Short echo MRSI at 7 Tesla in patients with major depressive disorder

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Introduction Major depressive disorder (MDD) is one of the most common psychiatric conditions, and is characterized by impairments in mood regulation, motivation and cognition. Most patients with MDD have recurrent episodes that severely impact quality of life. The etiology and neuropathology of MDD is unclear; but is thought to be associated with chemical changes, such as decreased Glu or GABA, in corticolimbic brain circuits, including subregions of the anterior cingulate cortex (ACC) and thalamus (Thal). Proton magnetic resonance spectroscopic imaging (H-1 MRSI) is a powerful noninvasive tool for investigating brain metabolism. The availability of ultra high field MR systems offers the advantages in higher SNR and improved spectral resolution, which can be used to improve the detection of J-coupled metabolites such as mI, Glu, Gln and GABA. The purpose of this study was to compare relative metabolite levels between unmedicated patients with MDD and healthy controls in the ACC and anterior/mediodorsal Thal using 3D short-echo MRSI at 7 Tesla. Multiple regions of interest (ROIs) were included in the study to assess the importance of voxel position in the analyses and to examine the correlation between metabolite levels in the subregions of ACC and Thal and patients with MDD.

Methods 13 depressed patients (10F/3M, 31±7 years) who met the DSM-IV criteria for MDD and who had been medication-free for at least 6 weeks were recruited into the study, and 10 healthy controls (7F/3M, 32±9 years) who had no history of neurologic illness, traumatic brain injury or DSM-IV Axis I or II diagnosis were also studied. All MR scans were performed using a volume transmit head coil and 32-channel receive-only array on a GE 7 Tesla scanner (GE Healthcare, Waukesha, WI). Anatomical imaging consisted of a T1-weighted sagittal scout, T1-weighted fast spoiled gradient echo and T2*-weighted gradient recalled echo (GRE) images. 3D H-1 MRSI was obtained using spectrally-selective adiabatic inversion recovery lipid suppression, CHESS water suppression, 8 VSS outer volume suppression that was automatically prescribed based on the location of the box [1], spin echo slice selection with TE/TR=20/2000ms, spectra array=18x22x8 and spatial resolution = 1cm^3 [2]. An interleaved flyback echo-planar trajectory was applied in the A/P direction to shorten the total acquisition time to ~10 min. The spectral slice was placed parallel to the ACPC-line with full coverage of the thalamus. The 32 channels of data were combined, processed as described previously [2] and quantified using LCModel. Metabolite signals for the basis set, which included PC, GPC, Cr, PCr, NAA, Glu, Gln, mI, Gly, GABA, GSH, PE, Glc, Scyllo, Tau and Asp, were generated using GAMMA simulations with prior knowledge of chemical shift and J-coupling. ROIs including 8 voxels in ACC (A1-8) and Thal (T1-8) are illustrated in Figure 1. Ranksum tests of significance were utilized to compare metabolite ratios between patients and controls.

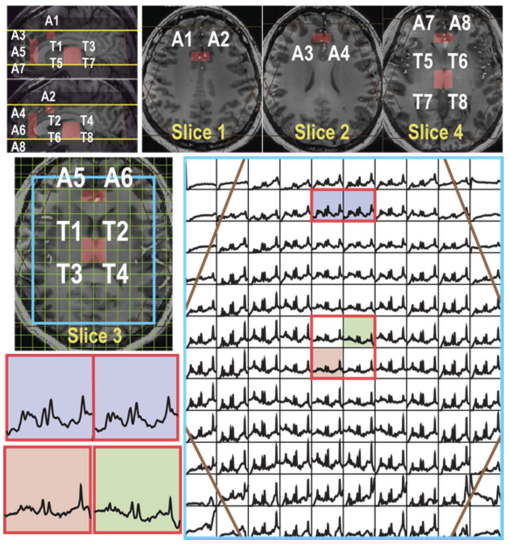

Figure 1. MRSI data shown without baseline subtraction from a patient with MDD showing regions that were studied (ACC 1-8, Thal 1-8).

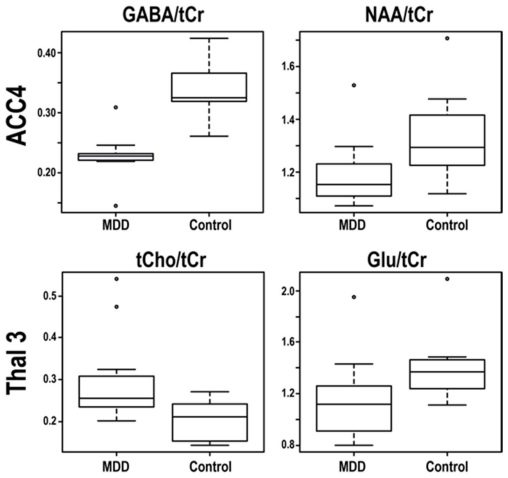

Figure 2. Boxplots of GABA/tCr and NAA/tCr in ACC4, tCho/tCr and Glu/tCr in Thal 3 for patients with MDD and controls.

Results Figure 1 shows H-1 MRSI data acquired from one of the patients. Metabolite ratios that were significantly different between patients and controls are given in Table 1. Compared to controls, patients had significantly decreased levels of GABA/tCr and NAA/tCr in a subregion of the left ACC (ACC4), significantly elevated tCho/tCr and lower Glu/tCr in the right mediodorsal Thal (Thal3) (Figure 2), and lower mI/tCr in the anterior/mediodorsal Thal.

Discussion This study has successfully demonstrated the application of 7 Tesla H-1 MRSI to patients with MDD. Glu and GABA are known to act as brain neurotransmitters and were found to be abnormal in patients with MDD. Decreased Glu in the limbic regions appears to be associated with depressive episodes [3]. The reduction in GABA/tCr suggests impaired GABAergic function in a subregion of the left ACC, which might play an important role in the pathophysiology of MDD. Regional differences within the ACC and Thal suggest accurate tissue segmentation is important in the interpretation of such data. These observations, as well as the study changes induced by therapy will be useful in better understanding how to manage patients with MDD.

	ROI	Metabolite (/tCr)	Patients	Controls	P-value
ACC	A4	GABA	0.23±0.04 (N=9)	0.34±0.06 (N=5)	0.0005
	A4	NAA	1.19±0.13 (N=11)	1.34±0.18 (N=8)	0.0409
	A2+A4	GABA	0.28±0.08 (N=11)	0.37±0.06 (N=7)	0.0346
Thalamus	T3	tCho	0.30±0.11 (N=12)	0.20±0.05 (N=8)	0.0021
	T3	Glu	1.16±0.33 (N=11)	1.42±0.30 (N=8)	0.0409
	T2 *(T8, T1+T2+T5+T6, T2+T4+T6+T8, T1-8)*	mI	0.64±0.17 (N=10)	0.88±0.17 (N=8)	0.0044 *(<0.05)*

Table 1. Metabolite ratios that were significantly different between patients with MDD and healthy controls.

References 1. Ozhinsky E, et al. J Magn Reson Imaging 2011; 2. Li Y, et al. ISMRM 2012; 3. Yuksel C. et a. Biol Psychiatry 2010.

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