Low-dose alcohol effects on neural timing, an fMRI study

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Introduction: FMRI is currently being used to investigate the acute effects of alcohol administration on the central nervous system. The two main aims of this project are 1) to determine the regional specificity of acute alcohol administration and its temporal dependence, and 2) to determine the influences of alcohol ingestion on behavioral task performance and the task-dependent brain activation. The experimental design allows subjects to be scanned, before and after drinking a cocktail, while performing two tasks associated with a traffic light model. Our preliminary results show that even a low dosage (≤ 0.25g/kg body weight) of alcohol ingestion may modulate both the subjects' performance in the tasks and the fMRI BOLD signal in detecting brain activation.

Materials and Methods: Eight healthy adult volunteers (7 males, 1 female; aged 25.1 ± 4.0) underwent anatomical and functional MRI's in a 3T Siemens Allegra head dedicated scanner. T1 weighted anatomical images (Matrix=256x256, TR=1.5s, TE=4.38ms, FA=8°, FOV=240mm, 160 slices, slice thickness =1.2mm without gaps) were obtained for co-registration with functional images acquired with a gradient-echo EPI sequence (TE=30ms/TR=3000ms, FA=90, Matrix=64x64, FOV=240mm, 36 slices, slice thickness=3.8 mm without gaps). All eight subjects participated in a Traffic Light (TL) task paradigm that was created and implemented with E-Prime (Psychology Software Tools) and consisted of two task conditions: counting and timing. Both the counting and timing tasks were briefly practiced outside of the scanner and then performed inside of the scanner before and after drinking a cocktail. Each task consisted of flashing one of four lights (blue, yellow, red, and green) in a random sequence. Using a right-handed response button glove (MRI Devices), the subjects answered each trial by determining if there was 4 flashes or 6 flashes in the counting task and if the light was flashed for a period of 4 seconds or 6 seconds in the timing task. The sequence of trials and tasks was counterbalanced for all subjects. In between the two scans, all of the subjects were served a 200mL cocktail with a variable amount of 80 pf Vodka (Stolichnaya) according to 0.25g/kg of their body weight (0.36mL per pound) mixed with diet 7UP (no caffeine or sugar). BAC measurements were taken at the beginning and end of each scan and 5 minutes after finishing the cocktail. BAC was measured using the Digital Alcohol Breath Analyzer/AlcoScan CA2000 and an average of 0.053 ± 0.029 was obtained at the end of the experiment. Both the counting and timing tasks were each performed two times: (1) immediately before drinking and (2) twenty minutes after finishing the cocktail in order to include the declining phase after reaching peak BAC. The imaging data was processed using Brain Voyager 2000 and analyzed with a general linear model based on a time course and an estimated hemodynamic response.

Results: ***Fig. 1*** shows an increased reaction time (RT) in the timing task compared to the counting task. We found no significant difference in the average percentage of correct responses (data not shown). ***Fig. 2*** compares the BOLD signals of the timing task during the pre-drink (***Fig. 2b***) and post-drink (***Fig. 2c***) conditions using a time-locked averaging approach. The color-coded region inside the cerebellum (Talariach: -35, -58, -35) in ***Fig. 2a*** indicates higher neural activation (functional images had a threshold at $P < 1.1 \times 10^{-5}$ and a minimum cluster size of 6 voxels) from the timing task in the post-drink condition relative to the pre-drink condition. The rise (Fig.2b – pre-drink) and drop (Fig. 2c – post-drink) in BOLD signals during the resting blocks further substantiates the changes pertaining to this ROI.

Discussion: In a Motor-Free Visual Perception Task (Calhoun 2004), alcohol induced dose-dependent activation increases in the insula, dorsolateral prefrontal cortex, and precentral gyrus regions while inducing dose-dependent activation decreases in the anterior and posterior cingulate, precuneus, and middle frontal areas. The findings in the data resulting from the TL paradigm of our study can be used to substantiate future explorations that involve isolating the neuroanatomical regions associated with reduced cognitive function due to alcohol intoxication, specifically such as diminished time perception. We are still speculating as to whether the increase in the reaction time of the timing task reflects a corresponding increased level of difficulty in the timing task or if it reflects a longer demand for judging the perception of time. In our upcoming future trials, we will attempt to preserve the flexibility of the subject's acute tolerance to alcohol by implementing the B_rAC clamping procedure developed at the Indiana University School of Medicine (O'Connor 1998). Our results will further enhance the present understanding of the neural pathways affected by alcohol in performing driving related tasks. Ultimately, this knowledge could have a tremendous impact on both societal attitudes and legislation involving DUI cases.

References:

Calhoun, Vince D. et al. "Alcohol Intoxication Effects on Visual Perception: An fMRI Study." Human Brain Mapping (2004) Vol. 21:15-25, pp. 15-25.

O'Connor S, Morzorati S, Christian J, Li TK. Clamping breath alcohol concentration reduces experimental variance: application to the study of acute tolerance to alcohol and alcohol elimination rate. Alcohol Clin Exp Res. 1998 Feb;22(1):202-10.

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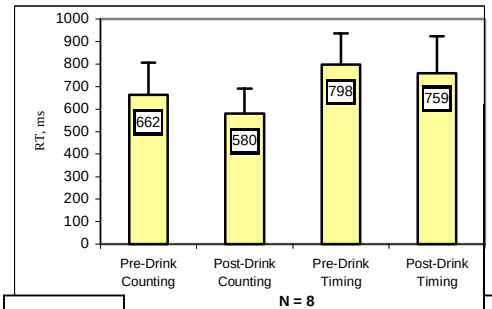

Fig. 1

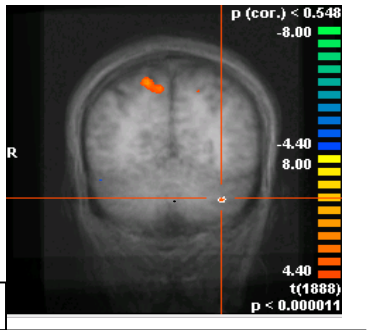

Fig. 2a

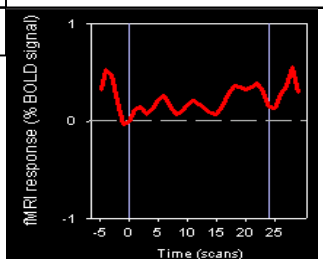

Fig. 2b

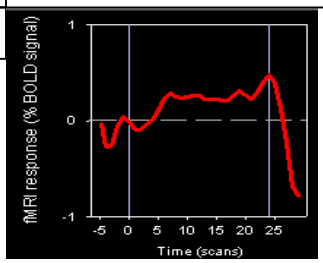

Fig. 2c