Age dependence of the downfield region of cerebral ^{1}H MR spectra

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Introduction

^{1}H-MR spectroscopy has been used to study human brain development in situ. Metabolic changes have been noted in the fetal, neonatal, pediatric, and even adult periods. Changes in the appearance of the normal spectrum are of course also relevant for the judgment of pathologic states. All these investigations have been based on the high-SNR, upfield part of the brain spectrum, where most features are well identified. The downfield part of the spectrum is still ill-defined, with most peaks only tentatively assigned, and there is no information on age-dependence of the spectra. It would be well possible that 1) the visibility of amide protons, which depends on the exchange rates and hence on the intracellular milieu, is different in early childhood, or that 2) the content or visibility of macromolecular compounds depends on age. In terms of established applications, it is essential to define the age-dependent normal down-field spectrum in order to extend the measurement of brain phenylalanine (Phe) [1] to the pediatric population.

Methods and Subjects

37 healthy subjects (newborn to 48 y) were investigated by ^{1}H-MRS using a protocol focused on the downfield part of the spectrum. For statistical analysis, the subjects were collected in age groups 1 to 6: 1 (<2 weeks old, N=3), 2 (6-10 yrs, N=5), 3 (10-15 yrs, N=6), 4 (15-20 yrs, N=6), 5 (20-30 yrs, N=9), 6 (30-50 yrs, N=8), and an adult group combining group 5 and 6. All spectra were recorded on a clinical 1.5T MR scanner (Signa, GE) using a quadrature head coil. Data acquisition and processing was as described in [1]. In brief: PRESS localization (20ms TE, 2.0 and 2.5 s TR for adult and neonates, respectively, 128-256 acquisitions/spectrum, 1-3 spectra per subject, supraventricular ROI of 17-70 cm^3 for neonates and adults) including non-water-suppressed scans for referencing (eddy current correction, compartment information, quantitation standard). Spectral fitting was performed with TDFDfit [2]. An averaged control spectrum obtained from adult subjects was used to set up the initial fitting model using 10 Voigt lines to describe obvious spectral features in the raw spectrum or necessitated by non-random residuals. No prior metabolite information was enforced, except for a peak at 7.8 ppm to define the NH peak of NAA and an additional metabolite pattern for Phe (aimed at PKU patients in a different study and kept at physiologic concentration in initial optimizations). In the final analysis to define the age dependence of these peaks in all subjects, the relative frequency differences and the linewidths were enforced to remain constant. Two variable lines were used to define the residual water peak. The spectral phase was automatically defined using the water reference and not fitted. The water scans were also used to define the lineshape [3] and to scale the metabolite peak areas into institutional molal units –without relaxation corrections. Group differences were tested by unpaired t-tests, where the threshold for significance was set at 0.01 to accommodate multiple testing.

Results

Fig. 1 presents averaged spectra for all age groups. Obvious differences are only seen for the neonatal group. The small residues show that the fitting model is sufficient for an initial analysis. However, there are small non-random features in the summed residues indicating that the fitting model can be improved. Detailed age-dependence for peak intensities is given in Fig. 2. Statistical analysis confirms that the NAA peak (mainly represented by a line at 7.8 ppm, but also influencing 2 further overlapping peaks in the fit model) shows the strongest age dependence (significant differences for groups 1, 2 and 3 compared to the adults, p<<0.001). The neonatal group featured several other significant differences, incl. the peaks at 6.8, 7 and 7.3 ppm. The 7 ppm peak was also below adult levels in group 2 (<10 y). The major baseline peak for Phe measurements at 7.3 ppm did not show any significant changes apart from the neonatal group.

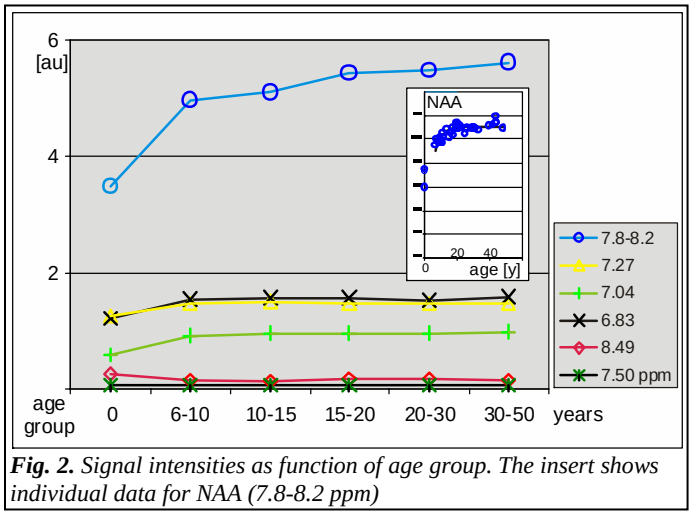

Fig. 2. *Signal intensities as function of age group. The insert shows individual data for NAA (7.8-8.2 ppm)*

Discussion & Conclusion

Normal downfield spectra are presented as a function of age. Major differences are evidenced for neonates, but one should note that presented results are in molal units, such that part of the apparent changes is due to the larger water content in neonatal brain. For older children, the NH peak of NAA is still increasing up to age 15, while no significant changes were found from 15 to 50 years. The averaged spectra can now serve as age-dependent norm for determination of Phe [1], or in diagnostic MRS. The fitting model can be refined to include spectral information based on suspected assignments e.g. restrictions for ATP peaks at 8.2 and 8.45 ppm.

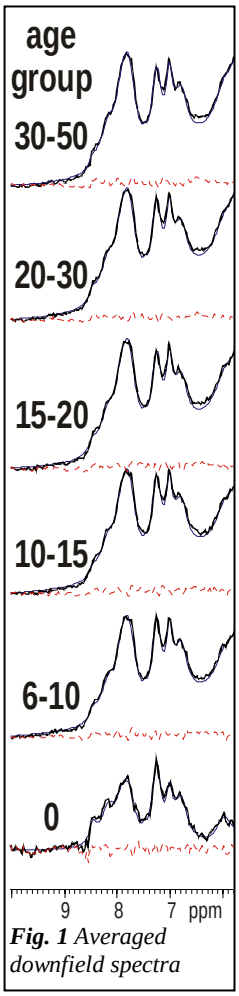

Fig. 1 *Averaged downfield spectra*

References

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