Scan time reduction and selective maximization of three metabolites of interest with ^{31}P LFA-MRS in human brain at 3T

R-A. Blenman[1], and J. Port[1]

[1]Radiology, Mayo Clinic, Rochester, MN, United States

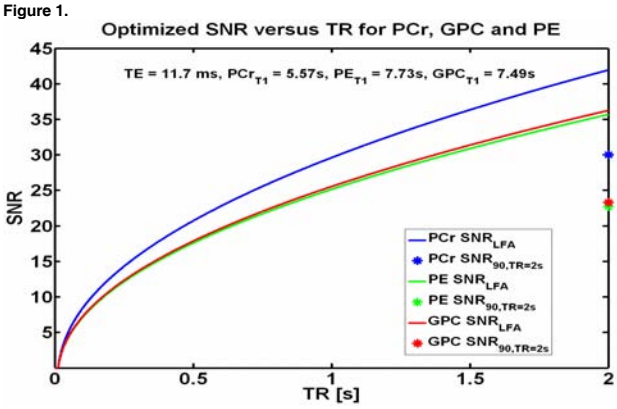
Introduction: Past ^{31}P studies of bipolar disorder suggest altered membrane turnover (↑ PDEs) and synthesis (↓ PMEs), and abnormal cell energetics (↓ PCr) in bipolar patients [1, 2, 3]. The changes in PMEs and PDEs could point to mechanisms that involve intracellular communication or signal transduction (PMEs), activation of several enzymes (phosphoserine), regulation of cytokinesis, correct protein folding of membrane proteins lipid homeostasis (PE), delivery of the essential nutrient choline, which is a precursor in the synthesis of the neurotransmitter acetylcholine (PC and GPC), fluidizing effect on cellular membranes (PC), and regulation of osmosis (GPC). If ^{31}P MRS diagnostic tools that specifically measure the levels of the metabolites indicated in bipolar disorder could be developed, the clinical diagnosis and understanding of bipolar disease could be improved. To address the selective signal maximization of these specific metabolites, the large flip angle (LFA) technique was developed. LFA MRS uses an α°-180°-echo scheme where $180° > \alpha > 90°$. This technique, implemented at 3T, has been shown to selectively increase the signal of materials that have T_1 relaxation times greater than the TR times of the scan by as much as 93%[4]. In this work, a decrease in TR by as much as 60% is shown to be possible without loss of SNR.

Materials & Methods: All experiments were conducted on a GE 3T SIGNA scanner (GE Healthcare, Waukesha, WI) using a dual-tuned ^{1}H-^{31}P head coil (Clinical MR Solutions, Brookfield, WI). To validate our techniques, phantom experiments were conducted with the GE MRS-sphere (GE Healthcare, Waukesha, WI). In vivo measurements were acquired for three healthy subjects who gave written informed consent (IRB#98-05). After fast ^{1}H MR 3-plane localizers were obtained for ROI placement and shimming, all first- and second- order shim currents were adjusted on tissue water with an automated shim protocol. Linewidths of the PCr resonance observed from the 240mm × 240 mm × 20 mm axial slice placed above the brain ventricles were 7-10 Hz without Gaussian line broadening. ^{31}P acquisitions were taken at TR=2s and 0.8s with a standard spin echo scheme and LFA scheme respectively. The LFA acquisitions were optimized for the selective enhancement of the metabolites GPC, PE and PCr. For each measurement at TE=11.7 ms, 128 scans were acquired with 2048 data points and a spectral width of 5000 Hz. The half echoes were summed, reconstructed (Gaussian filtered, Fourier transformed and zero-order phase corrected) and the spectral peaks integrated.

Results & Discussion:

Figure 1 shows the simulated behavior of peak area-to-noise for the three peaks of interest – GPC, PE and PCr – as the TR is minimized. The large flip angle that corresponds to the minimum TR that is required to give the SNR of a standard 90°-180° spin echo sequence acquired with a 2s-TR is then determined by solution of the simultaneous equations shown in figure 1. Given the echo time of the spin echo sequence, and the respective mean T_1 values measured in 10 healthy subjects[5], the excitation angles that were found to maximize the GPC, PE and PCr peaks were theoretically predicted to be 153° if a TR_{min} of 0.84s was used, 153.9° (TR_{min} = 0.82s) and 145.8° (TR_{min} = 1s) respectively. Total scan time was predicted to be reduced by as much as 60% for the three peaks. Characteristic human brain localizer and spectral data from one volunteer are shown in figure 2. Comparable spectral quality was obtained for the LFA scheme (flip angle = 153°) as compared to the gold standard (flip angle = 90°). Additionally, total scan time was reduced from 4.3s to 1.7s as the TR was minimized to 0.8s.

Figure 1.



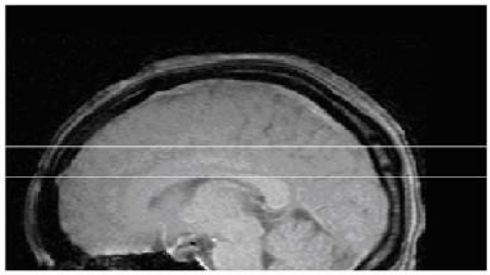
$$M_{xy} = \frac{\sin\alpha\,(1-2e^{-TR/T1}e^{TE/2T1}+e^{-TR/T1})}{(1+\cos\alpha\, e^{-TR/T1})}$$

$$M_{xy}(\alpha_{opt} = \cos^{-1}(-e^{-TR/T1}), TR) = M_{xy}(\alpha = 90°, TR = 2s)$$

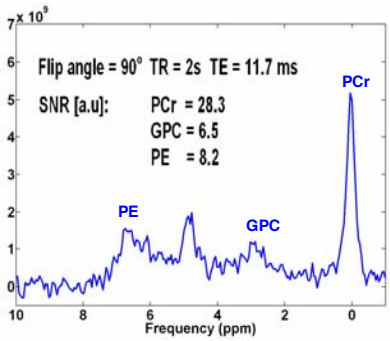
Conclusion:

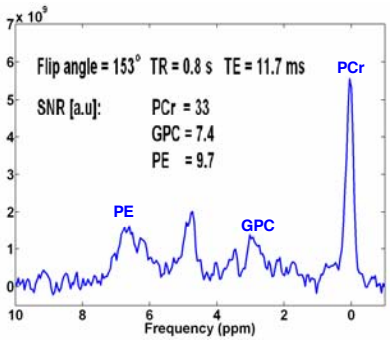
^{31}P MRS scan times are currently too long for routine clinical use because of issues with patient comfort and motion. As such, the SNR gain due to the LFA technique can be used to substantially shorten scan times. This work shows a 60% decrease in total scan time for a clinically reasonable SNR. Future work will involve the optimization of ^{31}P LFA-MRSI as preliminary results also confirm that ^{31}P LFA-MRSI results in a more time-efficient in vivo method than single slice ^{31}P LFA MRS. In addition to providing spectral-spatial information, scan time can be reduced from 34.1s in a standard spin-echo MRSI sequence that yields adequate SNR, to 13.7s with LFA-MRSI. ^{31}P LFA-MRS and LFA-MRSI may be valuable for future clinical applications in bipolar disorder.

Figure 2.



20 mm axial slice placed above brain ventricles on sagittal localizer





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