Global NAA/Cr measured by multi-slice echo planar spectroscopic imaging correlates with cognitive impairment in multiple sclerosis

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Introduction: Cognitive impairment occurs in approximately 50% of patients with multiple sclerosis (MS), with somewhat lower incidences in the early stages of the disease. There is no unambiguous pattern of cognitive deficits, but some cognitive functions are more frequently impaired than others, such as memory, information processing, attention, executive functions and verbal fluency. The pathophysiology of neuropsychological deficits is not clear. However, they are believed to be related to the overall disease burden of the brain. To assess pathology in normal appearing brain which goes undetected with conventional MRI, non-conventional MRI techniques, such as MR spectroscopy (MRS), are needed. Multi-slice EPSI can assess pathology in specific areas which might be associated with specific cognitive functions and in the same session assess diffuse global pathology associated with the overall cognitive function of the patient [1].

Subjects and Methods: The multi-slice EPSI sequence described in [1] was applied to 20 patients (16 females, 4 males), with newly diagnosed relapsing-remitting MS (disease duration < 5 years). The mean age was 36 years (range 22-48) and the mean EDSS score was 2.5 (range 0–4.5). 15 out of 20 patients received immunomodulatory therapy.
To evaluate cognitive dysfunctions, the patients completed a battery of 18 neuropsychological tests resulting in 29 derived test scores. The tests were grouped in 6 cognitive domains: 1) Abstract thinking/mental flexibility, 2) Mental processing/speed, 3) Working memory/attention, 4) General memory function, 5) Visuospatial memory, and 6) Naming/verbal retrieval. A General Cognitive Factor generated from 26 neuropsychological test scores and a Cognitive Dysfunction Factor including the 16 measures which best distinguished between MS patients and normal controls were also constructed.
The spectroscopic measurements were preceded by fully automated global high order shimming and a non-suppressed single acquisition water reference signal for alignment and spectral processing. Lipid signal nulling was provided by inversion recovery and water suppression was obtained using a 32 ms chemical shift selective radiofrequency pulse. To increase signal-to-noise ratio in the measurements of the metabolites, the sequence was repeated four times with two phase cycled acquisitions in each. TE/TR = 144/4300 ms, matrix 32 x 32. Eight 10 mm axial slices covered most of the cerebrum with 1 ml isotropic voxels. The visible metabolite (i.e. N-acetyl aspartate (NAA), choline (Cho) and creatine (Cr)) measures are reported as ratios which are insensitive to cerebrospinal fluid (CSF) content, coil sensitivity variations and oedema. Only brain parenchyma suitable for global spectroscopy was selected. Poorly shimmed areas (e.g. the inferior frontal lobes and inferior parts of the temporal lobes) and CSF were excluded (Fig. 1). The total scan time was 20 minutes.

Results: A number of strong correlations between spectroscopic measures and neuropsychological measures were found. Global NAA/Cr correlated with the General Cognitive Factor ($r = 0.64$, $p = 0.004$) and the Cognitive Dysfunction Factor ($r = 0.68$, $p = 0.002$). Furthermore, significant correlations were seen between global NAA/Cr and the following cognitive domains: Mental processing/speed ($r = 0.66$, $p = 0.003$), Working memory/attention ($r = 0.73$, $p = 0.001$) and Naming/verbal retrieval ($r = 0.56$, $p = 0.015$).

Discussion and Conclusion: When implemented at the diagnostic phase of MS, multi-slice EPSI might provide information about early cognitive impairment and indicate the need for neuropsychological evaluation; it might also be of importance in future clinical trials as a surrogate marker in order to assess if early treatment can prevent the development of further cognitive impairment.

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References:
[1] Mathiesen HK, Tscherning T, Sorensen PS, Larsson HB, Rostrup E, Paulson OB, Hanson LG. Multi-slice echo planar spectroscopic imaging provides both global and local metabolite measures in multiple sclerosis. Magn Reson Med (in press).

Fig. 1 Brain areas suitable for spectroscopy were evaluated to provide information on global NAA, Cho and Cr.