Neural Dynamics of Alcohol Effects on Cognitive Control: Eriksen Flanker Task

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Abstract—**Alcohol intoxication interferes with the capacity to inhibit maladaptive reactions and execute correct responses. In order to investigate alcohol's effects on cognitive control, a group of healthy subjects (N = 20, 9 women) participated in both alcohol (0.6 g/kg ethanol) and placebo conditions in a color version of the Eriksen flanker task. MEG signal was recorded from the whole head and the noise-normalized minimum norm inverse estimates were anatomically constrained to each person's cortical surface reconstructed from MRI. Alcohol increased error rates in the response-conflict condition. Under placebo, the anterior cingulate (AC) was sensitive to the level of conflict, supporting an optimized response strategy. Alcohol blunted this conflict-induced differentiation in AC activity. This suggests that alcohol impairs cognitive control by affecting top-down regulation of response preparation and execution. Alcohol-induced impairment of executive functions may result in poor self-control, expressed as socially-inappropriate behavior and an inability to refrain from drinking.**

Keywords— **MEG, Eriksen flanker, cognitive control, alcohol, anterior cingulate gyrus.**

I. Introduction

Chronic alcohol abuse is associated with deficits in executive functions, with the frontal lobes being especially vulnerable to its adverse effects [1]. Similarly, acute alcohol intoxication disrupts executive abilities in situations of increased complexity as it interferes with cognitive assessment of the environment and the capacity to inhibit maladaptive responses and use an appropriate response strategy [2]. Indeed, the inability to maintain inhibitory control over harmful levels of drinking is considered to be fundamental to alcohol abuse [3]. Though subsuming diverse functions, "executive capacity" refers to the ability to sustain focus on a goal in the face of changing contextual demands [4].

Neuroimaging studies indicate that different executive tasks regularly engage highly overlapping regions centered primarily in the anterior cingulate (AC) and lateral prefrontal (LPF) cortices. Conflict-monitoring theory [5] describes how this strategy-driven regulatory function arises from their functional interplay. Alternatively, the "Reinforcement Learning" theory proposes that a dopamine-dependent signal acting through the basal ganglia permits the AC to engage in top-down regulation [6]. In both cases, the AC is essential to subserving goal-oriented actions especially those that are not well rehearsed or habitual, under contextually-challenging circumstances. Its anatomical connections include the spinal cord, motor and limbic cortices, and prefrontal association areas, supporting this multifaceted role [7]. The AC is sensitive to task difficulty, response conflict, and error processing [8] and its activity has been probed in a series of cognitive control tasks.

The Eriksen flanker task was devised to investigate the effects of compatibility between irrelevant information (flanker letters) and targets (central letter in a letter array) on decision making [9]. Event-related potential (ERP) studies suggest that response conflict evokes a N2 component at ~350ms after stimulus onset, and error-related negativity (ERN) at ~50ms after response, presumably generated in the AC [10]. The ERN is attenuated by alcohol intoxication [11], indicating impaired performance monitoring. In order to investigate spatio-temporal characteristics of alcohol's effects on cognitive control, we used anatomically-constrained MEG (aMEG) method. It combines whole-head high-density MEG and a distributed source modeling approach with high-resolution structural MRI to estimate the anatomical distribution of the involved neural networks with high temporal resolution [12, 13]. The task version employed in this study included comparison between the stimulus-level vs. response-level incongruity, permitting assessment of alcohol's effects on these two aspects of processing.

II. Methods

A. Subjects

Young, healthy volunteers (N=20, 9 women; age (mean ± st. dev) = 25 ± 3.4 years) served as their own controls as they participated in both alcohol and placebo conditions in a counterbalanced manner. They were all right-handed native English speakers and were prescreened for a negative history of alcoholism and drug use. They were non-smokers and reported moderately low alcohol use, imbibing 3 ± 1 drinks per occasion, 2 ± 1 times per week on average. They all came from non-alcoholic families. All participants gave written informed consent to participate in the study.

B. Task

A color version of Eriksen flanker task was employed in this study [14]. Two flanker squares were presented in green, red, blue, or yellow for 200ms, followed by a target square presented in central location (Fig. 1, left panel). Subjects were instructed to respond to the color of a target square by pressing left button to green or red and right button to blue or yellow. On congruent (CO, 50%) trials the target and the immediately preceding flankers were of the same color. The incongruent trials were of two types: on stimulus-level incompatible (SI, 25%) trials the flankers and targets were different but used the same response hand; on response-incompatible (RI, 25%) trials the flankers and targets differed in color as well as response mapping. A total of 512 trials were presented every 1600ms with Presentation® software (Neurobehavioral Systems).

