Title

E006 Ultrashort echo time magnetic resonance imaging of myelin and iron in Huntington's disease (HD)

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254 directions) data were acquired on an ultra-strong gradient (300 mT/m) 3T Siemens Connectome system in n = 30 individuals with premanifest and manifest HD and n = 30 age- and sex-matched healthy controls. The caudate, putamen, pallidum, and thalamus were segmented bilaterally from T1-weighted images using FreeSurfer v6. Median values of proxy soma density, soma size, and extracellular water were extracted for each subcortical region and compared between the groups. SANDI measures were correlated with Q-motor2 speeded tapping performance.

Results HD was associated with increased extracellular water and soma size and reduced soma density in the BG but not the thalami (figure 1) consistent with ex vivo morphometric evidence of neuronal soma loss and astrocyte swelling in the HD brain.[3] Speeded tapping correlated negatively with soma density and positively with soma size and extracellular water (figure 2).

Conclusion SANDI-derived measurements may provide in vivo biomarkers of cellular BG changes that are associated with the loss of motor function in HD.

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E006 ULTRASHORT ECHO TIME MAGNETIC RESONANCE IMAGING OF MYELIN AND IRON IN HUNTINGTON'S DISEASE (HD)

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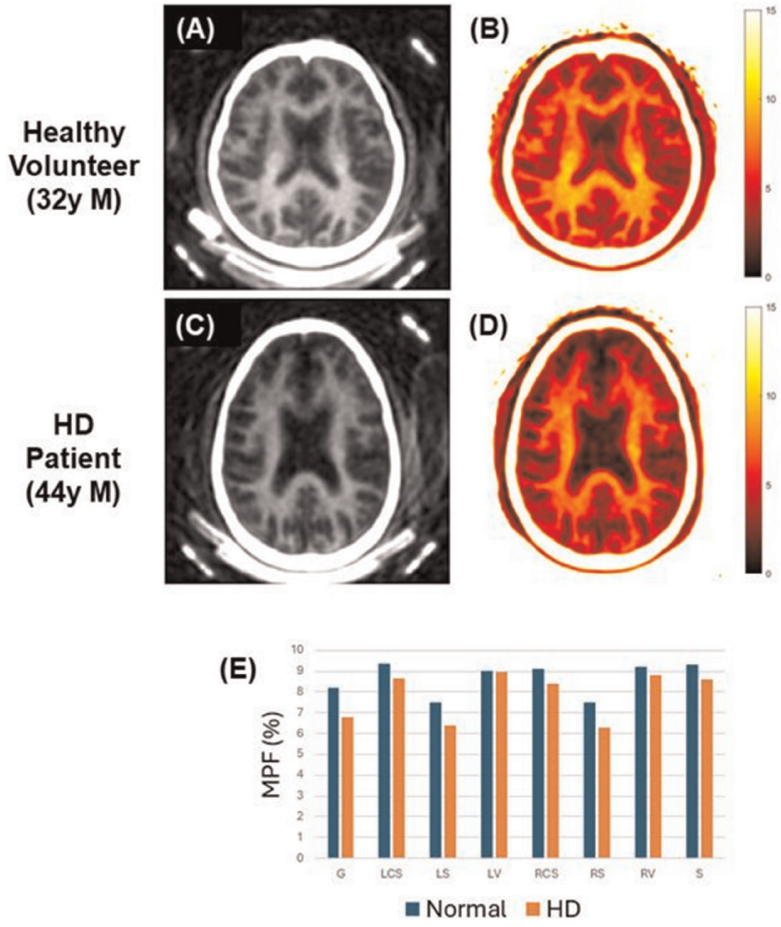
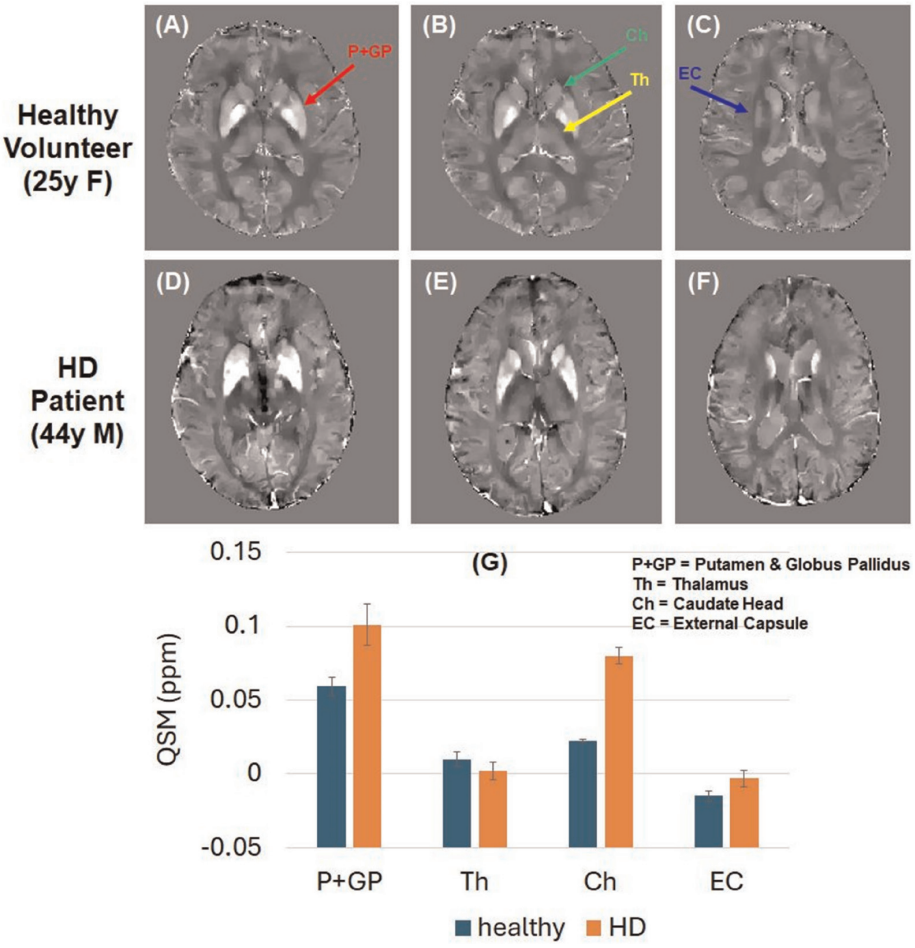
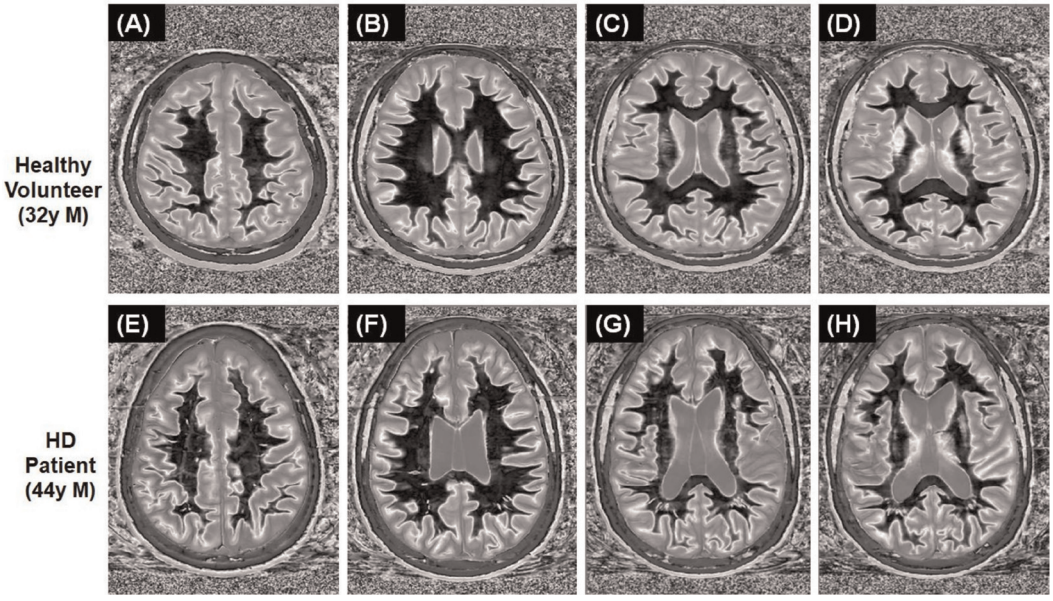
