Investigation of the Effects of Concurrent Chronic Cigarette Smoking in Alcoholics– a Preliminary Diffusion Tensor Imaging Study

S. Gazdzinski[1], T. C. Durazzo[1], P-H. Yeh[1,2], G-H. Jahng[2], P. Mukherjee[2], D. J. Meyerhoff[1,2]

[1]NCIRE, San Francisco, CA, United States, [2]Radiology, UCSF, San Francisco, CA, United States

Introduction: Previous studies of alcohol dependent individuals indicated decreased fractional anisotropy (FA) and increased mean diffusivity (MD) in the genu, body, and splenium of the corpus callosum, as well as in the centrum semiovale [1,2], with FA and MD inversely related [2]. Although, approximately 80% of alcohol-dependent individuals are regular smokers [3,4] and cigarette smoking was associated with higher incidence of WM pathologic changes [5] in non-alcoholic population, the effects of concurrent cigarette smoking on white matter integrity in alcoholics were not considered. Moreover, we have demonstrated with ^{1}H MR spectroscopic imaging that chronic cigarette smoking is associated with additional neuronal injury and cell membrane damage in frontal WM of alcoholics [6]. Therefore, we hypothesize that concurrent alcohol dependence and cigarette smoking would be associated with larger MD and lower FA than alcohol dependence alone.

Methods: We studied 18 alcohol dependent individuals (ALC) in treatment, sober for 6±3 days, and age-matched 11 healthy light drinking, non-smoking control participants (nsLD, 46 ± 8 years of age). In the ALC, 10 were smokers (sALC, 48 ± 9) and 8 non-smokers (nsALC, 50 ± 9). We used a single shot EPI DWI sequence (TR/TE/TI=5000/100/3000ms, 2.4x2.4x5mm^3) with a double refocusing SE acquisition and bipolar external diffusion gradients [7] to minimize eddy-current artifacts without sacrificing SNR, six encoding directions and five b-values (0,160, 360, 640, and 1000 sec/mm^2) to determine the ADC and diffusion tensor matrix for each voxel using a 1.5T MRI system. T1-weighted 3D MPRAGE images, segmented into gray matter (GM), white matter (WM), and cerebrospinal fluid (CSF) of bilateral major lobes, were co-registered to the b_0 images for calculations of mean regional WM DTI indices. Diffusion voxels were restricted to those with FA>0.2 and WM>95%. Regions visually affected by susceptibility artifact were manually removed. Additionally, in co-registered T1-weighted images we manually traced genu and splenium of corpus callosum. We used regional median MD and FA values for analyses, because MD and FA distributions within particular regions of interest were not Gaussian. Also, analyses of lobar WM regions and of corpus callosal regions were performed separately.

Results: Multivariate analysis of variance (MANOVA) comparing MD in lobar WM regions indicated significant group differences ($p = 0.007$). The follow-up analyses indicated a significant group effect in frontal WM ($p=0.009$) and a trend for a group effect in occipital WM ($p=0.06$), with nsLD having lower MD than nsALC and sALC (all $p<0.05$). No differences between sALC and nsALC were observed. MANOVA comparing lobar WM FA was not significant, however the follow-up analyses showed a pattern of lower FA in sALC vs. nsLD in frontal, parietal, and temporal WM (all $p < 0.05$, not corrected for multiple comparisons). Lobar WM MD and FA were not different between hemispheres ($p>0.27$).

MANOVA on genu and splenium showed a trend for group differences in MD ($p=0.06$), with nsLD showing lower MD than nsALC in genu and splenium ($p<0.05$) and nsLD having lower MD than sALC in genu ($p=0.04$). No differences in MD between sALC and nsALC were detected.

Discussion: Our results are consistent with previous DTI research demonstrating elevated MD in genu and splenium corpus callosum in alcoholics [1,2]. However, likely due to relatively large voxel size and lack of fluid attenuation in our sequence [8], our FA measures in genu and splenium were not significantly different between groups. Within large lobar regions, MD and especially FA measures are influenced by crossing fibers within voxels and partial volumes [e.g., 8,9]. Nevertheless, increased MD and decreased FA within WM tracts are reflected in median measures of these parameters within lobes. Among lobar WM regions, we found increased MD in frontal and occipital WM in both ALC groups, with no difference between nsALC and nsLD. Thus, in this cohort, alcohol dependence, not chronic cigarette smoking, has detrimental effects on WM structural integrity.

References:

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