C. Data Acquisition and Analysis

Continuous MEG signals were recorded from 204 channels (102 pairs of planar gradiometers) at 600 Hz with a whole-head Neuromag instrument (Vectorview, Elekta Neuromag), at the Martinos Center in Boston. Averages for each condition included only trials on which correct responses were given that were free of eyeblinks or artifacts. Digitizing positions of the main fiduciary points, magnetic coils, and a large array of random points spread across the scalp with 3Space Isotrak system (Polhemus Inc.) permitted co-registration with structural MRI images. For each participant a high-resolution structural 3D MPRAGE T1-weighted scan was obtained with a 3 T Trio body scanner (Siemens, Erlangen), with TR = 2.54 sec, TE = 3.25 msec, flip angle = 7^0, FOV = 256, 128 sagittal slices, 1.33 mm thickness, in-plane resolution 1 x 1 mm. Each person's cortical surface was reconstructed with an automatic segmentation, tessellation and inflation FreeSurfer tool (http://surfer.nmr.mgh.harvard.edu/), subsampled to ~2500 dipole locations per hemisphere and used to constrain inverse solution. The atomically-constrained MEG (aMEG) estimates were calculated with the MNE software (http://www.nmr.mgh.harvard.edu/martinos/userInfo/data/sofMNE.php). Averages contained only correct responses and were equated for the number of included trials across beverage conditions. Activity estimates were averaged to stimulus onset (Fig. 2) and to response execution (Fig. 3) in order to estimate alcohol effects on stimulus evaluation vs. response-preparation processing stages. The forward solution was based on a boundary element model and dipole strength power was estimated at each cortical location and each time point with a linear noise-normalized minimum norm estimation approach with no constraints on dipole orientation [15, 16]. The resulting "brain movies" consist of frames of statistical parametric maps displaying the statistical tests of the null hypothesis that, at each latency and location, there is no difference in the activity evoked by the condition and the baseline period. Group averages were obtained by averaging the inverse estimates using cortical surface alignment [17, 18]. Figures 2 and 3 show the group average estimates of the overall activity patterns evoked by each stimulus type at selected latencies for the stimulus-locked and response-locked averages respectively. Additionally, timecourses of estimated dipole-strength moments in the regions of interest in the cortical source space are presented in Fig 4.

D. Experimental Procedure and Design

All subjects first participated in an introductory session during which they were familiarized with the recording setup and provided detailed information about their medical status, history of alcohol and drug use, handedness, and dispositional profile. In each of the subsequent two sessions, scheduled 31 days apart on average, participants were given either alcohol or placebo in a counterbalanced order. Ten out of twenty subjects were given alcohol in the first session and placebo in the second. Prior to each session women were given a pregnancy test to ascertain that they were not pregnant. Blood alcohol concentration (BAC) was measured with a breathalyzer (Draeger, Inc.) on several occasions outside the magnetically shielded room. During the actual measurement, Q.E.D. Saliva Alcohol Test (OraSure Techn. Inc.) was used to estimate BAC. Alcohol was administered as a cocktail containing vodka (Grey Goose®, Bacardi), 0.6 g/kg of ethanol for men and 0.55 g/kg for women, mixed with orange juice in 20%v/v [19]. The average BAC just before the task reached 0.056 ± 0.01 and measured at 0.053 ± 0.01 upon the completion of the task. On a 1 to 5 Likert scale, the subjects reported being moderately intoxicated (2.7 ± 0.7) and rated the task as being moderately easy (2.7 ± 0.9). No gender effects were observed.

III. Results

A. Performance

Performance accuracy was affected by flanker-target compatibility, as indicated by the main effect of Condition, $F_{2,36} = 7.4$, $p < 0.005$ (Fig 1). Participants were least accurate on RI trials as compared to both CO, $F_{1,18} = 7.5$, $p < 0.05$, and SI conditions, $F_{1,18} = 7.7$, $p < 0.05$. The significant Beverage x Condition interaction, $F_{2,36} = 7.9$, $p < 0.005$, was due to more accurate responding under placebo than alcohol on RI trials, $F_{1,18} = 12.6$, $p < 0.005$. Reaction times (RTs) indicated that the condition difficulty increased from the CO to SI, $F_{1,18} = 114.6$, $p < 0.0001$, and from the SI to RI condition, $F_{1,18} = 64.0$, $p < 0.0001$, Fig 1. The Beverage x Condition interaction, $F_{2,36} = 4.2$, $p < 0.05$, reflected slower responses under alcohol than placebo on RI trials, $F_{1,18} = 3.3$, $p < 0.1$.

