

Abnormal White Matter Organization in Huntington's Disease Evaluated with Diffusion Tensor MRI

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Synopsis

Six presymptomatic subjects with Huntington's disease and six normal controls were examined with diffusion tensor magnetic resonance imaging. The fractional anisotropy (FA) images were normalized using a nonlinear elastic registration method. The group difference of FA was compared using a voxel-wise nonparametric statistics and a regions of interest analysis. In a whole brain voxel-by-voxel comparison, reduced FA values were observed in the thalamic nuclei, frontal and occipital forceps, splenium of corpus callosum and centrum semiovale, bilaterally. In region specific analysis, the right limbic area of HD group, which contains ventral putamen and thalamus, showed statistically meaningful FA reduction.

Introduction

Huntington's disease (HD) is a neurodegenerative disease which is known to primarily affect the caudate and putamen [1]. Although previous CT and MR imaging studies demonstrated indirect evidence of volumetric decreases in striatum, neuroimaging has played little role in early diagnosis or in researching pathophysiology. Diffusion tensor MR imaging (DT-MRI) has been shown to provide unique information about the microstructural integrity of white matter [2]. We investigated usefulness of DT-MRI in quantification of white matter abnormality in the brain of HD.

Method

We examined 6 presymptomatic, genetic marker-positive persons for HD and 6 matched normal controls (NC). DT-MRIs were acquired using a 1.5T GE Signa Horizon EchoSpeed and a single-shot spin echo EPI sequence (TR/TE=2500/67ms, FOV=24cm, acquisition matrix=96x96, reconstruction matrix=256x256, slice thickness/number=2.5mm/50, diffusion sensitizing directions=9, b=1000s/mm², NEX=4). Fractional anisotropy (FA) calculation was followed by linear tensor estimation. FA maps were spatially transformed into a standard Talairach template using nonlinear spatial normalization method (HAMMER, Hierarchical Attribute Matching Mechanism for Elastic Registration) [3] and white matter segmentation was performed using HMRF-EM (Hidden Markov Random Field Model and the Expectation Maximization) algorithm [4]. An individually adaptive automatic labeling was performed with respect to 22 predetermined regions of interest (includes orbitofrontal, dorsal-anterior frontal, ventral-posterior frontal, dorsal-posterior frontal, dorsal parietal, ventral parietal, dorsal occipital, ventral occipital, mid-dorsal temporal, ventral temporal, and limbic cortical areas for both hemispheres, respectively) (Figure 1). Whole brain FA maps from each group were assessed on a voxel-by-voxel basis using Wilcoxon signed rank statistics. The average values of respective regions of interest FA were statistically compared using two sample t-test.

Results

FA values of HD subjects (mean \pm SD) including overall white matter were 0.383 ± 0.038 and those of NC were 0.391 ± 0.037 . The global white matter FA difference between HD and NC was statistically insignificant ($p=0.081$). In a voxel-by-voxel comparison using nonparametric statistics, we observed areas with decreased FA in the thalamic nuclei, frontal and occipital forceps, splenium of corpus callosum and centrum semiovale, bilaterally ($p<0.05$) (Figure 2). However, power analysis showed insufficient statistical power with our sample size (the effect size of 0.95 and 46% of statistical power with alpha of 0.05 for a one-tailed t-test) and some false positive results were also observed due to residual anatomic variability. In region specific analysis, which allowed improved detection sensitivity, the variance of FA measure in HD brain was significantly higher than in NC ($p=0.0003$). The HD group showed decreased mean FA values in most white matter areas except for the right dorsal-anterior frontal cortex. However, FA decreases in the right limbic area, which contains ventral putamen and thalamus, were the only statistically significant difference ($p<0.05$) between-group (Figure 3).

Conclusion

Anisotropy is known to reflect intravoxel incoherence of axonal orientation. The result of our study possibly supports a hypothesis of a connectivity deficit between right ventral putamen and thalamus in the brain of HD. DT-MRI might be useful for early diagnosis and monitoring of disease progression in HD patients.

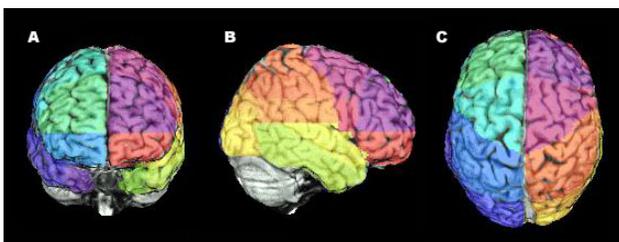


Figure 1. 22 predetermined regions of interest corresponding functional anatomical groups.

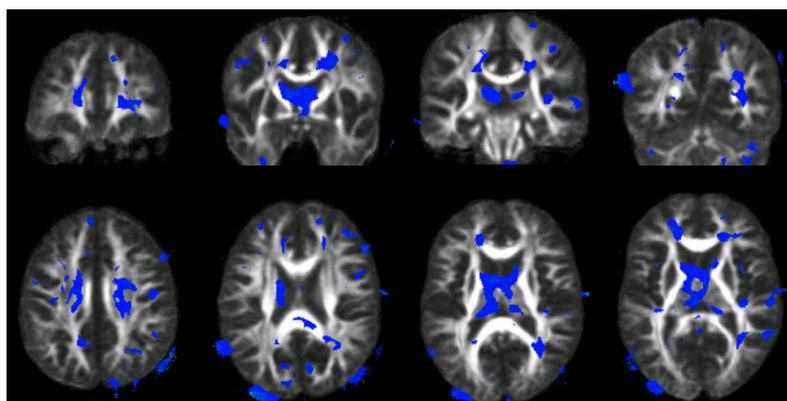


Figure 2. Statistical difference map of FA value between-group (NC-HD). Blue clusters represent reduced FA in the HD group ($p<0.05$).

Reference

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3. Shen D, Davatzikos C. *IEEE Trans. on Medical Imaging* 2002 (in press).
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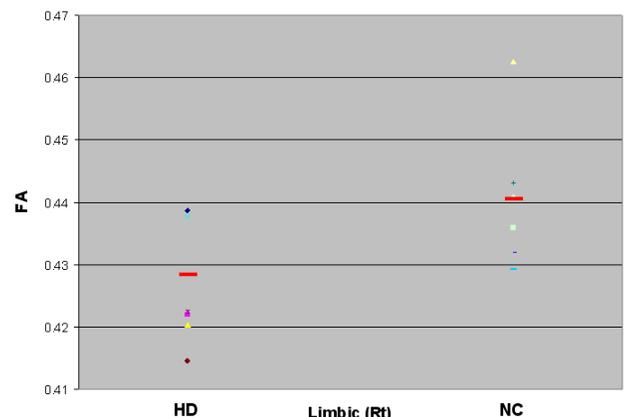


Figure 3. A scatter plot of FA value in the right limbic area. (region specific analysis). Group means of FA are represented by red colored lines.