Proton MR spectroscopy of the hippocampus at 3 Tesla in patients with major depression under pharmacological treatment

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Introduction:

Several studies using proton magnetic resonance spectroscopy (^{1}H-MRS) have described varying metabolic alterations in major depression in different brain regions. Most of these studies performed MRS in frontal lobe, basal ganglia or cingulum, only a few dealt with the hippocampus or amygdala regions. Due to the important role of the medial temporal lobe in the pathogenesis of depression, we performed single volume spectroscopy of the hippocampus with long and short echo times in an untreated patient group before and after medication.

Material and methods:

Examinations were done at our clinical 3T whole-body MR system (Gyroscan Achieva 3.0 T, Philips Medical Systems) with a transmit/receive head coil designed for imaging and proton spectroscopy. We studied patients with major depression (n=18) before, and 6-8 weeks (n=11) after standard pharmacological treatment. Single-volume proton MRS of a 6 ml VOI placed in the left hippocampus was performed including acquisition of water-suppressed PRESS spectra with TE/TR 140/2000 ms and 30/2000 ms. Metabolite ratios and absolute metabolite concentrations of N-acetyl-aspartate (NAA), total creatine (tCr), of choline (Cho) and inositol (Ins) containing compounds, glutamine (Gln) and glutamine/glutamate/GABA (Glx) were calculated using the unsuppressed water signal of the VOI as an internal reference. Data were compared to findings of 10 sex and age-matched healthy controls. Group comparisons between patients and healthy controls were performed using analysis of variance using age and gender as covariates. Treatment effects were analyzed with a nonparametric paired Wilcoxon test. Correlations of metabolite parameters and depression severity determined by Beck Depression Inventory (BDI) Rating Scale score were tested by Pearson correlation analysis.

Results: Pre-medication concentrations of total creatine and relative Glx and Gln were significantly reduced in the hippocampus in the patient group compared to healthy controls. Absolute NAA and Cho seem to be slightly reduced; differences however did not reach statistical significance. No changes were observed in inositol containing compounds (Table 1).

Table 1:

	n	[NAA]	[Cho]	[tCr]	[Ins]	NAA/Ins	Glx/tCr	Gln/tCr
controls								
mean	10	9.87	2.74	9.81	6.16	1.85	2.38	0.41
SD		*1.25*	*0.28*	*1.28*	*1.55*	*0.65*	*0.36*	*0.19*
pre-medication								
mean	18	9.43	2.49	8.90	6.32	1.46	1.87	0.25
SD		*1.35*	*0.37*	*1.43*	*0.93*	*0.22*	*0.39*	*0.14*
post-medication								
mean	11	9.78	2.54	9.03	5.93	1.81	1.82	0.27
SD		*1.18*	*0.40*	*2.20*	*1.65*	*0.58*	*0.32*	*0.14*
p (pre vs controls)		*ns*	*ns*	*< 0.05*	*ns*	*ns*	*< 0.01*	*< 0.05*
p (post vs controls)		*ns*	*ns*	*ns*	*ns*	*ns*	*< 0.01*	*ns*

Correlation analysis of depression severity vs MRS showed a significant correlation (r=-0.675, p=0.006) between NAA/Ins and BDI (Fig 1). Intra-individual comparison of pre- and post-medication examinations showed a trend towards recovery of [NAA] and [Cho]; no changes were found for relative Glx or Gln. A significant negative correlation was found between δ values (post- minus pre-medication) of BDI and [NAA] (r=-0.615, p=0.044) and [Cho] (r=-0.762, p=0.006) (Figs. 2, 3). That means, patients with improvement in depression rating score (decline in BDI) showed an increase in absolute hippocampal NAA and choline concentration after treatment.

Figure 1:

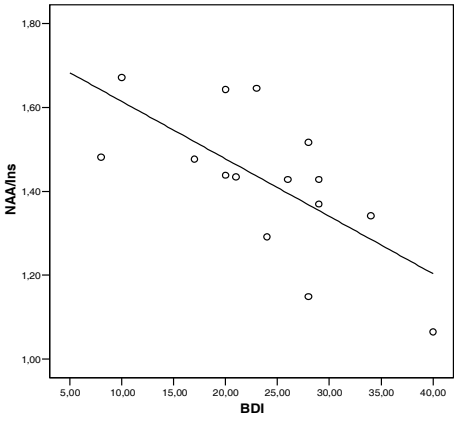


Figure 2:

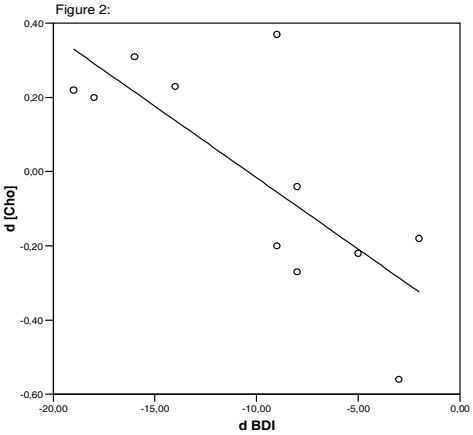
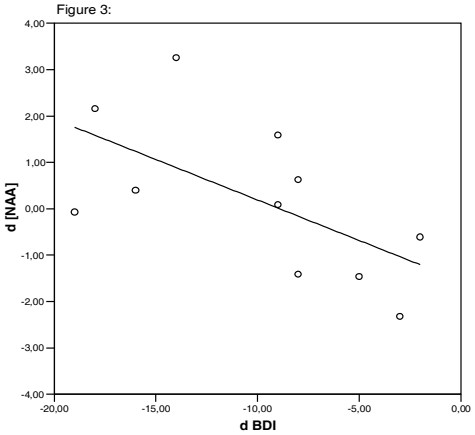


Figure 3:



Discussion:

In accordance with findings obtained in other brain areas, we found a significant reduction in Glx resonances in the medial temporal lobe of untreated patients, indicating a disturbed glutamergic metabolism in major depression disorder. Decreased NAA/Ins correlates well with the severity of depression. NAA and Cho recovery suggests that these alterations are reversible in patients who benefit from treatment.

References: F. Träber , Block W., Gieseke J., Gür O., Lamerichs R., Schild H., Proc Intl Soc Mag Reson Med 12 (2004) 2279