NOE Enhancements of Phosphorylated Metabolites in Human Brain at 1.5T

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Introduction: ^{31}P MRS of the brain allows the detection of phosphocreatine (PCr), ATP, inorganic phosphate (Pi), phosphomonoesters (PME), and phosphodiesters (PDE). From the chemical shift difference of PCr and Pi, the pH of tissue can be calculated. Standard ^{31}P MRS is compromised by low signal-to-noise (S/N) and complex multiplet structures caused by J-coupling. Proton-decoupling simplifies the complex pattern by separating multiplets into single peaks and improves the S/N due to the Nuclear Overhauser Effect (NOE) (1). For the absolute quantitation and for the interpretation of differences in peak ratios of proton-decoupled 31P spectra the knowledge of NOE factors in normal and diseased state are required.

Materials and Methods: Fifteen subjects (twelve healthy controls and three patients with normal MRI) were studied with non-decoupled and decoupled spectroscopy. A clinical 1.5 T GE scanner was equipped with a stand-alone decoupling unit (GE Medical Systems, Fremont, California). Standard 31P and proton-decoupled 31P spectra were acquired using a double-tuned head coil (Advanced Imaging Research Inc, Cleveland Ohio). Before acquiring 31P spectra, the regions of interest were identified on MRI, an automated shim procedure was carried out, and the resonance proton frequency for subsequent proton-decoupling was obtained. Spectra were acquired using a slice-selective spinecho sequence with a self-refocusing RF pulse at TE = 2.5 ms and TR = 1.5s. The 30 mm slab was centered at the level of the ventricles. In three subjects, two-dimensional phase encoding (CSI, 6×6, FOV=180-200mm) was applied. Acquisition times were 2.2 min for slice selective acquisition without phase encoding and 21.6 min for CSI acquisitions, respectively. For decoupling, a WALTZ-4 sequence (2) was used with a decoupling bandwidth of 500 Hz. The irradiation of WALTZ-4 pulses was continued at a 10-fold reduced power level during the recovery period to generate NOE. RF power deposition was monitored throughout the studies and did not exceed the limits defined by FDA guidelines (3). Data were post-processed using Sage 7^{TM} (GE Medical Systems, Fremont, California). 31P spectra were Fourier transformed after 4 Hz Gaussian apodization in the time domain. Spectra were then analyzed using the frequency domain fitting routines incorporated in Sage 7^{TM} program. Gaussian lines were fitted to the resonances of PE, PC, inorganic phosphate (Pi), GPE, GPC, PCr, γ-ATP (two lines), α-ATP (two lines), dinucleotides (DN), and β-ATP (one broad line) and peak areas, amplitudes, and linewidths were analyzed. Regions in the occipital cortex mainly containing grey matter (GM) and in the parietal cortex mainly containing white matter (WM) were analyzed separately for each subject undergoing a CSI study and treated as separate measurements.

Results: Low S/N compromised the accurate determination of peak areas in some spectra and caused large standard deviations in the results. However, when all data were pooled, significant NOE enhancements were measured for Pi, PCr, γ-ATP, and α-ATP (Fig.1, Table). A significant line narrowing for α-ATP (-21±15%, $p<0.000003$, paired t-test) was measured while the linewidths of other resonances were not affected significantly by decoupling. The combined effect of NOE enhancement and line narrowing resulted in a 50% increase in peak amplitude for α-ATP. There was no significance difference in NOE between WM and GM spectra nor between CSI and brain slice spectra. NOE enhancement for β-ATP was not determined in all data. γ-ATP and α-ATP NOE enhancements were not determined for WM and GM data sets because of low S/N.

Table: NOE enhancement of phosphorylated metabolites in the brain

	PCr	Pi	γ-ATP	α-ATP
All Data Pooled (n=18)	34±10%***	25±25%**	11±24%*	19±18%**
Brain slice (n=12)	32±13%	23±24%	11±24%	19±18%
WM (n=3)	42±19%	38±35%	ND	ND
GM (n=3)	50±12%	18±20%	ND	ND

*p<0.05, **p<0.01, ***p<0.00001 paired t-test: decoupled vs. non-decoupled studies

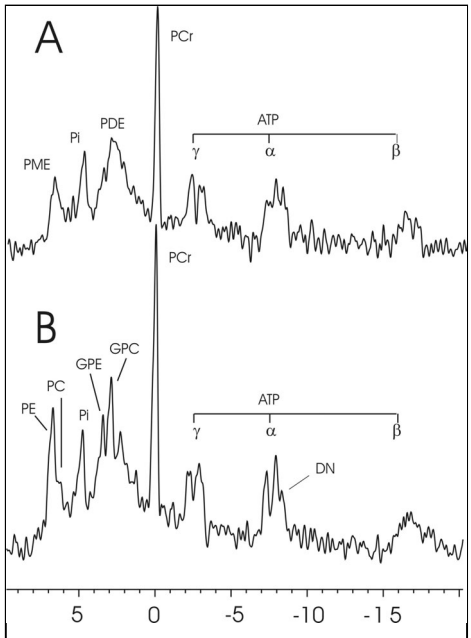

Fig.1: Standard 31P MRS (A) and proton-decoupled 31P MRS (B) from a 30 mm slab of the human brain.

Discussion: PCr, Pi, γ-ATP, and α-ATP showed significant NOE enhancement, however, with very different reproducibility. NOE of PCr is consistent with results obtained in a single control by Murphy-Boesch et al. (4) at 1.5 T and is slightly larger than what has been reported in recent study at 7T for the occipital cortex (5). In contrast to previous studies we measured a significant line narrowing of α-ATP.

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