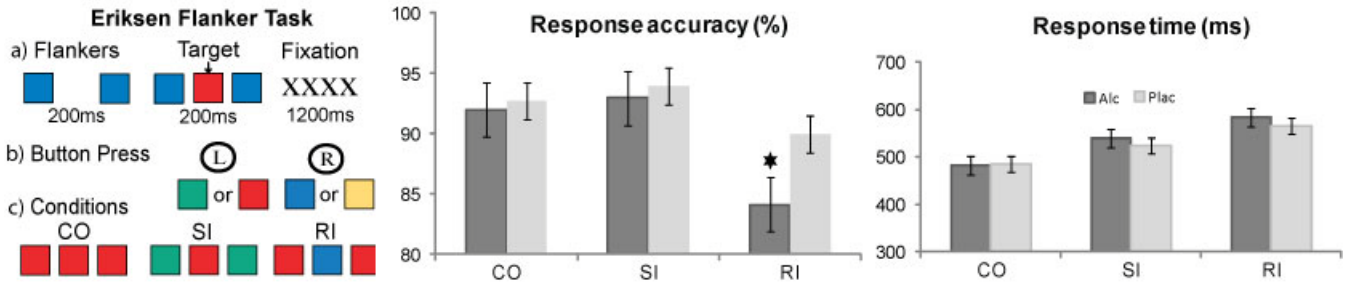

Fig. 1. left panel illustrates the task. a) Two flanker squares are presented for 200 ms. Target square is presented in the central location for 200 ms, followed by fixation for 1200 ms. b) Participants respond to the color of the target square by pressing left button to green *or* red and right button to blue *or* yellow. c) Examples of the Congruous (CO), Stimulus-level incongruous (SI), and Response-incongruous (RI) trials. Middle and right panels show response accuracy and RTs.

Stimulus-level incompatibility increased task difficulty but that was offset by slower RTs. In contrast, response-mapping incompatibility was not mitigated by slower RTs as participants made the most errors on such trials. Furthermore, alcohol selectively affected performance in this condition, indicating deficits on neural systems supporting response preparation and execution. No gender effects were observed on any measure.

Even though all the participants reported drinking in moderately low doses, those with higher drinking levels had slower RTs overall, $r = 0.45$, $p < 0.05$. Self-reported impulsivity was related to response accuracy. Scores on Thrill and Adventure Seeking (TAS) sub-scale of the Sensation Seeking Scale [20] were negatively correlated with accuracy under both alcohol ($r = -0.62$, $p < 0.01$), and placebo conditions ($r = -0.52$, $p < 0.05$), suggesting a dispositional tendency to make errors.

B. aMEG estimates

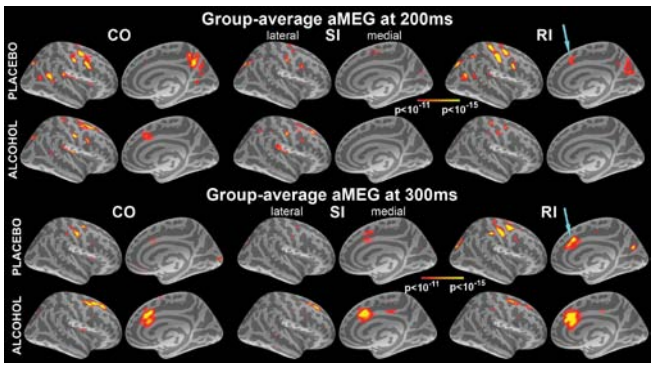

Fig. 2. Group average dynamic statistical parametric maps of estimated responses to all three trial types at 200 ms and 300 ms after stimulus onset under both placebo and alcohol conditions.

Stimulus-locked averages (Figs 2 and 4a) indicate that the AC is sensitive to conflict with strongest response to RI starting at 200ms after target onset under placebo, suggesting its importance in stimulus evaluation and top-down regulation. Even though the activity was stronger under alcohol at this stage overall, there was more conflict-related differentiation under placebo. Under placebo, RI selectively activated the AC after ~400ms, perhaps embodying AC contributions to executive regulation under the response-conflict condition. AC activation was also present under alcohol but did not differentiate strongly between conditions. Overall, the AC and motor/premotor cortex (MC) were the main foci of estimated activity.