Background Past studies have demonstrated extensive white and gray matter degeneration in Huntington's Disease (HD), including demyelination and iron accumulation.[1–4] Demyelination disrupts axonal transport, integrity, and structural plasticity,[5–7] and plays a major role in HD.[8–10] Iron accumulation contributes to neurodegeneration.[11–13] However, myelin has an



Abstract E006 Figure 1 STAIR-UTE imaging of a healthy volunteer (32y, male) (A) and an HD patient (44y, male) (C), as well as the corresponding MPF maps (B, D). Lower MPF values were observed in the HD patient across the white matter of the whole brain, including the genu (G), left centrum semiovale (LCS), left subcortical white matter (LS), left (peri) ventricular white matter (LV), right centrum semiovale (RCS), right subcortical WM (RS), right (peri) ventricular WM (RV), splenium (S)



Abstract E006 Figure 2 Selected 3D UTE-QSM images of a healthy volunteer (25y, female) (A-C) and an HD patient (44y, male) (D-F). The HD patient shows increased QSM values or iron accumulation in the globus pallidus and putamen (P+GP), head of the caudate nucleus (Ch), and external capsule (EC), but no significant iron accumulation in the thalamus (Th)



Abstract E006 Figure 3 dSIR imaging of a healthy volunteer (32y, male) (A-D) and an HD patient (44y, male) based on 2D IR-FSE imaging with a TI of 400 ms and 500 ms. Signal rebound in the anterior and posterior central corpus callosum of both the control and HD patient indicates that the shorter TI is slightly too long. A shorter TI of 350 ms will be tested in future studies. Even so, the dSIR images show obvious structural abnormalities in white matter of the HD patient as well as a smaller globus pallidus and putamen, and caudate nucleus

ultrashort T2, and is 'invisible' with conventional MRI, which provides no quantitative information on iron.

