Prefrontal and Peripheral Stress Mechanisms Affecting Addiction Relapse and Recovery.

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Background: Growing evidence indicates that chronic alcohol and drug abuse results in multilevel peripheral and brain adaptations in stress and homeostatic pathways that significantly impact cognitive, affective, alcohol craving and reward processes. However, identification of such measures as biomarkers of alcohol relapse and recovery has not been well studied.

Methods: Data from multimodal neuroimaging and human laboratory experiments combined with a prospective clinical outcomes design will be presented. Participants included inpatient treatment engaged individuals with alcohol use disorders (AUD) and cocaine use disorders (CUD) who were 3-4 weeks abstinent and in early recovery during separate laboratory and neuroimaging experiments. Healthy social drinking volunteers were included as control subjects. Multimodal neuroimaging using structural and functional magnetic resonance imaging (MRI and fMRI) assessing structural gray matter volume and functional neural responses to brief script-driven guided imagery of stress, alcohol cues and neutral relaxing states, and a laboratory experiment assessing autonomic and hypothalamic pituitary adrenal (HPA axis) basal states and responses to stress, drug/alcohol cue and neutral states were conducted in both patients and controls. Patients with CUD and AUD were followed prospectively after inpatient discharge with repeated assessment of substance use outcomes over a 90 day followup and recovery period.

Results: Findings indicate hyperactive basal and neutral state autonomic and HPA axis measures (heart rate, cortisol, cortisol/ACTH ratio), higher brain derived neurotrophic factor (BDNF), lower medial frontal brain volume and hyperactive neutral state ventromedial prefrontal cortex (VmPFC) and blunted VmPFC response to stress and drug/alcohol cue, with each predicting greater risk of future relapse and poor recovery outcomes. In the AUD group, we found a significant association between the cortisol/ACTH ratio and VmPFC disruption with VmPFC changes accounting for 33% of the HPA axis disruption in abstinent patients. Using receiver operating characteristics (ROC) to assess future relapse versus recovery outcome prediction accuracy, we found that VmPFC hyperactivity in neutral state showed the most optimal prediction characteristics across measures in sensitivity and specificity for alcohol relapse/recovery prediction.

Conclusions: These findings support both multimodal neuroimaging to assess addiction-related neuroadaptations in clinical samples, and also the need for further biomarker development to validate optimal biomarkers of addiction relapse risk so as to improve addiction recovery outcomes. (Supported by UL1-DE019586, R01-AA013892; PL1-DA24859).