

MR Spectroscopy without Water Suppression for the Determination of Proton Exchange Rates in the Human Brain

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Introduction

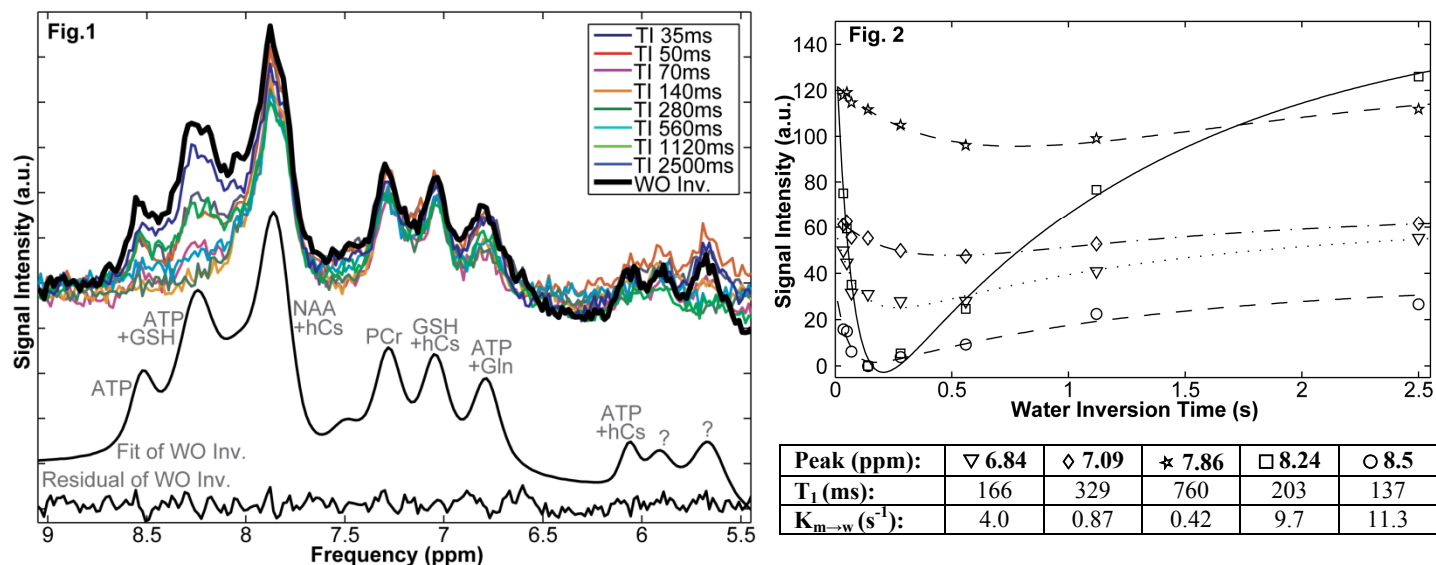
Water suppression (WS) abates resonances originating from protons that exchange magnetization with water. Recently, a method for simultaneous acquisition of water and metabolite spectra without WS has been demonstrated in healthy rat brain¹. It employs two asymmetric adiabatic pulses² to invert the metabolite peaks prior to their measurement in alternate scans, and it was further adapted into a scheme with alternate inversion of the up- and down-field spectrum to reduce T_1 effects³. The goals of this project were to apply the latter technique to the *in vivo* human brain, to determine what additional metabolites are visible in the spectrum downfield from water if no WS is applied, and to calculate their exchange rates with water.

Methods

12 healthy volunteers (20-30 y, mean 24 y) were recruited, and informed consent was obtained prior to scanning on a 3T Siemens TRIO system. Sagittal and axial images were acquired to prescribe a mixed gray and white matter supraventricular region of interest (ROI). A large volume (mean size of 54 ml) was used to detect low concentration metabolites. Spectra were acquired using a PRESS sequence (TE/TR=20/4000ms, 64 acquisitions) preceded by an RF pulse to invert the upfield or downfield metabolites in alternating acquisitions³. The experiment was performed with and without (WO) an additional selective 180° prepulse to invert water at varying times before the PRESS sequence (TI = 35, 50, 70, 140, 280, 560, 1120, 2500 ms). Individual spectra were stored, and each acquisition was Fourier transformed, then frequency and phase corrected. Pure metabolite and water spectra were obtained from either summation or subtraction. Both were eddy current corrected using the water spectrum. Metabolite spectra summed over all volunteers were fit in the frequency domain using FiTAID⁴ (which modeled peak areas as Voigt lines at all water inversion delay times simultaneously) after an HLSVD peak removal of the residual water with jMRUI⁵. Finally, to calculate proton exchange rates, the peak areas with varying TI were fit using non-negative least squares minimization to a two-site Bloch-McConnell model that included two phases during which magnetization transfer can occur, saturation recovery between PRESS and water inversion, followed by inversion transfer. Water T_1 was obtained from the water data. Metabolite T_1 values were constrained to lie between 0.05 and 50 s, and steady-state reaction fluxes were enforced.

Results

Fig. 1 shows the downfield spectrum summed over all volunteers, with and without water inversion. The bottom traces show the FiTAID fit of the spectrum without water inversion, with potential assignments taken from the literature⁶. Adenosine triphosphate (ATP), N-acetylaspartate (NAA), phosphocreatine (PCr), homocarnosine (hCs), glutathione (GSH), and glutamine (Gln) may cause some or parts of some of the observed peaks. Fig. 2 demonstrates the fit of the exchange model to a few example resonances, with the resulting exchange rates of protons from metabolite to water ($K_{m \rightarrow w}$), as well as T_1 values, in the table below. Resonances that have higher T_1 relaxation rates tend to also have higher exchange rates. Lifetimes ($1/K_{m \rightarrow w}$) range from 90 ms to >2 s. Short lifetimes give rise to magnetization transfer curves with a deep minimum at short TI times.



Conclusions

These preliminary results suggest that ¹H-MRS via simultaneous metabolite and water measurement enables the detection of more resonances downfield of water in the human brain spectrum, which promises the ability to detect metabolites not visible in the upfield spectrum, such as ATP and hCs, and to better resolve Gln from Glu. In addition, metabolite proton exchange rates can be measured through experiments employing a water inversion preparation pulse, offering information about pH and the chemical microenvironment *in vivo*. A separate fit of spectra from each subject will allow estimates of the intersubject variability, and errors on T_1 and $K_{m \rightarrow w}$. This information may be helpful in the investigation of brain pathologies, as well as in the understanding of proton transfer enhancement in chemical exchange dependent saturation transfer imaging.

References

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