Aims We report a 3D Short TR Adiabatic Inversion Recovery UTE (STAIR-UTE) sequence for Myelin Proton Fraction (MPF) mapping,[14] a UTE Quantitative Susceptibility Mapping (UTE-QSM) sequence for iron mapping,[15] and a divided Subtracted Inversion Recovery (dSIR) sequence[16] for high contrast imaging in HD.

Methods The STAIR-UTE sequence included: FOV=220×220×240 mm^3, matrix=92×92×80, resoltion=2.4×2.4×4.0 mm^3, TE=0.032/1.2ms, TR/TI=154/67ms, bandwidth=125 kHz, 7.5 min. The UTE-QSM sequence included: FOV=220×220×160 mm^3, matrix=220×220×80, resolution=1.0×1.0×2.0 mm^3, TR=28ms, six-echo (TE=0.032,4.4,8.8,13.2,17.6,22ms), 7 min. The dSIR sequence included two inversion recovery FSE acquisitions with TIs of 400/600ms. Five HD patients and five controls were scheduled (four participants already scanned) for this feasibility study.

Results/Outcome Figure 1 shows MPF maps that display myelin loss in white matter of the HD patient compared with the control. Figure 2 shows UTE-QSM maps. These show significant iron accumulation in putamen, globus pallidus, caudate, and external capsule of the HD patient compared with the control. Figure 3 shows dSIR images which depict abnormal structural changes in white matter of the HD patient and smaller globus pallidus, putamen and caudate nucleus compared with the control.

Conclusion STAIR-UTE, UTE-QSM, and dSIR sequences can depict myelin loss, iron accumulation, and structural changes in HD patients.

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E007 THE ROLE OF TEMPORAL WHITE MATTER IN HUNTINGTON'S DISEASE COGNITIVE DEFICITS

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Background Cognitive decline, including language and memory deficits, in Huntington's disease (HD) has traditionally been associated with fronto-striatal circuits neurodegeneration, while temporal regions involved in these functions were thought to be preserved. However, recent studies suggest that HD pathology extends to temporal and hippocampal regions. The extent to which cognitive deficits in HD are explained by alterations in temporal white matter connections remains unclear.

Aims This study investigates the vulnerability of macro- and microstructural changes in medial temporal lobe (MTL) pathways and hippocampal interhemispheric connections (fornix), and whether variability of these connections explains cognitive deficits in HD patients.

Methods Forty-six HD individuals (23 premanifest, 23 manifest) were evaluated for memory and language using Hopkins Verbal Learning Test and Boston Naming Test, respectively. Diffusion tensor imaging was used to delineate temporal projections through probabilistic tractography. Macrostructural (volume) and microstructural diffusion biomarkers (Fractional Anisotropy, Radial diffusivity) were extracted for each tract, and Principal Component Analyses (PCA) were conducted to identify patterns of alterations. These patterns were related to clinical symptoms using multivariate linear models.

Results We observed both memory and language changes, as well as widespread structural changes in temporal white matter, when comparing premanifest and manifest HD individuals. PCA identified three factors differentiating MTL pathways and fornix microstructural variability. Fornix volume predicted language and memory bilaterally. Additionally, while language deficits were related with bilateral MLT miscrostuctural patterns, memory changes were associated with the right MTL.

Conclusions These results underscore the importance of temporal white matter connectivity in HD cognitive symptoms and may help to better understand the associated fronto-striatal deficits.

E008 DELINEATING STRIATAL PATTERNS ASSOCIATED TO CORTICO-STRIATAL CONNECTIONS IN HUNTINGTON'S DISEASE: IMPLICATIONS FOR COGNITIVE PROFILES

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Background Despite a common genetic etiology, Huntington's Disease (HD) presents individual differences in onset, severity, and progression of motor, cognitive, and psychiatric symptoms. The neurobiological basis for this variability remains poorly understood. The striatum, a hallmark of early degeneration in HD, regulates unique motor, associative and limbic functions through topographically organized cortical connections.

Aims This study investigates whether symptomatic differences in HD are related to specific patterns of cortico-striatal neurodegeneration. Thirty-eight individuals (19 manifest and 19 premanifest) were evaluated for clinical symptoms. Diffusion tensor imaging was used to analyze cortico-striatal white matter connectivity and perform connectivity-based segmentation