Metabolite and Baseline Characterization in the Downfield Region of the Human Cerebral ^{1}H-MR Spectrum in Healthy Subjects and Patients with Phenylketonuria

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Introduction

The upfield region of the human cerebral ^{1}H-MR spectrum is fairly well characterized in terms of contributing metabolites and the macromolecular baseline. In contrast, in the downfield region, i.e. between 5 and 10 ppm, peak assignment and distinction between signals from low-molecular weight metabolites and macromolecular baseline have not been properly established. This differentiation is particularly challenging in the downfield region, because 1) contributing metabolites are of low concentration and/or 2) the contributing protons are exchangable (influenced by water presaturation and may have intrinsically larger linewidths). In-vivo characterization of saturable protons was possible in animal brain, but clear assignments were not feasible[1,2,3]. Pharmacological and supplementation studies yielded exact resonance positions for phenylalanine (Phe, 7.37 ppm)[4], homo-carnosine (Cs, 7.05, 8.02 ppm)[5], and histidine (His, 7.07, 7.83 ppm)[6], but also implied that from these only Cs contributes substantially to a healthy control spectrum. The other undisputed contributor is the N-H proton of NAA at ~7.89 ppm. Further potential contributors include glutamine (6.8 ppm), creatine (6.8 ppm), tryptophane (7.3 ppm), and ATP (8.22, 8.45 ppm). Macromolecular resonances are usually characterized by short T_1 and T_2. The T_2 effect attenuates their contribution at longer TE[6]. The T_1 dependence has been exploited in the upfield region to define macromolecule and metabolite spectra separately[7,8] and is used in this work to characterize the downfield spectrum.

Methods

All spectra were recorded on a 1.5T scanner (GE) using a quadrature head coil. 7 healthy subjects (mean age 30.1 y) and 5 patients with phenylketonuria (PKU, 30.6 y) were investigated in a ROI in centrum semiovale (70 cm^3). Two series of 16 saturation recovery (SR) PRESS spectra were obtained as described in [8] (TE 20 ms, water presaturation, 16 SR delays spaced logarithmically from 0.2 to 7 s, 16 acquisitions per delay, adiabatic saturation pulse, 11.5 min per spectrum. ROI compartmentation analysis used the T_2 decay of water (TE 20 to 1500 ms)). For eddy current correction and frequency alignment SR spectra were aquired without water suppression (1 NEX). Modelling of the SR data was performed point by point without any assumptions on lineshapes[8]. A distribution of T_1 values between 0.1 and 1.7 s was enforced. T_1 components < and > 0.5 s were collected to constitute the baseline and metabolite spectra, respectively.

Results

Averaged metabolite (A), baseline (B), and total spectra (C) are shown in Fig. 1, as obtained for healthy control subjects (left), PKU patients (middle) and their difference (right). The baseline spectra for controls and PKU patients are very similar, in spite of the large contribution from Phe that manifests itself in the metabolite (top) and total (bottom) spectra.

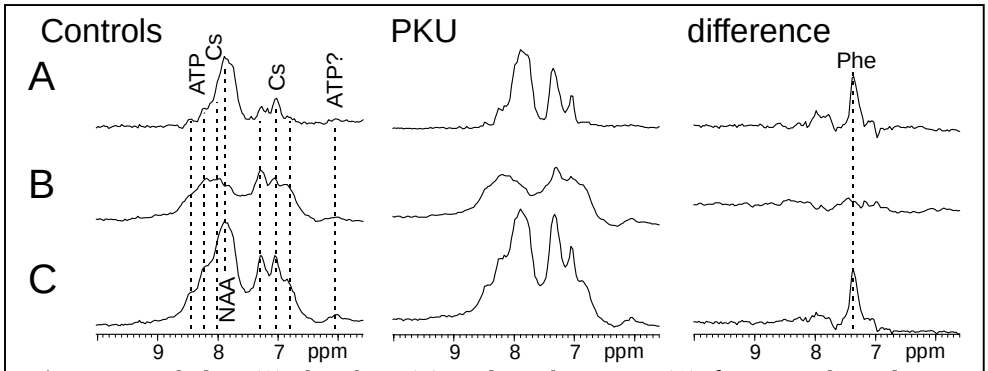

Fig. 1: *Metabolite (A), baseline (B) and total spectra (C) for controls and PKU patients differentiated by a SR sequence*

Discussion

- A substantial part of the downfield spectrum is constituted by short T_1 components.
- The segregation obtained by the proposed algorithm appears to work reliably, as the baseline determination is largely unaffected by a big overlapping signal from Phe in PKU patients.
- Based on the literature, it is likely that peaks from NAA, Cs, and ATP form most of the metabolite spectrum, while Cr and Gln do not seem to contribute with long T_1 signals (probably invisible because of water saturation).
- Most of the 7.3 ppm signal overlapping with the Phe resonance at 7.37 appears to originate from short T_1 components. This is surprising, given the fact that the 7.3 ppm peak has been shown not to disappear rapidly with increasing TE[6].

Acknowledgement: *Supported by the Swiss National Foundation (31-059082)*

References

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