The Effect of Ethanol on Resting State Brain BOLD Signal

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Introduction:

Functional magnetic resonance imaging (fMRI) has been instrumental to the advancement of our understanding of the human brain *in vivo*. Most fMRI experiments have focused on changes in neural activity before and during/following a stimulus, giving information on the modular functional neural organization. Recent investigations have used fMRI to look at spontaneous low frequency synchronizations between different areas of the brain. This technique, referred to here as 'resting state blood oxygen level dependent' (rsBOLD), is currently believed to give information on the brain's spontaneous functional connectivity. This method has further been shown to be useful in various pathologies and mental illnesses, (e.g. Alzheimer's, Schizophrenia, and ADHD). Few studies, however, have looked at changes in resting state conditions before and after alcohol or other mood altering drug use.

Hypothesis:

Ethanol's short-term deleterious effect on human behavior and thinking is familiar to non-scientists and scientists alike. We wanted to look at the differences in the rsBOLD signal before and after the onset of inebriation using a novel approach to resting state BOLD analysis: fractal dimension (FD) mapping **[1]**. We hypothesized that significant disorganization in the inebriated brain, determined from rsBOLD FD analysis, will be observed. We also hypothesized that ethanol will be quantifiable using a standard clinical PRESS MRS sequence, and its concentration would be correlated with FD changes.

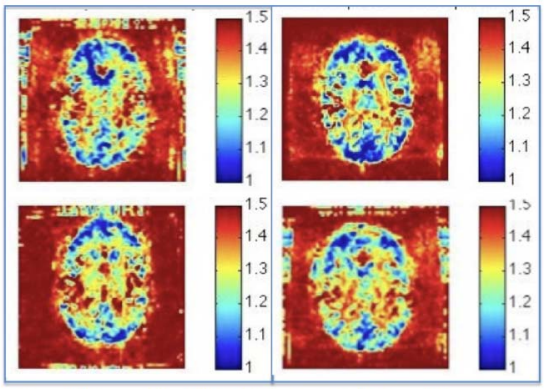

Figure 1: Effects of alcohol on BOLD signals in the brain. Power spectrum of the fractal dimensional map, prior to (top) and during (bottom) inebriation of subject 1 (left) and 2 (right). Index on side represents the degree of structure in signal (1 for structured, 1.5 for unstructured).

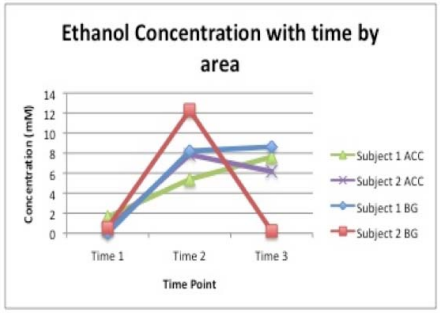

Figure 2: Ethanol concentration by area by time. Subject 1 (ACC in green, BG in blue) shows a pattern of increasing concentration, indicating a lack of ethanol clearance, whereas subject 2 (ACC in purple, BG in red) demonstrates a wash-in-wash-out ethanol concentration pattern.

Methods:

Two 24-year-old healthy male subjects (weights between 167-177 lbs.) were scanned, before and after the consumption of 5 ounces of 40% ethanol (by volume) taken in the span of 2 minutes. Three separate rsBOLD scans were taken: one before alcohol ingestion, and two following ingestion (30 and 70 minutes post consumption). For each rsBOLD scan, three slices (GE HD 3T signa MRI (GE Healthcare, Milwaukee, WI), 8 channel phased array head RF coil, gradient echo EPI, TE/TR=35/250ms, flip angle=70^o, 64x64, 5mm thick, FOV=24cm, 7200 scans) from the brain were acquired in the mid sagittal region. Images were analyzed using AFNI, and in-house programs written in Matlab (The Mathworks, Natick MA) for FD analysis. FD analysis was performed pixel-wise to determine the degree of temporal structure in the BOLD signal. After each rsBOLD scan, two PRESS MRS scans (TE/TR=30/2000ms, 256 NEX, 8cm^3 voxel, scan time = approx. 9mins) were acquired, first in the anterior cingulate cortex (ACC), which is implicated in rational cognitive functions, as well as autonomic regulation. The second MRS voxel was acquired from the basal ganglia (BG), implicated in inhibitory motor control. Significant ethanol concentrations in either of these structures could provide a partial explanation for the deficits characteristic of an inebriated state. Both of these structures were located on an axial fSPGR. Data was analyzed with LCModel **[2]**, using a simulated basis set including a 100mM ethanol spectrum for data deconvolution. Absolute metabolite concentrations were obtained using LCModel's water-scaling algorithm.

Results and Discussion:

After FD analysis, it was found that alcohol consumption led to an increase in unstructured BOLD signal (**Fig.1**), specifically in the frontal and visual cortexes. Structured BOLD signal, based on FD analysis, is represented by FD values approaching 1.5. Values nearing 1.0 represent periodic, or structured BOLD signal variation. This was also accompanied by a significant increase, defined as SD%<20, in ethanol signal as measured in the ACC at time points 2 and 3 for both subjects, and at time points 2 and 3 for subject 1, and time point 2 for subject 2 (**Fig.2**). These findings, although only suggestive, shed further light on alcohol's effect on the brain, specifically the brain's functional connectivity.

References:

[1] Wardlaw G, Wong R, Noseworthy MD. (2008) Phys Med.24:87-91.

[2] Provencher S (1993) Magn Reson Med 30:672-679.