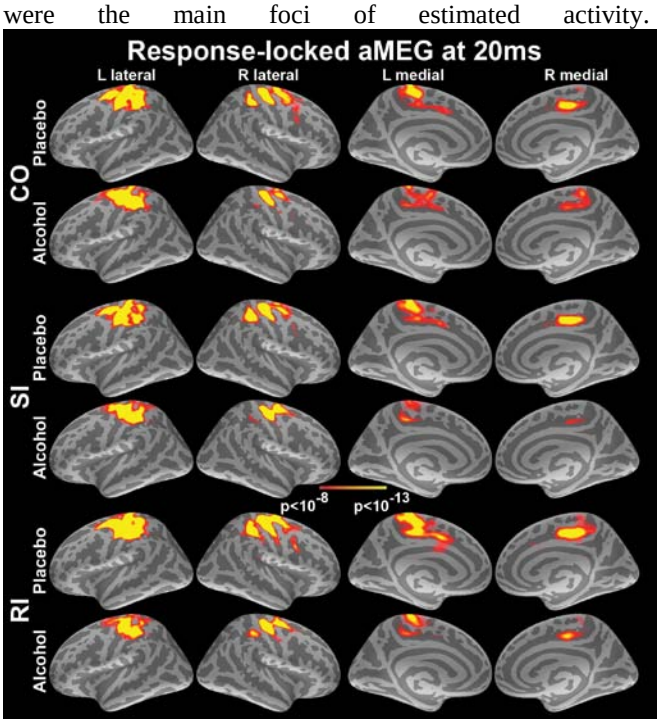

Fig 3 Group average aMEG time-locked to button press responses

In order to explore response preparation and execution processing stages, response-locked aMEG estimates are presented in Fig 3. Together with the timecourses extracted from the MC and AC (Figs 4b,c), they indicate stronger activity under placebo overall. Conflict-related differentia-

tion is expressed under placebo only, whereby the executive involvement of both the AC and MC are dependent on the level of incongruity between flankers and targets. Moreover, the preparatory increase in MC activity to SI and RI at ~80 ms before the response is visible only under placebo (Fig 4b), indicating optimized response strategy.

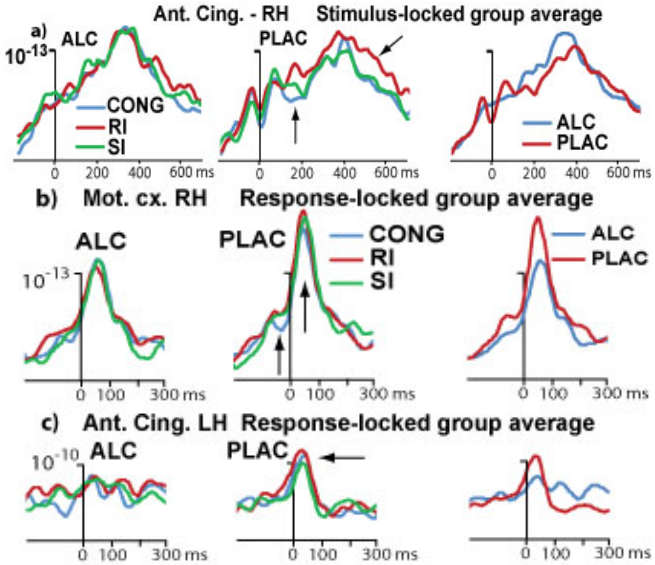

Fig. 4. Group average timecourses of the estimated dipole strengths in the AC and MC regions locked to stimulus onset (a) and button-press response (b,c).

IV. CONCLUSIONS

Moderately low intoxication affected executive capacity, particularly in the response-level incompatibility condition, wherein a primed response needed to be inhibited in favor of the opposite motor mapping. Whereas slower RTs successfully offset increased difficulty on SI trials, response-level incompatibility on RI trials resulted in significant increase in errors, particularly when intoxicated. Under placebo, the AC was sensitive to the level of conflict both during stimulus evaluation (~200ms) and response preparation (~400ms) processing stages, whereas alcohol blunted that conflict-induced differentiation. Moreover, increased activity during conflict under placebo during response preparation and execution in the AC and MC indicates a contribution to optimized response strategy. In contrast, alcohol intoxication impairs the regulative (AC) and motor executive circuitry, resulting in behavioral deficits under conditions of response conflict.

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