3T MR Spectroscopy and Neuropsychology of Bipolar Disorder

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The goal of this work was to correlate the underlying biochemical changes with neuropsychological results in bipolar disorder during the manic episode using a 3T MR scanner. STEAM localized MR spectra were recorded in three brain locations: anterior cingulate (AC), basal ganglia (BG) and occipito-parietal white matter (OP). The BG NAA/Cr was significantly lower in manics compared to controls ($p<0.01$). Performance on the Wechsler Adult Intelligence Scale (WAIS) letter-number sequencing was positively correlated with BG NAA/Cr.

Introduction:

Abnormalities in NAA biochemistry in bipolar disorder have been reported in the anterior cingulate and dorsal lateral prefrontal cortex (1,2). Previous studies have used both single and multi-voxel MR spectroscopy. The primary goal of this study was to further evaluate the biochemical changes in bipolar patients with mania using a 3T MR spectroscopy, and to correlate with the neuropsychological deficits.

Materials and Methods:

Sixteen patients currently receiving mood stabilization treatment for bipolar disorder, manic or hypomanic state, underwent a structured clinical diagnostic interview (SCID, DSM-IV). Age matched controls (n=12) were also interviewed. A $2x2x2cm^3$ voxel was selected in the AC, BG and OP locations. Other MRS parameters were: TR/TE=2s/20ms, NEX=128, and TM=8ms using a STEAM sequence. MRS raw files were processed using the LC-Model software package. Both absolute concentrations (mM) and metabolite ratios with respect to creatine were calculated. The MRS results were not corrected for T_1, T_2 saturation and gray/white/CSF partial volume effects. Means +/- standard deviation, t-test, and analysis of variance were calculated. A 3T GE MRI/MRS scanner (GE Medical Systems, Waukesha, WI) with a quadrature head coil was used.

The neurocognitive battery consisted of California Verbal Learning Test (CVLT), Wisconsin Cord Sorting Test (WCST), Trails A/B and additional tests of verbal fluency and working memory.

Results:

The 3T MR spectra had better dispersion than 1.5T as expected, however the resonances were slightly broader due to the decreased T_2 of metabolites on a 3T scanner (3). Comparing manic patients vs. controls, there was a significant reduction in the BG NAA/Cr ratio (0.98 +/- 0.17 vs. 1.17 +/- 0.23; df=25, t=-2.36, p=0.02), but not the absolute BG [NAA] (5.4 +/- 1.2 vs. 5.95 +/- 1.45; t=-1.17, p=0.25) as shown in Table 1 and 2. The AC NAA/Cr was also decreased in bipolar manics, however the decline was not statistically significant. The BG NAA/Cr ratio, controlling for age and years education, was significantly lower in manics vs. controls (adjusted mean: 0.98 vs. 1.18; ANOVA by diagnostic group: F=7.47, p=0.01: years education: F=6.87, p=0.02: and age: F=1.28, p=0.27). Except in FAS verbal fluency, there was no significant impairment of bipolar patients compared to controls. There was no difference in the BG NAA/Cr ratio in 6 patients who had a second scan while euthymic (N=6, paired t=-0.40, p=0.71). There was no significant difference between diagnostic groups in FG [NAA], OP [NAA], or OP NAA/Cr.

Locations	Metabolites	BIPOLAR (mM)	CONTROL (mM)
Anterior Cingulate	NAA	7.58 ± 2.03	8.32 ± 1.50
	mI	4.78 ± 2.72	4.65 ± 0.89
	Glx	14.69 ± 3.82	14.12 ± 1.95
Basal Ganglia	NAA	5.28 ± 1.29	5.95 ± 1.15
	mI	2.48 ± 0.68	2.14 ± 0.67
	Glx	9.32 ± 2.76	8.64 ± 2.32
Occipital Parietal	NAA	6.37 ± 0.83	6.29 ± 0.52
	mI	3.49 ± 1.35	3.49 ± 0.88
	Glx	6.90 ± 2.06	6.50 ± 0.75

Table 1 Metabolite concentrations in Bipolar vs Controls

	Metabolite ratios	Bipolar Patients	Healthy Controls
Anterior Cingulate	NAA/Cr	1.00 ± 0.22	1.12 ± 0.20
	mI/Cr	0.63 ± 0.32	0.63 ± 0.15
	Glx/Cr	2.09 ± 0.93	1.94 ± 0.43
Basal Ganglia	NAA/Cr	0.98 ± 0.17	1.17 ± 0.23
	mI/Cr	0.46 ± 0.13	0.43 ± 0.16
	Glx/Cr	1.74 ± 0.45	1.66 ± 0.33
Occipital Parietal	NAA/Cr	1.31 ± 0.32	2.04 ± 1.71
	mI/Cr	0.68 ± 0.13	1.05 ± 0.70
	Glx/Cr	1.40 ± 0.51	2.16 ± 1.91

Table 2 Metabolite Ratios in Bipolar vs Controls

Conclusion: This data suggests basal ganglia NAA pathology in bipolar patients undergoing treatment for acute mania. The neurochemical changes have been correlated with the neuropsychological deficits. The limitations of this study include the lack of medication free scans and the small sample size. Further work is necessary to clarify state vs. trait phenomena and whether NAA abnormalities can be modulated by treatment intervention.

References

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