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EEG coherence related to fMRI resting state synchrony in long-term abstinent alcoholics

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ABSTRACT

Recent work suggests that faulty co-activation or synchrony of multiple brain regions comprising "networks," or an imbalance between opposing brain networks, is important in alcoholism. Previous studies showed higher fMRI resting state synchrony (RSS) within the executive control (inhibitory control and emotion regulation) networks and lower RSS within the appetitive drive network in long-term (multi-year) abstinent alcoholics (LTAA) vs. non substance abusing controls (NSAC). Our goal was to identify EEG networks that are correlated with the appetitive drive and executive function networks identified with fMRI in our previous alcohol studies. We used parallel ICA for multimodal data fusion for the 20 LTAA and 21 NSAC that had both usable fMRI and 64-channel EEG data. Our major result was that parallel ICA identified a pair of components that significantly separated NSAC from LTAA and were correlated with each other. Examination of the resting-state fMRI seed-correlation map component showed higher bilateral nucleus accumbens seed-correlation in the dorsolateral prefrontal cortex bilaterally and lower seed-correlation in the thalamus. This single component thus encompassed both the executive control and appetitive drive networks, consistent with our previous work. The correlated EEG coherence component showed mostly higher theta and alpha coherence in LTAA compared to NSAC, and lower gamma coherence in LTAA compared to NSAC. The EEG theta and alpha coherence results suggest enhanced top-down control in LTAA and the gamma coherence results suggest impaired appetitive drive in LTAA. Our results support the notion that fMRI RSS is reflected in spontaneous EEG, even when the EEG and fMRI are not obtained simultaneously.

1. Introduction

The diagnosis of alcoholism requires the continuing engagement in dangerous or risky drinking in the face of recurring negative consequences of the drinking behavior in the social, physical, work, or family domains. This propensity toward continued hazardous drinking despite continuing consequences suggests that the short-term appetitive outcomes of drinking (e.g. intoxication, disinhibition) have greater control over behavior than do the potential short-term and long-term negative consequences of drinking (e.g., drunk driving arrests, liver disease, loss of family or job, etc.). From a neurobiological perspective this pattern implies weak "top-down" executive control over impulsive and compulsive urges to consume alcohol, and a strong "bottom-up" appetitive drive to impulsively and compulsively consume alcohol.

In 2013, we measured social deviance proneness, antisocial disposition, and both lifetime and current antisocial symptoms in both short-term abstinent alcoholics (STAA) and long-term abstinent alcoholics (LTAA) compared to controls (Fein and Fein, 2013). Lifetime antisocial symptoms, social deviance proneness, and antisocial disposition were highly elevated in both STAA and LTAA. Current antisocial symptoms were dramatically reduced in LTAA compared to STAA, close to levels observed in controls. In contrast, social deviance proneness and antisocial disposition remained highly elevated in LTAA, comparable to STAA. These findings suggest that antisocial behaviors are reduced in extended abstinence despite continued social deviance proneness and antisocial disposition, consistent with the notion that extended abstinence requires strong "top-down" executive control to inhibit deviance-prone tendencies.

The brain regions associated with executive control and appetitive drive have been extensively probed using functional magnetic resonance imaging (fMRI), and many observed differences in activation in these brain regions have been associated with alcohol use, abuse, and dependence, suggesting that multiple brain regions can contribute to the poor decision making and risky behaviors seen in alcoholism (for a

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review, see (Camchong et al., 2013a)). Recent work suggests that faulty co-activation or synchrony of multiple brain regions comprising "networks," or an imbalance between opposing brain networks, is important in alcoholism. Network synchrony is often referred to in the literature as "functional connectivity," and resting state fMRI (rs-fMRI), electroencephalography (EEG), and magnetoencephalography (MEG) can be used to investigate different properties of brain networks, such as spatial specificity, magnitude of the synchrony among its constituent components, or timing of event processing.

We previously observed in fMRI, higher resting state synchrony (RSS) within the executive control (inhibitory control and emotion regulation) networks and lower RSS within the appetitive drive network in long-term (multi-year) abstinent alcoholics (LTAA) vs non substance abusing controls (NSAC) (Camchong et al., 2013b). We found similar effects, although to a lesser degree, in short-term (~6–15 weeks abstinent) abstinent alcoholics (STAA) (Camchong et al., 2013c). We believe these cross-sectional differences reflect adaptive changes that support abstinence both because of the observation of graded effects in short-term vs. long-term abstinence and because these networks play important roles in the changes needed for continued abstinence, where inhibiting behavior and reducing appetitive drive are central (Hare et al., 2009; Medalla and Barbas, 2009; Naqvi and Bechara, 2010). If it can be confirmed in longitudinal studies that the degree of these changes in the appetitive drive and executive control networks is associated with and predictive of successful abstinence, then interventions that directly augment these changes, such as neurofeedback that "feeds back" measures of brain network synchrony, may have treatment potential for recovering alcoholics.

