Eicosapentanoic acid supplementation alters ^{1}-H MRS metabolite profiles in first episode psychosis

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Introduction

Bioactive lipids are molecules that have both intra- and intercellular roles, including mediation, modulation and control of neurobiological processes, such as ion channel and receptor activity, neurotransmitter release, synaptic plasticity, second messenger pathways and neuronal gene expression[1]. The essential fatty acid arachidonic acid (AA) and its metabolites, known collectively as eicosanoids comprise a major fraction of bioactive lipids in the brain. Bioactive lipid metabolism has been implicated in the etiology of psychosis[2] with depletion of bioactive lipids (eg. AA) in cell membranes of patients with schizophrenia [3], independent of drug treatment[4].

This study investigated the effect of EPA (eicosapentanoic acid) supplementation on the metabolite profile of the brain, *in vivo*, in first episode psychosis.

Methods

Twenty-four patients in the first episode of a psychotic disorder were studied. After an initial ^{1}H-MRS examination and in addition to standard treatment with atypical antipsychotics, 12 took a course of 2g oral EPA supplement and 12 patients placebo (mineral oil) for 12 weeks prior to a second MRS study. Short echo (30 ms) MRS was performed on a GE 3 T LX Horizon scanner (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 using a basis set of 15 metabolites acquired on-site. Metabolite concentrations (institutional units) were estimated following calibration of the analysis software with a 50 mM NAA solution. Metabolite data were rejected if the Cramer-Rao lower bounds of the LCModel fit were greater than 30%.

Results

Using ANCOVA, there was a change in trimethylamines and total creatine with treatment ($p < 0.05$), independent of EPA supplementation. EPA supplementation produced a significant interaction between treatment and time for myoinositol and glutathione ($p < 0.05$). The results are summarized in the table.

Table 1: Metabolite concentrations measured in the temporal lobes of 24 first episode psychosis patients at diagnosis and again after 12 weeks of treatment comparing placebo and essential fatty acid supplementation.

		TMA	Cr	GSH	MI
Placebo (n = 12)	Baseline	1.24 ± 0.02	4.27 ± 0.54	2.01 ± 0.40	3.60 ± 0.52
	12 weeks	**1.20 ± 0.19**	**4.03 ± 0.58**	1.80 ± 0.47	3.19 ± 0.54
EPA (n = 12)	Baseline	1.09 ± 0.02	3.59 ± 0.54	1.71 ± 0.40	3.08 ± 0.83
	12 weeks	**1.21 ± 0.19**	**3.92 ± 0.58**	**2.32 ± 0.47**	**3.45 ± 0.87**
Control values (n = 20)		1.21 ± 0.20	3.76 ± 0.65	1.89 ± 0.38	3.22 ± 0.61

Results are mean and standard deviations, with metabolites showing a significant difference between groups and time shown in bold. Abbreviations: Cr, creatine + phosphocreatine; Glx. Glutamine + glutamate; GSH, glutathione; MI, myoinositol; NA, total N-acetylaspartyl groups (NAA + NAAG); TMA, trimethylamines (total choline-containing compounds)

Discussion

The significant increase 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 in schiqophrenia[5]. An increase in TMA is consistent with higher turnover of lipids or an increase in the pool of precursors or breakdown products. Changes in myoinositol with EPA supplementation and normal treatment are also consistent with changes in glial metabolism. The elevated concentration of glutathione may also reflect increased oxidative stress and increased glial and to some extent neuronal progenitor cell apoptosis accompanying the onset of the disorder[2]. These data provide support for the proposal that altered lipid metabolism occurs in first epiesode psychosis and that EPA supplementation can alter the metabolite profile in first epiesode psychosis.

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