Brain Metabolite Abnormalities in Alcohol Dependent Patients Using Proton MR Spectroscopy at 3T

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Introduction

Chronic alcoholism is associated with cognitive impairments affecting executive functions, verbal/visual memory, and visuospatial functions [1]. These impairments are moderate to severe but usually remain undiagnosed. Previous proton magnetic resonance spectroscopy (^{1}H-MRS) studies at 1.5T of the dorsolateral prefrontal cortex (DLPFC) in alcoholic dependents have revealed lower levels of N-acetyl aspartate (NAA), phosphocreatine plus creatine (PCr+Cr, tCr), choline containing compounds (GPC+PC, tCho), and higher levels of glutamate plus glutamine (Glu+Gln, Glx) [2, 3]. However, these findings were not consistent across different ^{1}H-MRS studies. More studies are still needed to confirm those observations. In this study, we performed *in vivo* short-echo time (TE) ^{1}H-MRS to investigate brain metabolite levels in the left DLPFC of alcohol-dependent patients and healthy controls. For quantitative spectral analysis, metabolite basis sets were acquired in-house on the same 3T MRI scanner.

Materials and Methods

This study included 50 subjects, 26 male alcohol dependents (mean±SD, 51±8.3 years) and 24 healthy control subjects (mean±SD, 52±8.4 years). Single-voxel ^{1}H-MRS was performed using a PRESS sequence at 3T (e.g., Philips Achieva TX System with a 32-channel receive-only array head coil). The examinations (voxel size, 2×2×2 cm^3) were measured from left DLPFC in patients with alcohol dependents and healthy subjects. After shimming procedure water suppression was accomplished with "VAPOR" pulses. The acquisition parameters were TR/TE = 2500/35 ms, and 128 acquisitions for averaging. A fully relaxed, unsuppressed spectrum was also acquired to measure the water peak (16 averages). LCModel fitting was conducted using in-house measured basis spectra of 16 metabolites. For multivariate statistical analysis, SIMCA-P 13.0 software (Umetrics Inc.) was used to process the numeric data. Principal component analysis (PCA) and partial least squares regression discriminant analysis (PLS-DA) were performed to distinguish between the two groups. To identify which variables were responsible for the separation, the variable influence on the projection (VIP) parameter was used.

Results

In vivo quantification result of LCModel using experimental metabolite basis set is shown in Figure 1. LCModel reliably quantified NAA, tCho, tCr, Glu, Glx, myo-inositol (Ins) (CRLB<10%) and somewhat reliably quantified aspartate (Asp), glutathione (GSH) (CRLB=10~20%) in the left DLPFC of alcohol-dependent patients and healthy controls. Gln was quantified (CRLB<30%). Significantly decreased tCho and Ins concentrations were found in the alcoholics as compared to the controls (p=0.001, p=0.008, in Figure 2). In addition, there was a trend towards increasing Gln in alcoholic dependents (p=0.059). In a PLS-DA model, the relative discriminatory potential of the ^{1}H-MRS parameters in the differentiation of the two groups are shown in Figure 3 (bottom) in terms of VIP. 6 ^{1}H-MRS parameters (e.g., tCho, Ins, Gln, tCho/tCr, Ins/tCr, Gln/tCr) with VIP>1 are those detectable in ^{1}H-MRS spectra. Using these 6 ^{1}H-MRS measures an optimal model was constructed, but it did not allow a significant separation between the two groups (Figure 3(top)).

Discussion

The present study demonstrated that *in vivo* ^{1}H-MRS can be used to detect the brain metabolite abnormalities in alcoholic dependents. The main observation in this work was the significant reduction of tCho and Ins concentrations in the left DLPFC of alcohol dependent patients compared to healthy control subjects. tCho levels are lower in prefrontal brain areas of recently detoxified alcoholic patients [4]. In this study, the decreased tCho levels are interpreted as indicating damage to cell membranes and/or myelin caused by chronic alcohol consumption [5]. The function of Ins is not well understood, but it is associated with cell growth, osmolite, and a storage form for glucose. The decreased Ins levels might reflect functional changes with a reduction of glucose metabolism or cerebral blood flow in prefrontal regions in alcohol dependent patients. Therefore, these metabolic abnormalities may be neurochemical correlate of an increased risk to develop alcoholism.

