Magnetic resonance spectroscopy (MRS) of the deep brain structures at 7.0T

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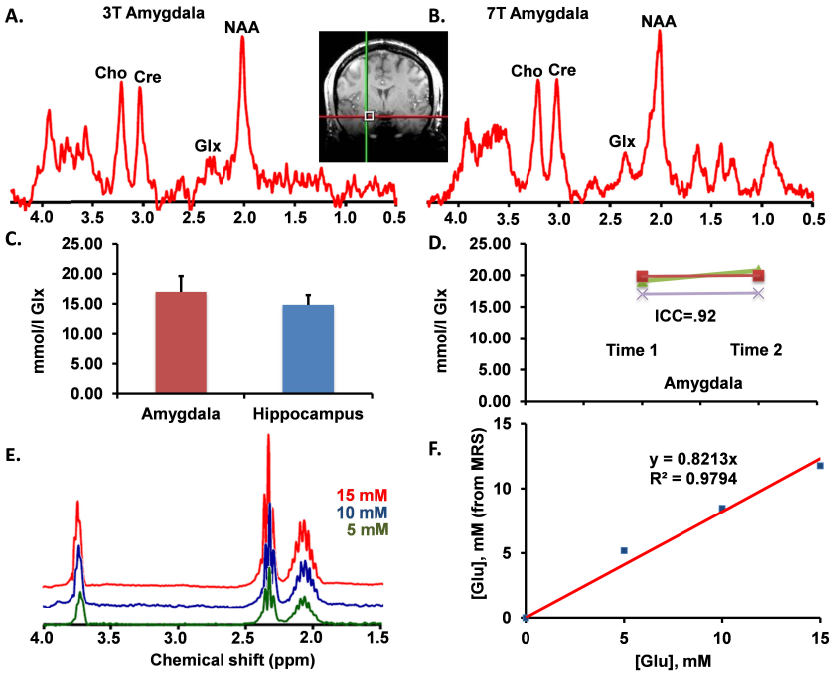
Introduction. Standard proton MRS at 3.0T allows for exceptional sensitivity to the neurochemistry of many regions of the brain (Nacewicz et al.,). However, direct quantification of specific neurotransmitters such as glutamate (Glu) within deep brain structures (e.g. amygdala and hippocampus) remains limited at this field strength. Recent advances in MRS, especially the use of ultra-high field 7.0T MRS, offer increased sensitivity and specificity for brain neurochemistry in deep brain structures. Thus, the use of 7.0T MRS to investigate brain metabolites may yield better quantification of brain neurochemistry since spectral dispersion is enhanced at this magnetic field. The goal of the current study was to determine if 7.0T MRS provides appreciable gain in Glutamate/Glutamine (Glx) signal to noise (SNR) as compared to 3.0T, measure the concentration of Glx in the amygdala and hippocampus, and determine the reproducibility of this measurement.

Methods. Standard MRS (Point RESolved Spectroscopy; PRESS) was used for acquisition at 3.0T Siemens scanner using 8-channel head coil (Parameters: TE: 30 ms; TR: 3000 ms; Voxel size: 10X10X10 mm^3; 128 averages). A modified MRS (PRESS) acquisition was used at 7.0T Siemens scanner using 32-channel head coil (Parameters: TE: 20 ms; TR: 3000 ms; Voxel size: 10X10X10 mm^3; 128 averages). MRS was collected from six male subjects (aged between 22-64 years) at two time points approximately at 90-day intervals. Data was collected from the amygdala and hippocampus (left and right). At 7.0T, Glu was measured in glutamate phantoms prepared using PBS buffer at pH 7.0 in three concentrations [5 mM, 10 mM, 15 mM]. Spectra obtained from 7T MRS were processed by exponential apodization (10 Hz) of the raw free induction decay data followed by Fourier transformation, phase correction and then baseline correction. Metabolite peaks from the deep brain structures were fitted as Gaussian functions with non-linear least squares fitting (MATLAB "nlinfit" routine) followed by integration and then normalized by water signal for absolute quantification of Glx concentration.

Results. 7.0T spectra showed an appreciable gain over 3.0T spectra in deep brain structures (Figure A, B; line broadening of 5Hz was used in both spectra for comparison). Qualitatively, the Glx peak at 2.35 ppm is clearly visible in the spectra acquired at 7.0T. Macromolecular peaks (from 0.7 to 1.8 ppm) seen in 7T spectrum arises most probably due to the shorter echo time used when compared to 3T. Mean Glx concentration was 16.99 (2.64) mM; [range (13.31-19.85); coefficient of variation (CoV = 15.5%)] in the amygdala and 13.52 (1.80) mM; [range (11.21-16.39); CoV = 13.3%] in the hippocampus (Figure C). These values are comparable to a recent study at 3.0T (Nacewicz et al.,; CoV = 15.42% in amygdala). Only three subjects had suitable data for longitudinal comparison in the amygdala (Figure D), however they showed high reliability from time 1 to time 2 (intra class correlation coefficient = 0.92). Finally, to confirm the stability of *in vivo* acquisition, Glu was measured *in vitro*. These data show that Glu has three resolvable peaks around 2.08ppm, 2.35ppm and 3.74ppm (Figure E). The 2.35 ppm peak is the only one used for Glx quantification *in vivo*. Quantified Glu concentration based on MRS method shows linearity to the actual Glu concentration (Figure F).



Conclusions. Despite the challenges due to field inhomogeneities in imaging deep brain structures, we demonstrated the feasibility of measuring high quality MRS from amygdala and hippocampus at 7T. In this limited study, we further showed that the 7T MRS has about 2.5 times SNR advantage over the corresponding 3T MRS and provides high quality Glx spectra. Repeated measurements showed high degree of precision (intra class correlation coefficient = 0.92) at 7T. Since the deep brain structures are invovlved in many important cognitive functions like memory, emotion and other behavioral domains, accurate quantification could provide insight into the well-documented volumetric and functional differences in a variety of neuropsychiatric disorders including schizophrenia and autism.

Acknowledgements. This work was performed at an NCRR supported Biomedical Technology and Research Center (P41 RR02305) and in part supported by R21-DA032256, T32 MH019112 (D.R.R.)-SCHIZOPHRENIA: A NEUROPSYCHIATRIC PERSPECTIVE, MH060722 and MH064045.

References. Nacewicz, B. M. et al., (2011) Reliable non-invasive measurement of human neurochemistry using proton spectroscopy with an anatomically defined amygdala-specific voxel. NeuroImage (In press).