Frontal white matter choline-containing compounds increase with alcohol consumption and glutamate decreases with increasing addiction criteria

G. Ende[1], D. Hermann[2], M. Hoerst[1], N. Tunc-Skarka[1], G. Oberthuer[1], S. Wichert[2], J. Rabinstein[2], W. Weber-Fahr[1], K. Mann[2], and S. Vollstaedt-Klein[2]
[1]Neuroimaging, Central Institute of Mental Health, Mannheim, Germany, [2]Addiction Medicine, Central Institute of Mental Health, Mannheim, Germany

Introduction

It has been previously shown that frontal white matter (fWM) choline-containing compounds (tCho) increase with alcohol consumption in social drinkers but were found decreased in detoxified alcoholics [1,2]. With this study we aimed to investigate whether fWM tCho would still be elevated in heavy drinking as well as in non-abstinent alcohol dependent patients. Since Glutamate plays an important role in alcoholism [3] we further investigated correlations between glutamate concentrations and measures of alcohol addiction.

Methods

In this study non-abstinent alcohol-dependent subjects (N=15, 48.8±10 years), heavy but non-dependent drinkers (N=7, 53.7±11 years) and light social alcohol drinkers (N=6, 43.7±8 years) underwent single voxel 1H MRS of fWM. Heavy and dependent drinkers were classified according to ICD-10 and DSM IV diagnostic criteria. Additionally, a questionnaire of obsessive-compulsive alcohol-related thoughts and behaviour was completed by all participants (Obsessive Compulsive Drinking Scale, OCDS, German version,9). All subjects provided informed written consent according to the declaration of Helsinki and the study was approved by the local ethics committee. All subjects had zero breath alcohol levels at the time of the MRS examination and no ethanol was detected in the spectra. Spectra were acquired on a 3T Siemens Magnetom TIM Trio. The position of the voxel was defined based on anatomical images from an isotropic 1 mm³ mprage data set (acquired in sagital planes and reconstructed in orthogonal transverse and coronal planes). It was positioned in the frontal white matter (15 x 40 x 15 mm³) and acquired with a PRESS sequence using the following parameters: TE = 80 ms [3], TR = 3000 ms. For T2 evaluation of the water signal additional 6 unsupressed water spectra were acquired from the same voxel at different TEs. Spectra were evaluated with LCModel using simulated data set. Glutamate fits were accepted when the Cramer Rao Lower Bounds of the fit were 20% or less. The results were scaled with the water signal at TE=0 ms which was extrapolated from a bi-exponential T2 fit. We also accounted for the different amount of grey matter (GM, mean 16.6 %), white matter (WM, mean 82.2 %) and CSF (mean 1.2 %) in the measured voxel and their different water concentration (GM: 45 mM, WM: 39.4 mM, CSF: 54.4 mM) by image segmentation of a T1-weighted MPRAGE. Metabolite data were corrected for CSF content. Chemical shift displacement results in a different measured voxel position for the different metabolites. This was accounted for in the in house developed segmentation tool which is based on the SPM2 algorithm [4].

Results

A positive correlation of tCho and alcohol consumption was replicated for the whole group (r = 0.425, p = 0.024). As shown in Figure 1. tCho, although higher in heavy drinkers and dependent drinkers, is very inhomogemous in heavy alcohol use and the variance is not explained by a difference between dependent and non-dependend alcohol abusers. (Drinks per day are the mean for the previous 90 days). Without the light drinking group this correlation is not significant any more.

Measures of addiction (OCDS, ICD-10 and DSM IV) did not explain tCho variances but showed significant negative correlations with Glu in the heavy drinking groups (Figure 2 and Table).

Figure 1

Figure 2
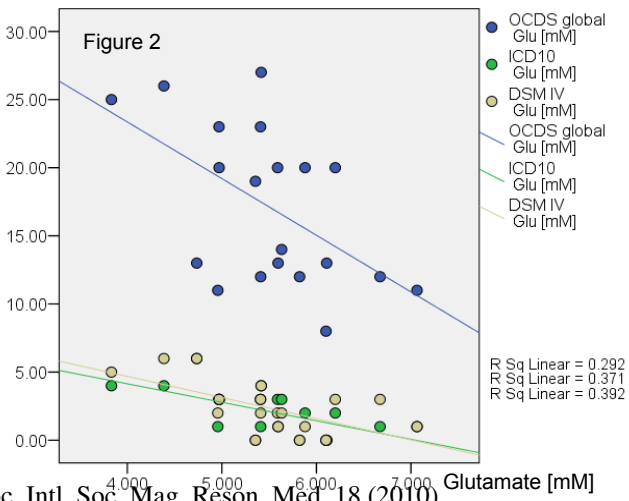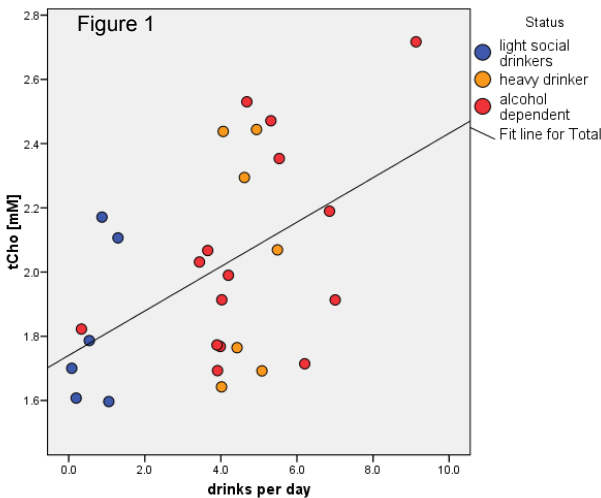
Correlations

			DSM IV	ICD10	OCDS global
Spearman's rho	tCho [mM]	Correlation Coefficient	.162	.118	-.121
		Sig. (2-tailed)	.472	.600	.591
		N	22	22	22
	Glu [mM]	Correlation Coefficient	-.561**	-.583**	-.470*
		Sig. (2-tailed)	.010	.007	.036
		N	20	20	20

**· Correlation is significant at the 0.01 level (2-tailed).
*· Correlation is significant at the 0.05 level (2-tailed).

References:
(1) Ende G et al. Neuroimage 15;32:740-6, 2006;
(2) Ende G et al. Biol Psychiatry, 15;58(12):974-80, 2005
(3) Pulvirenti L & Diana M, Rev Neurosci. 2001;12(2):141-58 ;
(4) Weber-Fahr W et al. Neuroimage 16:49-60, 2002