Quantification and Reproducibility of L-COSY in Human Brain at 7T

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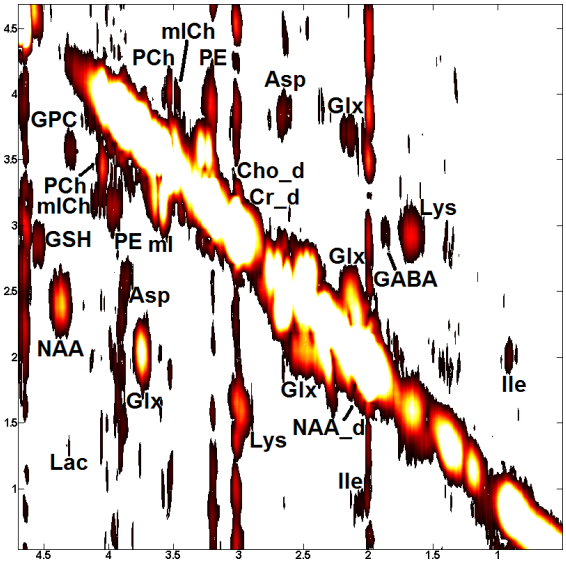
Introduction: Localized correlated spectroscopy (L-COSY) (1) detects J-coupling interactions by indirectly monitoring the t_1 evolution of coupled spin systems. This increases the specificity as L-COSY can resolve resonances that overlap on conventional 1D MRS methods (2). The sensitivity can additionally be increased at higher field strengths due to increased chemical shift dispersion and signal intensity. We demonstrate the ability of L-COSY in reliably identifying several metabolites from the human brain at 7T. The versatility of this method in assessing various anatomical regions of the brain is also demonstrated in this study using a whole body 7T scanner.

Materials & Methods: A single-voxel PRESS-based L-COSY sequence (1,3) was implemented on the Siemens whole body 7T MRI scanner with a 32-channel head transmit/receive coil. VAPOR-based water suppression (4) and FASTESTMAP shimming routines were employed to optimize signal quality. Reproducibility tests were performed on a phantom containing metabolites, typically observed from the white matter, at physiological concentrations. Scan parameters for the reproducibility studies were as follows: 18/2000ms TE/TR, 8 averages, 2048 F_1 points, 64 Δt_1 increments, 4000/2500 F_2/F_1 bandwidths and 2x2x2cm^3 (8ml) voxel size. The *in vivo* human brain reproducibility tests were performed by acquiring the L-COSY spectra from the occipital lobes of six healthy volunteers (all male, ages 30 to 72) using the same acquisition parameters except that a TE of 20 ms and a voxel size of 3x3x3cm^3 (27ml) was used. In two subjects, L-COSY spectra were also acquired from multiple locations such as the basal ganglia, frontal lobe, parietal lobe and dorso-lateral prefrontal cortex to test the viability of L-COSY in differing anatomy. These scans were acquired with a 18ms TE and 2.5x2.5x2.5cm^3 (15.6ml) voxel size and each scan took 17 minutes.

All data were post-processed offline using a custom MATLAB-based program, which applied zero-padding and line-broadening filters along both spectral dimensions. Metabolite concentrations were quantified using both simple volume integrals and Prior-knowledge fitting (ProFit), a 2D fitting program analogous to LC Model in 1D spectroscopy. Reliability was measured in terms of the coefficient of variation (CV) in the metabolite ratio with respect to the 3.0ppm peak due to creatine (S/S_{Cr}).

