J-Resolved Proton Echo Planar Spectroscopic Imaging of GABA in the Human Brain

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Abstract: Two-dimensional, J-resolved magnetic resonance spectroscopy (2D, JMRS) has been combined with proton echo-planar spectroscopic imaging (PEPSI) to drastically reduce the required scan time needed to sample enough k-space and TE-points to adequately resolve and quantify the gamma-amino butyric acid (GABA) resonance sideband at 2.95ppm from neighboring creatine (Cr) at 3.03ppm at 4 Tesla. This combination of techniques allows us to either drastically reduce the scan-time needed to acquire a whole J-resolved PEPSI (JEPSI) dataset at a modest spatial resolution of 16x16, or to vastly increase spatial resolution to 32x32 in a clinically-sound scan time. Our previous sequence using a sparse-reduced k-space sampling scheme required 49 minutes to sample 96 k-space points on a Cartesian grid (TR=1.25s), with 24 TE-steps/k-space point, yielding a 16x16 matrix of 4.5cc nominal voxels (1,2). In this work, we demonstrate that with our JEPSI sequence we are able to obtain quantifiable in vivo GABA spectra from 1.7cc voxels at 32x32 resolution (collecting all 1024 k-space points) in 45 minutes (TE steps = 24, TR=1.25s).

Introduction: Gamma amino butyric acid (GABA) plays a key role in many neuropsychiatric/neurological disorders such as epilepsy, panic/anxiety and drug/alcohol addiction. To measure GABA concentration in vivo throughout the brain is valuable in determining the spatial/anatomical distribution and nature of these disorders, as well as the effects of medications. To date, many methods have been devised to obtain in vivo GABA measures using MRS (3-6). The J-resolved method allows for a reasonably unobstructed measure of the GABA sideband resonance situated at 2.95ppm and J=7.5Hz, and is simple to implement on any MR scanner. J-resolved methods allow for the improved isolation of several J-coupled and uncoupled metabolites, as well as metabolite T_2 information. Combination of J-resolved techniques with MRSI (7) have proven useful in assessing tissue-specific GABA concentrations throughout the brain (1,2). However, the time needed to sample enough k-space points and TE-steps to provide adequate spatial resolution and quantifiable GABA spectra can be exceedingly long. Echo-planar spectroscopic imaging provides a means of rapidly obtaining an entire dataset compared to conventional phase encoding (8). By combining PEPSI with J-MRS, we are now able to obtain complete datasets in much shorter scan times, allowing for the implementation of signal-to-noise enhancing options such as k-space weighting during acquisition. In this work, we demonstrate that we can obtain quality J-resolved in vivo GABA from much smaller voxels from a 32x32 matrix in the same scan time as conventional phase-encoding (<1 hr).

Methods: All scans were performed on a Varian UnityINOVA 4 Tesla whole-body MR scanner, operating at 170.3MHz at the proton frequency, and used a volumetric, TEM-design head coil (Bioengineering Inc, Minniapolis, MN). High-resolution T_1-weighted sagittal and axial image sets (TE/TR=6.2/11.4ms, field-of-view (FOV)=24x24x16cm, readout-duration=4ms, receive bandwidth= ±32kHz, data matrix size=128x256x32, in-plane resolution=0.94x1.88mm, slice thickness=5mm, readout points=512, flip-angle=11/32°) were collected with a 3D-FLASH sequence for during-acquisition slab positioning and post-acquisition voxel placement. A standard spin-echo, slab-selective proton spectroscopic imaging sequence was modified with an echo-planar, spatial-spectral encoding readout gradient to collect an entire line of k-space for each shot in the readout direction. Standard phase encoding was done in the phase-encode direction, with variable k-space averaging for improved signal-to-noise in this dimension. For the JEPSI scan, the spatial-spectral gradient waveform used trapezoidal geometry with oscillating-polarity, collecting 1024 complex time-points/FID. Scan parameters for the 32x32 JEPSI acquisition used were: TR=1.25s, TE=30-490ms, slab-thickness=30mm, TE-steps=24 (20ms increments – 50Hz bandwidth in the J-dimension), readout-duration=512ms, FOV=24mm, nominal voxel volume=1.7cc, total complex points collected during readout=32768, acquisition bandwidth=64000Hz (15.625us dwell-time), averages/phase-encode step ranged from 1-6, Hanning-modulated filter, total scan time=45min. All JEPSI scans employed a WET water-suppression scheme for improved water suppression. A healthy human male volunteer was first informed/consented according to McLean Hospital and federal policies regarding research with human subjects, then screened for any MR-incompatible implants/devices. All JEPSI data were processed and reconstructed offline using C-code developed on-site. The raw JEPSI data were first reconstructed to produce even- and odd-echo images for each TE-step. Then, phase-correction factors for each real spectrum using the Cr-Cho complex at 3.00-3.20ppm from the spatially resolved image at the first TE-step were calculated, since the signal-to-noise is highest for this purpose. Then, the following TE image sets were phase-corrected using these initial phase-correction factors and all image sets were then back-FFT'd to k-space. Even- and odd-echo k-space FIDS were then combined to produce a single image set with the original 2kHz spectral bandwidth intact. JEPSI spectra were extracted from J=0.0Hz and J=7.5Hz (Figure 1).

