Niacin insensitivity is related to ^{1}H MRS abnormalities in drug-naive first episode psychosis

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Introduction

Psychotic disorders have been associated with MR spectroscopic abnormalities, although this is by no means a consistent finding (1). Findings of correlations between reduced arachidonic acid levels in red blood cell membrane and *in vivo* phosphorus MRS measures (2) support the hypothesis of a dysfunctional lipid metabolism, at least in a subgroup of patients (3). The skinflush reaction to topical niacin is an easily administered way of measuring relative arachidonic acid levels, and it has been shown that patients with psychosis exhibit a bimodal distribution, with around half reacting normally and half having a markedly reduced reaction (4). The aim of the study was to investigate the relationship between niacin sensitivity and in vivo brain abnormalities in acutely ill, neuroleptic-naïve first-episode psychosis patients.

Method

This study examined 20 patients in the first episode of a psychotic disorder (all antipsychotic drug naïve) and compared them with 23 controls. Short echo (30 ms) MRS was performed at 3T (GE, Milwaukee, USA) using a PRESS sequence with two chemical shift selective imaging pulses for water suppression. Spectra were acquired with 128 transients of 2 k data points over a frequency width of 5000 Hz with a repetition time of 3 sec. A single voxel (2x2x2 cm) was placed in each temporal lobe. This region of interest included the hippocampus, amygdala and lateral aspect of the temporal lobe. Spectra were analysed with LCModel (5) using a basis set of 15 metabolites acquired on-site. Metabolite concentrations were estimated following calibration of the analysis software with a 50 mM NAA solution.

Niacin flush response was assessed by a semi-quantitative rating scale (6), and patients divided into 'sensitive' and 'insensitive' depending on whether they scored below the normal range.

Results

The niacin-insensitive patient group showed significant increases in creatine and phosphocreatine (Cr) and glutathione (GSH), and a difference in trimethylamines (choline + phosphocholine + glycerophosphocholine, TMA) that approached significance (see table 1). NAA, myo-inositol (mI) and glutamate/glutamine (Glx) were not different between groups.

Table 1: Metabolite concentrations for the three groups. Results are means and standard deviations, with metabolites showing a significant difference between groups shown in bold.

	Cr	Glx	**GSH**	MI	NA	TMA
Niacin-insensitive (n = 9)	**4.28 ± 0.47**	6.58 ± 0.89	**2.45 ± 0.52**	3.40 ± 0.62	6.02 ± 0.71	1.27 ± 0.18
Niacin-sensitive (n = 11)	**3.64 ± 0.47**	6.67 ± 0.89	**1.71 ± 0.51**	3.25 ± 0.62	5.78 ± 0.71	1.08 ± 0.18
Control (n = 23)	**3.66 ± 0.47**	6.60 ± 0.89	**1.82 ± 0.51**	3.11 ± 0.62	6.04 ± 0.71	1.19 ± 0.18
p =	**0.005**	0.972	**0.020**	0.490	0.601	0.068

Discussion

The elevated concentration of glutathione, a strong antioxidant, may reflect increased oxidative activity associated with emerging psychotic disorders in the subgroup of patients who are niacin-insensitive. The significant increases in creatine containing compounds is consistent with observations recently describing elevated creatine in association with reduced cognitive performance and may reflect a reduced ability to utilize phosphocreatine (7). These data support the notion that first episode psychosis groups are heterogenous and that this may be explained in part by biochemical differences.

References

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