Impaired Dynamic Neural Response Underlying Alcoholism and Early Life Adversity

Dongju Seo, Cheryl M. Lacadie, and Rajita Sinha

Alcohol use disorder (AUD) patients with early life adversity (EA) suffer from severe clinical symptoms and worse treatment outcomes. Yet, mechanisms underlying the link between AUD, EA and high relapse risk remain unclear. The current research investigated neural mechanisms of co-occurring AUD/EA and their prediction of relapse in two data sets using functional magnetic resonance imaging.

Methods: In Study 1, we conducted a secondary analysis on data from our 2013 paper (Seo et al., 2013) to examine the effects of early trauma on alcoholism. In Study 2, utilizing a sustained emotion provocation (SEP) task, we investigated dynamic neural response in AUD patients with early adversity (AUD/EA, N=8), without adversity (AUD/NA, N=10), and healthy controls (N=9) during stress and alcohol cue exposure. Early life adversity was determined using the Childhood Trauma Questionnaires.

Results: Study 1: we previously showed that AUD inpatients (N=45) exhibited hypoactive response to stress in the ventromedial prefrontal cortex (VmPFC) ($p<0.01$, whole-brain corrected), which was associated with high alcohol craving and early relapse after treatment (Seo et al., 2013). A secondary analysis focused on early adversity showed that hypoactive VmPFC response to stress was significantly associated with early trauma ($r =-.54$, $p<0.01$), indicating that the VmPFC hypoactivity might be an underlying factor of comorbid AUD and EA.
Study 2: To further investigate the nature of the VmPFC hypoactivity, we utilized the SEP task to detect dynamic response over time; a lack of dynamic VmPFC response during stress was associated with reduced coping skills and increased alcohol consumption (Sinha et al., 2016). The SEP task results indicated that AUD/EA showed a lack of dynamic VmPFC response during stress relative to AUD/NA and controls ($p<0.01$). During alcohol cue, significant group difference was found in the ventral striatum (VS), a reward brain region. AUD/NA showed increased VS response to alcohol cue, while AUD/EA and controls showed decreased responses ($p<0.05$). Finally, we examined whether neural responses during the SEP task predicts future relapse using Cox proportional hazard regression in 24 AUD patients who were prospectively followed for 90 days after treatment. We found that poor dynamic VmPFC response to stress predicted early relapse to heavy drinking (men: 5 drinks or more/occ., women: 4 or more/occ.) and resulted in 84% greater chance of early relapse to heavy drinking ($\chi2=5.3$, $p<.05$; HR=.16; 95%CI: .03-.78) during the 90-day follow-up period.

Discussion: The results indicate that AUD/EA show hypoactive VmPFC responses to stress with a loss of neuro-flexibility, while the AUD/NA showed hyperactive ventral striatal response to alcohol cues. In AUD/NA, increased VS response to alcohol cue may indicate their vulnerability to reward-driven, alcohol seeking behaviors. In AUD/EA, poor dynamic VmPFC response to stress suggests their vulnerability to cope with stress and a tendency to abuse alcohol as a maladaptive coping strategy. AUD/EA may be more vulnerable to relapse and engage in heavy drinking under stress, resulting from disrupted VmPFC control over stress-related emotional response. These data suggest differential vulnerability patterns in AUD/EA vs. AUD/NA during early abstinence and its subsequent effects on biobehavioral recovery from alcoholism.

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