Cerebral White Matter Recovery in Abstinent Alcoholics – A Multimodal Magnetic Resonance Study

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Introduction: Previous MRI and proton ^{1}H MRS studies of alcoholics demonstrated widespread volumetric and metabolic abnormalities [2], which are modulated by concomitant chronic cigarette smoking [3]. Also previous diffusion tensor imaging (DTI) studies of alcoholics demonstrated lower fractional anisotropy (FA) and elevated mean diffusivity (MD) in callosal fibers. The volumetric and spectroscopic abnormalities have been shown to be partially reversible with abstinence from alcohol [2], but with cigarette smoking potentially hindering these processes [3]. However, no longitudinal DTI studies in alcoholics were reported. The goals of this study were to assess WM volumetric, spectroscopy and DTI measures in alcoholics, evaluate their inter-relations, and their changes with abstinence from alcohol.

Methods: Sixteen non-smoking alcohol-dependents (**nsALC**) and 20 smoking individuals (**sALC**) were scanned at 1.5 Tesla, at approximately one week of abstinence from alcohol. Ten nsALC and 11 sALC were rescanned at approximately one month of abstinence. 22 non-smoking light-drinkers were also scanned only once. Structural and spectroscopy data were acquired with T1-weighted (TR/TI/TE=10/300/4 ms), and multislice ^{1}H MRSI (TR/TI/TE=1800/300/25 ms) sequences, respectively. The latter was obtained in 3 parallel planes through the centrum semiovale, nuclei of the basal ganglia, and cerebellum. Diffusion weighted images were acquired with a single-shot EPI sequence (TR/TE/TI=5000/100/3000ms, 2.4x2.4x5mm^3) with a double refocusing SE and bipolar external diffusion gradients [4] to minimize eddy-current artifacts without sacrificing SNR. Six encoding directions and five b-values (0,160, 360, 640, and 1000 sec/mm^2) were used. The T1-weighted images were segmented into gray matter, white matter (WM), and cerebrospinal fluid (CSF) of major lobes with automated probabilistic segmentation, aided by an automated atlas-based region labeling of major lobes, cerebellum, and subcortical structures. Regional atrophy-corrected metabolite concentrations of N-acetyl-aspartate (NAA, a marker of neuronal viability), choline-containing compounds (**Cho**), myo-inositol (**m-Ino**) and creatine containing metabolites (**Cr**), were calculated by combining spectroscopic and segmented MRI data. For DTI analyses, median FA and MD in frontal, parietal, temporal, and occipital WM were calculated using only diffusion voxels with FA>0.2 and WM>95%.

Results: At one week of abstinence, nsALC had higher MD in frontal, temporal, and parietal WM (all $p<0.008$) relative to nsLD, while sALC had elevated MD only in frontal WM ($p=0.03$) relative to nsLD. Even in the absence of significant atrophy, nsALC and sALC each demonstrated lower concentrations of NAA in frontal and parietal WM compared to nsLD (both $p=0.01$). Over one month of abstinence, MD decreased in all regions of nsALC ($p<0.04$), while FA increased only in temporal WM ($p=0.003$). No corresponding changes were observed in sALC. By contrast, WM volume in sALC increased over one month of abstinence in all WM regions ($p<0.04$), whereas there were no changes in nsALC. The longitudinal changes in concentrations of NAA and Cho were not significant in this sample.

Discussion: These data demonstrate significant WM changes with abstinence from alcohol, reflected either as microstructural recovery or volumetric increases depending on the smoking status of the participants. The changes in WM were not accompanied by changes in NAA, suggesting that these changes were driven by the glial component of WM. In conclusion, our results are important, as they demonstrate that 1) not controlling for smoking status may lead to varying results depending on the proportion of smokers in the cohort and 2) use of a single imaging modality provides an incomplete picture of neurobiological processes associated with alcohol induced brain injury and recovery thereof.

References:

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