used to obtain measurements of normalized caudate volume. Caudate volumes and mean LFS for controls and presymptomatic HD subjects were compared using the Wilcoxen ranked-sum test.

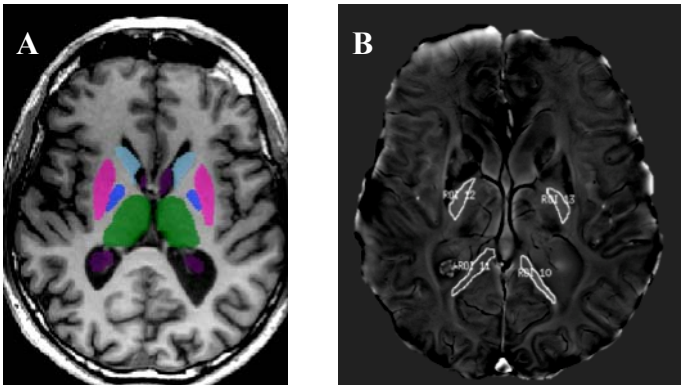

Figure 1. (A) Regions of interest (ROIs) were extracted with FIRST from the 3T T1; the caudate is show n here (cyan). **(B)** Phase images were used to trace white matter ROIs of the posterior internal capsule and the splenium.

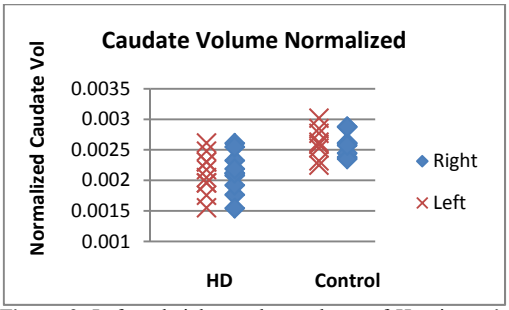

Figure 2. Left and right caudate volume of Huntington's patients and controls normalized by intracranial volume

Results and Discussion: Mean ages for patients and controls were 46.78 (range 26-78) and 42.43 (range 26-65), respectively; the mean number of genetic CAG repeats for HD was 42.72 (range 40 to 47). Presymptomatic HD patients showed significantly smaller left and right caudate volumes ($P<0.01$) as compared with controls (Figure 2). Presymptomatic HD subjects showed higher mean LFS than controls (Figure 3). Although not statistically significant ($p=0.3247$), the presymptomatic HD group exhibited a strong trend toward higher LFS when compared to controls.

LFS represents a composite measure of susceptibility effects, which are related to a number of factors including the presence of iron, calcium, and deoxyhemoglobin within vascular structures. We speculate that differences in caudate LFS in patients with presymptomatic HD are due to iron deposition and loss of neuronal cytoarchitecture. A direct relationship between caudate volume and LFS was not observed, suggesting that LFS and volume may represent different pathologic endpoints of neurodegeneration.

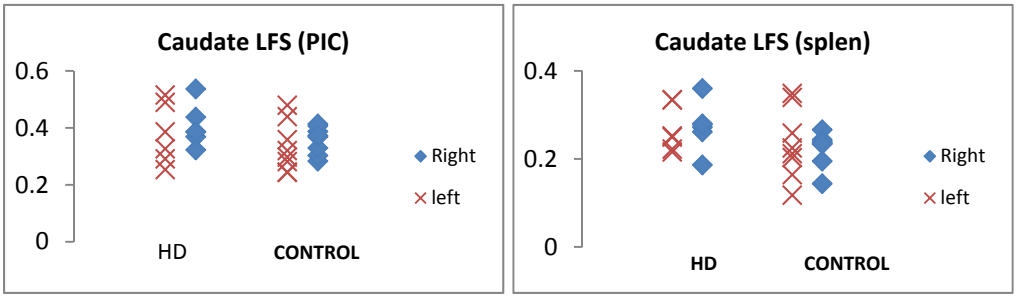

Figure 3. LFS of the right and left Caudate for HD and Controls; normalized by PIC and splenium phase values

Conclusions: Currently, the most studied method for evaluating disease progression in HD is volumetric measurement of the caudate. Although preliminary, our results suggest that LFS derived using from 7T phase imaging may also represent a useful biomarker for early stage HD.

References: [1] Bartzokis et al. Arch Neurol 1999; 56:569-574 [2] Hammond et al. Neuroimage 2008; 39:1682-1 [3] Weir DW et al. Lancet Neurol 2011; 10: 573-90. [4] M.W. Woolrich, et al.. NeuroImage, 2009 45:S173-186, 2009