Results/Discussion: These preliminary results indicate that we can successfully combine rapid echo-planar spectroscopic imaging with J-resolved MRS to obtain quantifiable J-resolved GABA spectra in vivo. The benefits are either a drastically reduced scan-time for a larger (4.5cc) voxel and 16x16 sampling grid, or much better spatial resolution (1.7cc) for a 32x32-sampling grid in the same scan-time as we have demonstrated here. Compared to our previous publications using conventional phase encoding, we have improved our spatial resolution to 1.7cc from 4.5cc for the same approximate scan-time (~45min). Remaining issues need to be addressed regarding our JEPSI acquisition. Combining even- and odd-echo data is susceptible to artifacts arising from disparity of even and odd gradient performance. Also, our gradients operate at a rather low slew-rate (300us ramp to maximum amplitude). Improved gradient performance would allow for less spatial and spectral artifact, as well as increased spectral bandwidth. Our eventual goal is to produce an actual image of GABA in the brain, showing the global distribution with the ability to quantify this distribution.

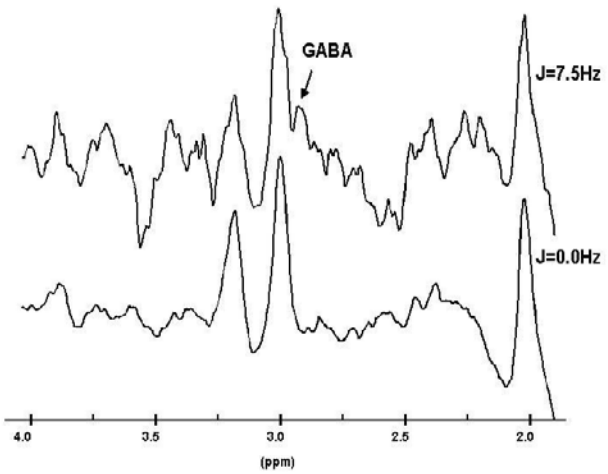

Figure 1 – JEPSI spectra from the brain of a healthy human volunteer. GABA-optimized (J=7.5Hz) and TE-averaged (J=0.0Hz) spectra displayed with 5Hz exponential filtering. Nominal voxel size is 1.7cc, 32x32 sampling grid, 45-minute scan-time. GABA spectrum has been vertically scaled for comparison to the TE-averaged spectrum.

Conclusions: J-resolved proton echo-planar spectroscopic imaging provides a rapid means of acquiring quantifiable in vivo GABA spectra, either greatly reducing scan-time requirements for a given voxel size, or vastly improving spatial resolution for a given scan-time. Our preliminary data suggest an approximate 3-fold improvement in spatial resolution in the same clinically reasonable scan time (< 1hr).

References:

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