References

[1] Bernardin, *et al.*, Frontiers in Psychiatry 2014;78:1-6. [2] Frey *et al*., Bipolar Disorders 2007;9:119-127. [3] Molina *et al*., European Psychiatry 2007;22:505-512. [4] Lee *et al*., Neuroreport 2007; 18:1511-1163. [5] Bartsch *et al*., Brain 2007; 130:36-47.

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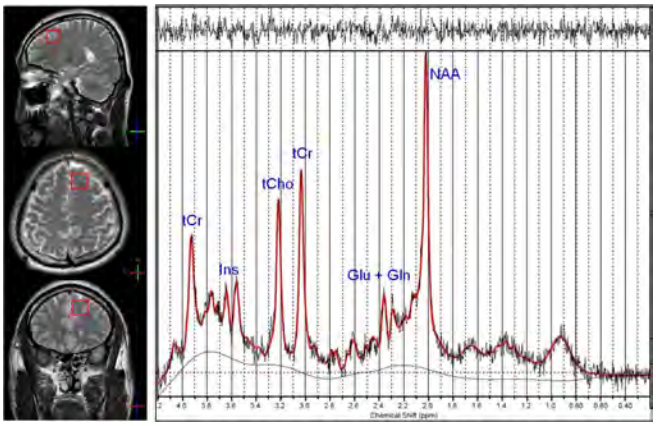

Figure 1. 3T MR imaging showing the volume of interest (Left) and in vivo spectrum of the left dorsolateral prefrontal cortex (DLPFC) of a representative subject processed using LCModel with experimental basis sets (Right).

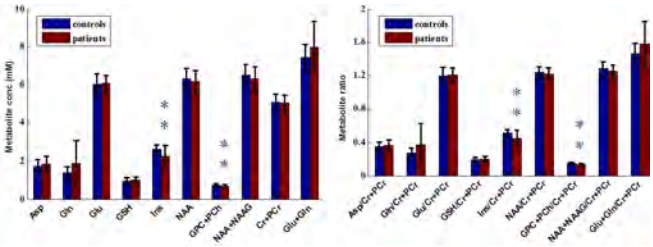

Figure 2. Metabolite levels quantified in left DLPFC of alcohol-dependent patients and healthy controls. Data shows mean±SD for each group using a two tailed *t*-test with significance threshold of **p < 0.01.

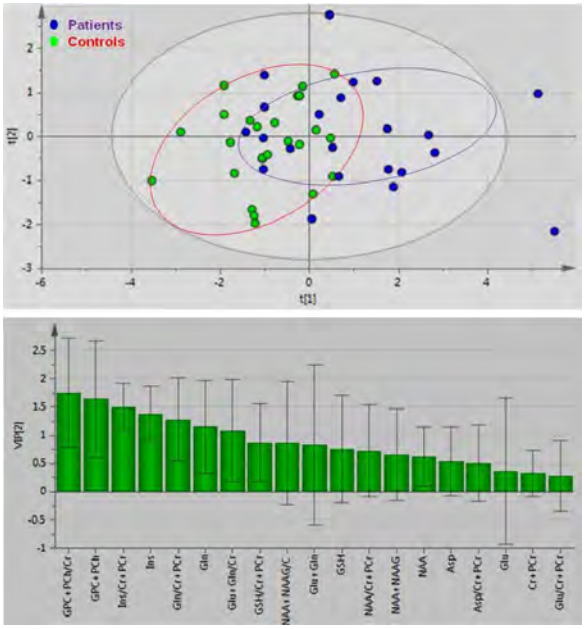

Figure 3. The variables with VIP values in PLS-DA model (bottom) and PLS-DA scores plot (top). The model did not allow a good separation of the two groups (e.g., alcohol-dependent patients vs. healthy controls).