Does Obesity Account for Brain Injury in Alcohol Dependent Individuals? – a Multimodal Magnetic Resonance Study at 1.5T.

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Introduction: Clinical [1] and epidemiological [2] studies demonstrated that alcohol dependence and excessive alcohol consumption are associated with increased rates of obesity, in particular abdominal obesity. Our group and others have previously demonstrated that elevated body mass index (BMI) in healthy cohorts is associated with lower N-acetyl-aspartate concentrations (NAA, marker of neuronal viability)[3], lower glucose metabolism [4], and structural brain alterations [5], mostly in frontal brain regions. However, no study evaluated the potential effects of BMI on regional structural, metabolite concentration, and perfusion measures in alcohol dependent individuals (ALC). We hypothesized higher BMI, cigarette smoking, older age, and more severe drinking are associated with smaller brain volumes, lower regional NAA levels, and lower gray matter perfusion.

Methods: We studied 54 ALC [32 smokers (sALC) and 22 non-smokers (nsALC), abstinent from alcohol for approximately one month, BMI between 20.4 and 37.1 kg/m²] with MPRAGE, (TR/TI/TE=10/300/4 ms); multislice 1H MRSI (TR/TI/TE=1800/300/25 ms) in 3 parallel planes through the centrum semiiovale, nuclei of the basal ganglia, and cerebellum; and with pulsed arterial spin labeling using single shot EPI [TR/TE/TI (time between labeling pulse and the excitation pulse) = 2500/15/1500 ms] in five 8mm thick slices 2mm apart, above the Circle of Willis and oriented as 1H MRSI. Regional white matter (WM), gray matter (GM) and CSF volumetry utilized automated probabilistic segmentation, combined with automated atlas-based region labeling of major lobes, cerebellum, and subcortical structures. Regional atrophy-corrected metabolite concentrations of NAA, choline-containing compounds (Cho, associated with membrane metabolism), myo-inositol (m-Ino, a putative marker glial cells) and creatine containing metabolites (Cr), were calculated by combining SI and segmented MRI data. Average cerebral perfusion in frontal and parietal GM was calculated over voxels containing at least 80% GM tissue. The outcome measures were modeled as a function of age, smoking status, BMI, and average number of alcohol drinks per months over lifetime. For BMI, the results were corrected for multiple comparisons (13 regions) and p = 0.05/13 = 0.0038 was considered significant.

Results: Linear regression analyses revealed that higher BMI was associated with lower NAA and Cho levels in frontal GM, thalamus, and cerebellar vermis (β<0.46, p<0.002) and lower NAA in frontal WM and brainstem (β<0.44, p<0.002). Additionally, higher BMI was associated with lower Cr in frontal GM, frontal WM, thalamus, caudate, and lenticular nucleus (β<0.45, p<0.004) and lower m-Ino in cerebellar vermis (β<0.47, p<0.002). Cigarette smoking was associated with lower NAA in frontal and temporal WM and in temporal GM (β>0.37, p<0.04). Regional brain volumes (scaled to total intracranial volume), or the cerebral perfusion measures were not associated with BMI or smoking. Higher m-Ino was associated with larger average number of drinks over lifetime in multiple brain regions (β>0.30, p<0.02); however, m-Ino did not explain the pattern of associations between BMI and regional NAA, Cho, and Cr concentrations. These results were not affected by excluding participants with co-morbid conditions such as hypertension, depression, or hepatitis C.

Discussion: These results replicate and extend the associations we observed between BMI and NAA concentrations in healthy control cohorts. However, unlike in healthy controls, higher BMI was also associated with lower concentrations of Cho, Cr, and m-Ino in various brain regions. Elevated BMI in men is often associated with abdominal obesity that might be related to peripheral insulin resistance, elevated levels of pro-inflammatory cytokines that may affect the neuronal metabolism [6]. Regional brain tissue volumes and cerebral blood flow were not associated with BMI. The positive associations between more drinking and higher m-Ino concentrations suggest that excessive alcohol consumption is associated with gliosis, consistent with [7]. However, m-Ino did not explain the associations between higher BMI and lower concentrations of NAA, Cho, and Cr.

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