Though technically possible, it is at present neither practical nor economically feasible to use neurofeedback to modify fMRI RSS. Furthermore, although fMRI provides high confidence in the identification of anatomical regions that contribute to the executive control and appetitive drive networks, it is unable to reflect the sequential neural activity underlying cognitive states of readiness or execution of a task due to the poor time resolution of the BOLD response, which at best is on the scale of hundreds of milliseconds, compared to the millisecond resolution of EEG. Converging evidence suggests that the fMRI BOLD response reflects the summed neural activity of several oscillatory EEG networks (for a review, see (Whitman et al., 2013)). These EEG networks may oscillate at multiple frequencies (e.g., theta, alpha, or gamma) and the activity of separate networks may vary as a function of cognitive states lasting only a few hundred milliseconds. fMRI networks involved in task processing are likely to be comprised of multiple oscillatory EEG networks reflecting both induced and evoked EEG responses, including those that derive from frequency-dependent changes in phase alignment (Burgess, 2012). Therefore, the identification of EEG networks underlying executive control and appetitive drive could potentially reveal more about the mechanisms underlying the processing and inhibition of the cascades consequent to alcohol cues that contribute to the maintenance of abstinence, because of the more complex nature of EEG measures of brain activity that dynamically change at the same pace as cognitive processes.

Other researchers have explored brain networks derived from scalp-recorded EEGs and their relationship to rs-fMRI networks. Earlier work used low-resolution electromagnetic tomography (LORETA) (Pascual-Marqui, 2002, 2007) to estimate cortical EEG sources and independent components analysis (ICA) to identify source networks, and demonstrated EEG networks involving similar cortical regions to those of rs-fMRI networks from the literature. More recent work studied the effect of acute alcohol intake on the brain's resting state network in social drinkers, by examining the magnitude squared coherence between the activity of cortical sources of EEG within different frequency bands (Lithari et al., 2012) to construct brain networks.

Our goal in this paper is to identify EEG networks that are correlated with the appetitive drive and executive function networks identified in our previous alcohol studies. We use parallel ICA (Liu et al., 2009; Meda et al., 2014; Narayanan et al., 2015) for multimodal data fusion between the rs-fMRI and resting state EEG for the 20 LTAA and 21 NSAC from our prior study (Camchong et al., 2013b) that had both usable fMRI and 64-channel EEG data. This approach is well accepted in the medical image processing community and has been used for joint analysis of fMRI, structural MRI, EEG, and genetic data. Parallel ICA allows us to consider two sets of extracted features from each subject's data (e.g., fMRI seed connectivity map and the resting state EEG coherence maps for each subject) and identify components that contribute in a similar way to each subject and are "linked." In addition, we examined social deviance proneness, antisocial disposition, and both lifetime and current antisocial symptoms in our participants, to determine whether identified networks were accompanied by behavioral changes that implied enhanced "top-down" control.

2. Methods

2.1. Participants

Twenty-three LTAA (abstinent 7.91 ± 7.80 years) were compared to 23 gender and age (35–60 years) comparable NSAC, as described in (Camchong et al., 2013b). LTAA met DSM-IV lifetime criteria for alcohol dependence (American Psychiatric Association, 1994) but not for lifetime abuse or dependence on any other drugs of abuse (other than nicotine or caffeine). Inclusion criteria for the NSAC group was a lifetime drinking average of < 30 standard drinks per month with no periods of drinking > 60 drinks per month, and no lifetime history of alcohol or substance abuse or dependence. Participants received monetary compensation for their participation. Exclusion criteria for both groups included: a) a significant history of head trauma or cranial surgery; b) current or lifetime history of diabetes, stroke, or hypertension that required medical intervention; c) current or lifetime history of a significant neurological disorder, including dementia; d) clinical or laboratory evidence of active hepatic disease; e) clinical evidence for Wernicke-Korsakoff syndrome, and f) lifetime diagnosis of schizophrenia or schizophreniform disorder, f) contraindications to MRI. All subjects completed signed informed consent, as approved by our institutional review board (E&I Review Services, LLC, Corte Madera, CA), before study procedures commenced.

Participants were studied with fMRI, EEG, clinical, and neuropsychological testing. Ideally, all study procedures were completed within one month, but due to scheduling difficulties time between EEG and fMRI acquisition was sometimes longer. For the 41 participants that had both usable fMRI and EEG, 31 (76%) were acquired within one month, with the time between acquisitions of 6.57 ± 8.24 weeks for NSAC and 4.65 ± 9.48 weeks for LTAA (no difference between groups). LTAA subjects were required to stay sober throughout the study and did not drink between EEG and fMRI acquisitions; NSAC were asked to abstain from alcohol for 24 h prior to any lab visit, but may have continued drinking at their usual low level of drinking between visits and their alcohol use between study procedures was not monitored. A breathalyzer test (Intoximeters, Inc., St. Louis, MO) and a rapid oral fluid drug screen test (Innovacon Inc., San Diego, CA) for THC, amphetamines, methamphetamines, cocaine, opioids, and PCP was administered to all participants, with a negative result required for all participants at all sessions.

2.2. Clinical and psychological measures

Participants were interviewed on the lifetime use of alcohol and each drug that they had taken (including nicotine) using a timeline follow-back and lifetime drinking history assessment (Skinner and Allen, 1982; Skinner and Sheu, 1982; Sobell and Sobell, 1992; Sobell et al., 1988). ASPD symptoms were obtained using the C-DIS (Blouin et al., 1988; Robins et al., 1998). For each symptom the subject endorsed, we asked about currency. Psychological measures of antisocial