

Diffusion tensor imaging (DTI) in Huntington's disease patients: analyses of fractional anisotropy (FA) maps and apparent diffusion coefficient (ADC) maps.

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Objective: Huntington's disease (HD) is an inherited neurodegenerative disease that predominantly targets the subcortical grey nuclei. Although MR imaging may be used to measure disease progression in HD patients, few investigations have been done with DTI, which supplies FA and ADC maps. We expect that DTI might provide additional information on the water movement, the demyelination or the loss of connections in the brain of HD patients, in comparison with control brains.

Methods: Fourteen patients with mild HD (aged 42 ± 8 years) were compared to 10 healthy controls (37 ± 11 years). All subjects underwent T1-weighted sequence and diffusion-weighted sequence (41 orientations, $b = 700$ s/mm², 0.9375×0.9375 mm² in-plane resolution, slice thickness 2 mm) on a 1.5T Signa imager (GEMS). Two analyses were performed: one based on a ROI approach, and a voxel-wise automated method using the SPM2 software (Ashburner, 2000).

In SPM2, we created an appropriate FA template containing both patients and controls FA -and symmetric FA- images. This FA template was obtained by applying to native FA images non-linear transformations determined by normalizing each T2-weighted EPI image onto the MNI EPI template. Then, all native FA maps were normalized to this adapted FA template. The resulting transformations were also applied to the native ADC maps. Then, normalized FA and ADC images were smoothed using an $8 \times 8 \times 8$ mm³ gaussian kernel. Regional differences in FA and ADC between controls and HD patients were analyzed using an ANCOVA, with age and sex as nuisance covariates.

Second, ROI in subcortical nuclei were manually segmented on T1-weighted images and then realigned to the native FA and ADC maps, providing FA and ADC mean values in each ROI (FA example in **Fig.1**). T-tests were carried out on these data to evidence differences between both groups in each ROI.

Results: SPM2 analysis showed that FA was significantly increased bilaterally in the lenticular nuclei of HD patients (FDR-corrected $p < 0.1$, **Fig.2**). The ROI analysis found significant bilateral FA increase in anterior ($p = 0.02$) and posterior ($p = 0.04$) putamen and in the body of caudate nuclei ($p = 0.03$). Besides, both methods evidenced a highly significant bilateral ADC increase in anterior and posterior putamen, head and body of caudate nuclei and globus pallidus (SPM2: FDR-corrected $p < 0.005$; ROI: $p < 10^{-4}$ except for globus pallidus: $p = 0.05$).

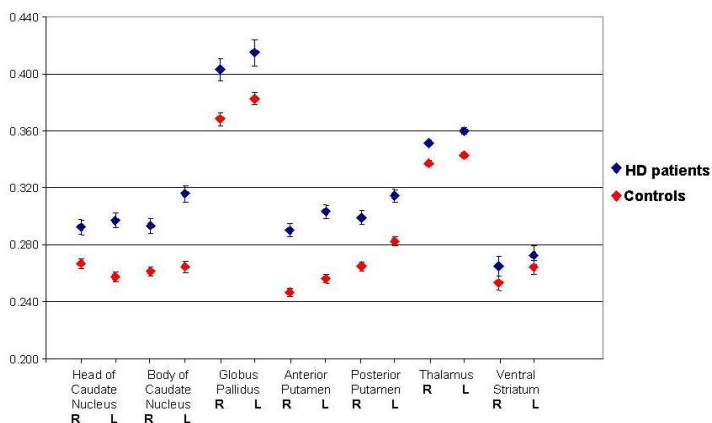


Fig.1 Fractional anisotropy for each ROI

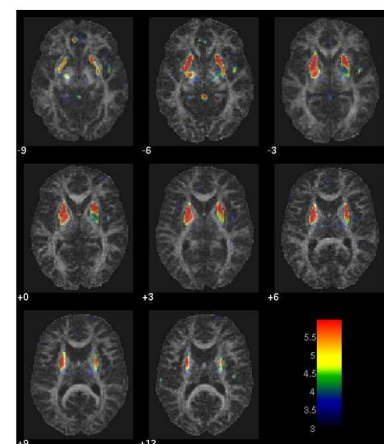


Fig.2 Significant increase of FA found in HD patients with SPM2

Discussion: The FA increase in the lenticular nuclei and body of caudate nuclei might be explained by the loss of dendrites in medium-spiny neurons that degenerate in HD: water movement in these regions appears to be more unidirectional since, at the beginning of HD, only dendrites degenerate, while axons are spared (Baquet, 2004). The dendritic loss, as well as the loss of bulk of neurons targeted by the degenerative process, might also explain the ADC increase in the striatum and globus pallidus, considering that ADC depicts extracellular water diffusion. Interestingly, neither FA nor ADC reductions were found in HD patients' white matter with SPM2, suggesting that no major axonal projections to or from the striatum have degenerated in early HD patients.

Conclusions: SPM2 is more sensitive to detect significant differences in FA or ADC between HD patients and controls, with no a priori on their location. Conversely, its main limit leans on an imperfect registration that does not handle correctly ventricular enlargement, which has repercussions on the interpretation of results in structures such as the caudate nucleus.