Metabolic aberrations underlying impaired abstract reasoning abilities in chronic alcoholism: A proton magnetic resonance spectroscopy imaging study

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Target audience: Researchers working in the field of drug abuse and neuroimaging.

Purpose: Excessive alcohol consumption over a period of years may lead to a variety of neuropsychological deficits, brain atrophy and altered regional brain metabolism.[1] The neurocognitive deficits are most evident in higher order cognitive functions, such as abstract reasoning, problem solving and visuospatial processing. A recent fMRI study at our centre has shown the role of right fronto-parietal network in abstract reasoning. This study showed the greater recruitment of fronto-parietal brain regions to compensate for impaired abstract reasoning abilities.[2] Considering this, we performed a ^{1}H MRS study on right frontal gyrus and right superior parietal lobule in alcohol dependent subjects in order to explore the yet largely unknown relationship between metabolic alterations in fronto-parietal brain regions and impaired abstract reasoning abilities. We hypothesized that metabolic alteration in these brain regions would be related to abstract reasoning deficits in these subjects.

Material and methods: The study included 25 alcohol dependent subjects (n=25) and 20 healthy non alcoholic controls (n=20) matched for age, sex and education. The study was carried out using 3T whole body MR system (Magnetom Skyra, Siemens, Germany) with a 32 channel head coil. MRS data was obtained with a single voxel (SVS) point resolved spectroscopy sequence (PRESS) (TR=3300ms, TE= 30ms, voxel size=10*10*10 mm, averages=256, Number of spectral points=2048) with water suppression. The voxel was positioned in right inferior frontal gyrus and right superior parietal lobe. LC model was used for data processing. Relative concentrations of N-acetylaspartate (NAA), choline-containing compounds (Cho), myo-inositol (mI) and combined glutamate-glutamine (Glx) were measured. The results were reported as ratios relative to creatine at p values ($\leq$0.05). A correlation analysis was carried out between the changes observed in metabolic ratios and the response accuracy (to assess the performance in abstract reasoning task) selected from the abstract reasoning based fMRI study carried out at our centre only. The subjects were abstained from alcohol at the time of study with an abstinent period of more than a week.

Results and discussion: Proton MRS results in frontal gyrus and parietal lobule showed alcohol-associated significant reductions in NAA/Cr and Glx/Cr ratios whereas there was a significant increase in Cho/Cr and mI/Cr ratios (p value $\leq$0.05). Reductions in NAA levels might be attributed to neuronal loss while reductions in Glx levels might reflect perturbation of Glu-Gln system in alcohol dependents which could represent a neuroprotective adaptation[3]. Raised mI may reflect astrocyte proliferation as well as an osmotic response to cell shrinkage whereas a significant increase in Cho ratios indicate altered cell membrane metabolism[1]. A significant correlation was also observed between the response accuracy variable for abstract reasoning task (data taken from a previous fMRI study at our centre) and changes in NAA and Cho levels. Response accuracy is a measure of performance of an individual for a particular task (in this study, the abstract reasoning task). The higher response accuracy reflects better performance for the task. The significant correlation between metabolic alterations and response accuracy suggests the probable contribution of metabolic alterations towards impaired abstract reasoning abilities in alcohol dependent subjects.

Conclusion: The neuronal compromise that these metabolic changes reflect may contribute to the abstract reasoning deficits in alcohol dependent subjects. Our study thus shows a possible relationship between altered metabolism and function in the fronto-parietal circuit in chronic alcoholism.

References:

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2. Bagga D et al. Assessment of abstract reasoning abilities in alcohol dependent subjects: A fMRI study. (Neuroradiology.DOI 10.1007/s00234-013-1281-3).
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Metabolite ratios	Frontal gyrus		Parietal lobule	
	Alcoholics	Controls	Alcoholics	Controls
NAA/Cr	1.241±0.13	1.611±0.09*	1.264±0.31	1.540±0.21*
mI/Cr	0.863±0.32	0.609±0.27*	0.942±0.13	0.892±0.17
Glx/Cr	0.988±0.24	1.016±0.23	0.971±0.14	1.421±0.02*
Cho/Cr	0.237±0.04	0.191±0.03*	0.280±0.02	0.228±0.06*

Table 1: Results of in vivo MRS studies on frontal gyrus and parietal Lobule of alcoholics and controls (*p value$\leq$0.05)

Metabolite ratios	Correlation between Frontal gyrus metabolite ratios and response accuracy(r value)#		Correlation between Parietal lobule metabolite ratios and response accuracy(r value)#	
	Alcoholics	Controls	Alcoholics	Controls
NAA/Cr	0.612*	0.412	0.521*	0.298
mI/Cr	0.157	0.121	0.221	0.319
Glx/Cr	0.243	0.179	0.337	0.035
Cho/Cr	-0.681*	-0.306	-0.587*	-0.145

Table 2: Summary of the correlations between response accuracy and metabolite ratios in frontal gyrus and parietal lobule in alcohol dependents and controls (*p value$\leq$0.05).

#Correlation was run only with 18 alcohol dependent subjects and 18 controls recruited for the fMRI study.