Brain Magnetic Spectroscopy Imaging and Hereditary Spastic Paraplegia (HSP)

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The search for biomarkers in HSP includes the possible use of imaging tools to differentiate HSP subjects from controls, to mirror clinical characteristics (at least in term of severity) and to possibly serve as indicator of disease progression and response to treatment.

MRI in its standard configuration doesn't provide much help, advanced structural imaging using Diffusion Tensor Imaging detects some pathology specific alterations but recent longitudinal studies failed to show sensibility to disease progression.

Brain magnetic resonance spectroscopy (MRS) allows the identification and measure of key brain metabolites in selected regions of the brain, thus offering a novel perspective to brain imaging potentially capable of identifying HSP type specific changes and monitor them across disease stages.

We conducted a focused review that provided insights on the current knowledge of brain metabolites in HSP. Fourteen MRS studies have been analyzed with overall 61 HSP patients, falling within a wide range of age at onset, disease duration and age at the MRS scan, including children and adults. The genetic diagnosis included several subtypes (SPG2/3a/4/5/10/11/28/31/54). Only SPG11 and SPG54 have been more frequently investigated. The MRS methodology included various scan field strength, not easily comparable spectra areas designed to assess the motor tracts varying from the whole brain sampling to various cortical areas, brain stem and cerebellum. No consistency in disease severity and other outcome measures was observed. The main MRS findings corresponded to the areas of White Matter (WM) abnormalities.

In parallel we conducted a pilot cross sectional and longitudinal study assessing by MRS 45 HSP subjects (22 SPG4) and 46 healthy controls measuring the following metabolites: N-Acetyl Aspartate, Myo-Inositol, Choline, Creatine/P-Creatine, Lipids. The scans were repeated at 18-36 month interval. Increased myo-inositol in the left motor area above 0.605 differentiated 75% of the HSP subjects from controls. 100% sensitivity could be obtained by adding other metabolites to the selection tree. Increased levels of Myo-inositol in the motor or pre-motor areas marked also the longitudinal assessment and were correlated with disease severity and disease duration.

These preliminary results need confirmation on a larger cohort and validation with a blinded assignment test. They are nevertheless encouraging and indicate that MRS is a valuable tool to explore the disease processes underlying HSPs. Brain metabolites, as assessed by MRS, could represent potentially useful diagnostic markers and prognostic indicators of disease progression in HSP. Specific recommendations regarding the MRS technical protocol, CNS areas sampling, study design and applicability of findings should be framed to consolidate this possibility.