Quantitative ^{1}H Magnetic Resonance Spectroscopy in Boys with Duchenne Muscular Dystrophy

R. Kreis[1], E. Giger[2], P. Vermathen[1], S. Strozzi[3], F. Kaufmann[2], C. Boesch[1], M. Steinlin[3]

[1]Dept. Clinical Research, University & Inselspital Berne, Berne, Switzerland, [2]Pediatric Neuropsychology, University Children's Hospital Berne, Berne, Switzerland, [3]Pediatric Neurology, University Children's Hospital Berne, Berne, Switzerland

Introduction

Duchenne muscular dystrophy (DMD) is characterized by absence or disruption of the protein dystrophin, which is normally found in muscle, the CNS (in particular cerebellum) and other tissues. The resulting muscle weakness usually leads to a need for a wheelchair by age 10 and death at ~ age 20. The absence of dystrophin has long been recognized as cause for cognitive impairment [1,2], although the role of dystrophin in the CNS is not finally elucidated. Earlier studies in DMD children and the *mdx* mouse model found altered bioenergetics [3] and increased cerebellar choline (Ch) levels in the form of increased Ch/Cr and Ch/NAA level ratios [4].

Methods

A group of 16 boys with DMD (12±4 years) and a matched group of 19 healthy boys (12±4 years) was investigated with a battery of neuropsychological tests (WISC/WAIS, attention tests, VLM, RVDLT, Rey figure, block tapping, fluency). In 11 of the patients and 14 of the healthy boys a quantitative ^{1}H-magnetic resonance spectroscopy (^{1}H-MRS) exam of the cerebellum and the functionally left temporal lobe was performed. All spectra were recorded on a clinical 1.5 T MR scanner using an optimized PRESS sequence (20 ms TE) [5]. Single voxel spectra were recorded from temporal cortex, centered on the posterior part of the Sylvian fissure (3s TR, 64 scans; 9.6 cm^3). In the cerebellum, 1D CSI spectra were acquired, yielding 5 spectra of nominally 2.5 cm^3 from a PRESS volume of 12.5 cm^3 (70 x 12 x 15 mm^3, 16 phase-encoding steps in L/R; TR 2.5s; 16 scans per step). Single voxel data were processed, fitted and quantitated as described earlier [5]: LC-Model with 22 model compounds including a peak at 0.9 ppm and a macromolecular baseline spectrum, quantitation based on unsuppressed water. Quantitation of SI data [6] was based on unsuppressed water and tissue composition information obtained from relaxometry (multi TE IR images). Spectra were rejected if error bounds were > 50% or the linewidth was > 0.07 ppm. Extrapolation, based on voxel composition provided tissue content of pure cerebellar white matter (WM).

Results

Typical CSI spectra of cerebellum from a 8 year old DMD patient and an age-matched healthy boy are plotted in Fig. 1, together with the LC-Model fit. Fig. 2 contains the averaged spectra from all DMD patients and healthy controls for the left temporal location. Patients with DMD had significantly lower total choline (Ch_{tot}) levels in both, the temporal location (-15%) and the cerebellum (~-10% overall and also extrapolated to pure WM, whereas the central voxel with largest GM contribution did not show a Ch_{tot} deficit, but a significant 8% increase in Cr_{tot}). A small, but significant increase in NA (=NAA+NAAG , +3%), (NA/Ch_{tot} (+23%), NA/mI (+8%)) was found in the temporal lobe for DMD boys. General intelligence assessment showed a mean IQ of 86 with 56% of boys showing an IQ < 85. In DMD patients a highly significant association was found between the Ch_{tot}/Cr_{tot} ratio in the left temporal lobe and visuo-spatial memory. Also significant were the correlations between NA/mI in the left temporal lobe and verbal performance as well as between NA/Cr_{tot} and Ch_{tot}/Cr_{tot} in the cerebellar WM and divided attention.

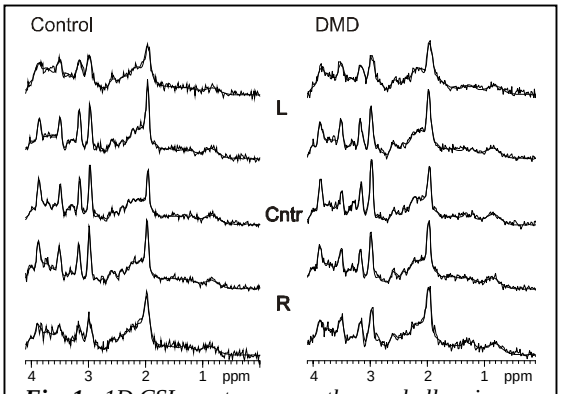

Fig. 1: *1D CSI spectra across the cerebellum in a healthy control and a DMD patient. (Experimental and fitted spectra, left to right).*

Discussion & Conclusion

Compared with the results of prior studies [4] we could not confirm an increase in the ratio of choline to NAA. In contrast, the patients in this study showed a consistent decrease in absolute Ch_{tot} levels and corresponding ratios in both the cerebellum and a temporal voxel. Spectral quality was excellent, guaranteeing the integrity of these findings. Virtually all other major metabolites and the macromolecular components were indistinguishable from normal for both locations in spite of very low within-group standard errors of 2-5% for most major metabolites. The abnormal Ch_{tot} levels are consistent with irregular membrane/myelin turnover in association with the missing dystrophin in DMD, although it is unclear why in this group of patients Ch_{tot} levels are lower and not higher as observed before. Accidental significance for some of the correlations found between metabolite levels and neuropsychologic test results cannot be excluded, but association between metabolite disturbance and visuo-spatial memory is in accordance with expectations.

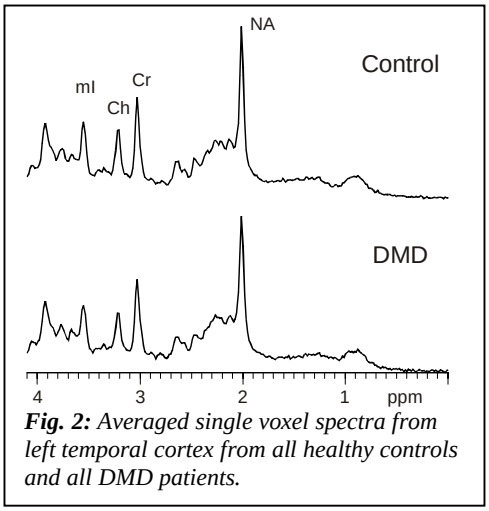

Fig. 2: *Averaged single voxel spectra from left temporal cortex from all healthy controls and all DMD patients.*

References

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