Cerebral Fiber Changes in Patients with Hereditary Spastic Paraparesis Assessed by Diffusion Tensor MRI

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Hereditary spastic paraparesis (HSP) comprises a heterogeneous group of congenital diseases with progressive spastic paresis of the legs. Most common are pure forms with autosomal dominant inheritance (HSP4 and HSP3). Pathological findings revealed degeneration and demyelinization of the corticospinal tract increasing from the cervical to the lumbal level of the medulla considering a dying-back axonopathy of these long axons. However, occasional extraspinal involvement like thin corpus callosum, cerebellar atrophy and cognitive impairment in HSP4 suggest other factors for neural degeneration beside axon length. No alterations of cerebral corticospinal tract fibers have been described so far. Diffusion tensor MRI provides an estimate of the orientation of fiber bundles in the white matter. The directionality of diffusion can be quantified by fractional anisotropy (FA) allowing an estimation of fiber coherence. The aim of this study is the assessment of cerebral fiber changes in patients with pure HSP. We investigated 8 HSP patients (HSP4/HSP3, autosomal dominant) with spastic paraparesis, hyperreflexia of legs and positive Babinski sign in comparison to 16 age-matched controls. Diffusion-weighted images were acquired on a 3 Tesla MR system with a STEAM sequence (voxel size 3 ´ 3 ´ 3 mm3, 24 directions, 4 measurements, whole brain scan). Additionally we obtained a T1-weighted MRI. Images were realigned and spatially normalized. We computed diffusion tensor images on normalized T1 maps and calculated the FA voxel-wise. FA maps of patients were compared in 2 sample t-tests versus healthy controls using standard voxel-based statistics (SPM02). We report areas of significantly reduced FA ($p < 0.05$ corrected, family-wise error) after small volume correction (sphere of 8 mm). In HSP patients the strongest FA decrease was located in the right crus cerebri of the mesencephalon (global maximum, $p < 0.001$, corr.). FA was also decreased in the left posterior limb of the internal capsule ($p < 0.026$, corr.), in the corpus callosum ($p < 0.008$, corr.) and bilaterally in the cerebellum ($p < 0.004$, corr.) and frontal lobe ($p < 0.004$, corr.). The strongest decrease of fiber coherence of the caudal cerebral pyramidal tract fibers is in accordance with the pathological findings increasing to the lumbal level. Additionally, our results suggest an involvement of the corpus callosum, cerebellum and frontal lobe in autosomal dominant pure HSP indicating more extensive fiber degeneration than has been described so far.

Voxel-Based Morphometric Investigations in Basal Ganglia Diseases: Structural Changes and Function