Altered Default Mode Network Connectivity in Alcohol Dependent Patients with DAT1 Gene Variant

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Background: Alcohol Dependence (AD) is a chronic relapsing disorder with high degrees of comorbidity and mortality. While multiple neurotransmitter systems are involved in the complex symptomatology of AD, alcohol induced dopamine (DA) release in the mesolimbic reward system has been implicated in reinforcing excessive alcohol intake and the consequent dependence (Volkow et al. 2009).

The DA transporter (DAT1) plays a key role in the regulation of dopaminergic neurotransmission through presynaptic DA reuptake. Previous studies have been in disagreement about the effect of this gene in alcohol dependence (van der Zwalum et al 2009). The 9-repeat allele of this gene was positively associated with alcohol misuse behavior and alcohol dependence (Lind et al, 2009); however, another study found a non-substantial impact of this gene on the severity of alcohol withdrawal symptoms (Franke et al. 1999). Because the dominant variant of the DAT1 gene is the 10/10 allele, we initially investigated the potential contribution of the major allele on resting state network connectivity differences.

Methods: Participants underwent a 5-minute, eyes-open resting state scan. We conducted resting state fMRI functional connectivity analysis using an independent component analysis (ICA) approach in 13 AD subjects and 30 healthy controls (HC). All subjects were genotyped for the 9-repeat and 10-repeat of DAT1 gene. In the preliminary portion of this study we performed functional connectivity analyses of the major allele (10/10 variant) of DAT1 between 13 AD and 14 HC.

Resting state functional connectivity was analyzed using FSL software. MELODIC (Beckmann and Smith, 2004) was used to identify independent components, and dual regression (Beckman et al., 2009) was used to conduct group analysis. The resulting statistical maps were threshold at p < 0.005 FWE-corrected for the main effect of group.

Results: In participants with the 10/10 allele of DAT1, HC showed higher network connectivity than AD in DMN only in the insula and anterior cingulate, thalamus and parahippocampus (p < 0.005, corrected).

Conclusions: AD showed decreased network connectivity in the DMN compared to HC, despite both groups only including individuals with the major allele of the dopamine transporter gene. Further work will be required to understand the effect of the 9-repeat variant of DAT-1 on resting state functional connectivity in AD.

Short Abstract: We conducted resting state connectivity analysis of 13 alcohol
dependent patients and 14 healthy controls with the 10/10 variant of the dopamine transporter (DAT1). We found higher resting state functional connectivity in DMN of the healthy control participants.