Different patterns of white-matter changes in pure SPG4 and complicated SPG7 forms of hereditary spastic paraplegia

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Background:

Hereditary spastic paraplegias (HSP) are genetically and clinically heterogeneous neurodegenerative disorders, categorized into pure (pHSP) and complicated forms (cHSP). Most MR-studies on HSP include very heterogeneous samples of patients, and findings were inconsistent. Here we aimed to characterize specific pattern of very early white matter (WM) changes in genetically proven groups of cHSP and pHSP patients with normal conventional MRI.

Methods:

Six patients with pHSP and SPG4 mutations and 4 cHSP patients with SPG7 mutations were examined by clinical evaluation, detailed neuropsychological testing, and neuroimaging analyses, including conventional MRI (FLAIR-, T1- and T2-sequences), diffusion tensor imaging (DTI) and brain volumetry. Differences of voxel-wise statistics and ROI-based analysis of DTI data between patients and 32 healthy volunteers were evaluated by analysis of covariance.

Results:

Whereas conventional MRI and brain volumetry were normal, DTI revealed widespread disturbance of WM integrity ($p<0.001$), with different pattern in both HSP-subgroups. The localization of WM changes was in considerable accordance with the clinical symptoms. Consistent with the more severe phenotype including extramotor clinical features, WM changes of the cHSP group were more widespread and more pronounced, particularly affecting in the frontal lobes and the brainstem.

Conclusions:

In both cHSP and pHSP patients, early multisystem affection of WM is evident, with a specific pattern of WM changes in both subgroups. These subtle WM abnormalities have functional relevance since they correlated with clinical symptoms. The early alterations of nerve fibres, which can be detected by DTI, could be used as a biological marker in HSP subtypes.