Results & Discussion: 2D L-COSY was successfully implemented on the 7T scanner and lead to acceptable CVs from brain phantom and human brain. The CVs quantified using prior-knowledge based peak fitting, shown in the second column in Table 1, ranged from 2-7% in diagonal peaks and 8-19% for cross peaks. Figure 1 shows a spectrum extracted from a 27ml voxel in the occipital lobe, showing diagonal peak resonances of choline (Cho_d), creatine (Cr_d) and N-acetylaspartate (NAA_d). The 2D spectrum also contained several cross-peak resonances, not typically resolved in 1D, including aspartate (Asp), γ-aminobutyric acid (GABA), glutamate/glutamine (Glx), glutathione (GSH), isoleucine (Ile), lysine (Lys), myo-inositol (mI), mI+free choline (mICh), phosphocholine (PCh), glycerophosphocholine (GPC), phosphoethanolamine (PE) (2). The same metabolite profile was also visible in other regions of the brain including the spectrum acquired from a much smaller voxel of 15.6ml in the parieto-occipital region shown in Figure 2. CVs of S/S_{Cr} for the occipital lobe, quantified using volume integrals are shown in the first column of Table 1, ranged from 4-16% for diagonal peaks and 6-28% for cross peaks.

Met	P	CV_{BP}	CV_{OL}
Cr39	d	3.7	14.1
mI	d	7.1	11.0
Cho	d	2.4	3.6
NAA	d	3.8	15.5
Car7	d		22.8
Car8	d		4.9
NAA	C	8.6	11.9
Asp	C	11.5	19.7
Lac	C	13.4	15.4
Glx	C	19.2	19.4
mI	C	14.0	14.2
PE	C	9.8	25.1
PCh	C	8.9	24.3
GPC	C		24.3
mICh	C	10.5	23.4
Lys	C		6.4
Tau	C	18.5	
GABA	C	15.5	15.4
Ile	C		24.6
GSH	C	9.8	28.3



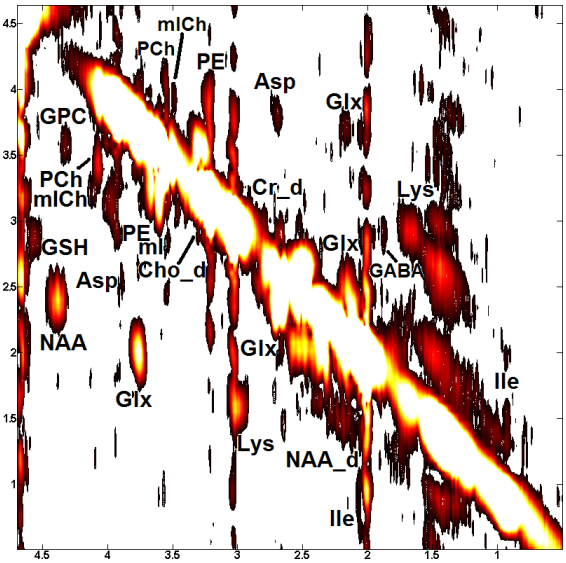


Table 1 (Left): CVs of S/S_{Cr} ratio taken from reproducibility studies of brain phantom (CV_{BP}, n=16) and occipital lobe (CV_{OL}, n=6) of normal subjects. Diagonal and cross peaks are indicated with a d or C, respectively, in the second column.
Figure 1 (Middle): Typical spectrum taken from a 27ml voxel extracted from the occipital lobe of a healthy volunteer.
Figure 2 (Right): A 2D L-COSY spectrum from a 15.6ml voxel in the parieto-occipital region of a healthy volunteer.

Conclusion: 2D L-COSY at 7T was able to uniquely resolve cross-peaks due to GABA, GSH, Lys and the choline group (Ch, PCh, GPC and PE), not typically seen in conventional 1D sequences or even 2D sequences at lower fields. Reproducibility studies resulted in CVs analogous to 2D L-COSY studies at lower fields (5). By incorporating more aggressive pulse timing and FASTESTMAP shimming, L-COSY sequence demonstrated similar resonance profile from other regions of the brain, even at a much smaller volume, indicating the versatility of this technique, which may aid in assessing metabolic profiles in pathological conditions.

References: 1. Thomas MA et al. Magn Reson Med 2001; 46:58-67, 2. Velan S., Magn reson Med 2007;26:405-409, 3. Thomas MA et al., NMR Biomed 2003:245-251, 4. Tkac et al. Magn Reson Med 1999; 41:649-656 5. Binesh N et al. Magn Reson Med 2002; 48:942-948