Exploring Relationships Between Brain Structure, Peripheral Cytokines and Neurofilament Light Polypeptide in a Sample of Heavy Drinkers

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Background. Chronic alcohol consumption is associated with structural brain changes and increased inflammatory signaling throughout the brain and body. In particular, heavy drinkers show increases in pro-inflammatory cytokines measured in blood (1). Preclinical evidence suggests that alcohol also causes increased inflammation in the brain (2), and neuroinflammation has been associated with structural brain damage (3). Recent studies have shown that neurofilament light polypeptide (NfL) is released into circulation following neuronal damage (4). Given that NfL is produced following axonal damage and can be measured in blood, it has been proposed as a biomarker for several neurodegenerative diseases but has not yet been explored in connection with alcohol use disorder (AUD). We tested associations between alcohol consumption, plasma cytokines (specifically the pro-inflammatory cytokine IL-6), NfL and brain structure in heavy drinkers. We hypothesized that alcohol consumption will be associated with increased IL-6, that IL-6 will be correlated with decreased frontal gray matter (GM) volume and compromised white matter (WM) integrity, and that these brain phenotypes will be positively associated with NfL.

Methods.182 individuals participated in a study examining the effects of Mindfulness-Based Relapse Prevention (MBRP) compared to Relapse Prevention (RP) on drinking outcomes, and a subset of participants underwent MRI scanning. These analyses focus on measurements (self-reported alcohol consumption, blood biomarkers, and structural MRI) taken at baseline, prior to the intervention. 74 participants provided blood samples and had useable scan data. GM thickness was extracted from frontal brain regions using Freesurfer. Axial, radial and mean WM diffusivity values were extracted from Tract Based Spatial Statistics and a composite score was created consisting of the body of corpus callosum, fornix, external capsule, superior longitudinal fasciculus, and cingulate gyrus. NfL and IL-6 were measured from blood. Regression models were used to test relationships between these variables, controlling for gender. **Results.** Models showed significant negative relationships between GM and percent heavy drinking days, IL-6 and GM, and NfL and GM. Significant positive relationships emerged between IL-6 and total drinking days, WM and percent heavy drinking days and NfL and WM (note that higher WM diffusivity suggests greater damage). No associations emerged between IL-6 and WM.

Discussion. Data suggest that drinking is associated with inflammation, which is linked with structural brain damage and circulating NfL. This is the first study to demonstrate an association between brain structure and NfL in heavy drinkers and suggests that NfL may be a useful AUD biomarker with potential research and treatment implications.

References.

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