Proton MR Spectroscopic Imaging in Neurofibromatosis Type-1: Relationship to Neuropsychological Testing

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Introduction
Neurofibromatosis type I (NF1) is the most commonly encountered phakomatosis. Cognitive impairments and learning disabilities are commonly reported in children with NF1. A prior proton MR spectroscopic imaging (MRSI) study found metabolic abnormalities in the thalamus in children with NF1 1; however, it was unclear if NF1-associated neuropsychological deficits were related to abnormal thalamic metabolism or not. The current study was therefore conducted to (a) confirm the prior findings of abnormal metabolism in NF1, and (b) to investigate whether or not there is an association of cognitive impairment/learning disability to brain metabolism in NF1.

Material and Methods
Thirteen children with NF1 (age range 7 to 15 years) and seventeen age-matched healthy controls underwent conventional brain MRI and proton MRSI. All subjects also underwent a battery of neuropsychological tests as described previously 2. Of these tests, NF1 subjects have been found to often perform poorly on the “Judgment of Line Orientation” (JLO) and “Boston Naming Test” (BNT), tests of visuospatial skill and object naming, respectively. These 2 tests were therefore selected for comparison to MRSI data.

All imaging was performed at 1.5 T. MRSI was performed using a multi-slice spin-echo pulse sequence (TR/TE = 1900/280 msec) with CHESS water suppression and outer-volume saturation (OVS) for lipid suppression. Three 15 mm thick slices (gap 2.5 mm) were recorded covering from the cerebellum to the centrum semiovale (with the central slice at the level of the thalamus) 3. With a field of view of 24 cm, 28x28 circularly-encoded phase-encoding steps were recorded giving a scan time of 20 minutes, and a 1.1 cm3 nominal voxel size.

Spectra from the brain stem, cerebellum, striatum, occipital white matter, mesial occipital cortex, centrum semiovale, parietal white matter, parietal gray matter and thalamus were bilaterally evaluated, and ratios of metabolite peak areas (for N-acetyl asparate (NAA), Creatine (Cr) and Choline (Cho)) were calculated. Student t-tests were used to determine between group differences, and regression analyses performed to determine correlations between metabolite ratios and neuropsychological tests.

Results
NF1 patients showed significantly lower NAA/Cr and NAA/Cho ratios in the thalamus (p=0.017 and 0.04 respectively) and in the parietal white matter (p=0.04 and 0.039 respectively) as compared to the controls. Also, there was significant positive correlation between the JLO scores and NAA/Cr ratios in the brain stem, striatum and thalamus (p=0.018, 0.03, 0.016 respectively), as well as significant positive correlations between JLO scores and NAA/Cho ratio in the brain stem, cerebellum, occipital white matter (p=0.004, 0.001, 0.019 respectively). There was also a significant negative correlation between JLO and Cho/Cr ratio in the cerebellum (p=0.015). Significant positive correlation was also found between the (BNT) and NAA/Cr and NAA/Cho ratios in the brain stem (p=0.016, 0.009 respectively), and in NAA/Cho in the cerebellum (p=0.02).

Discussion
Reduced ratios of NAA/Cho and NAA/Cr in NF1 confirm the previous observation of abnormal thalamic metabolism 1, and suggest possible neuroaxonal loss or dysfunction in NF1. Abnormal thalamic metabolism in NF1 has also been reported using positron emission tomography 4. Neuropsychological test scores, in particular JLO, showed correlations with NAA/Cho and NAA/Cr in multiple brain regions, including the thalamus, suggesting a link between (widespread) abnormal brain metabolism in NF1 and cognitive impairment. These data suggest that MRSI, in addition to MRI, may help understand the pathophysiology of brain involvement in NF1, and its relationship to cognitive impairment and learning disabilities.

References
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