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Alcohol-induced suppression of BOLD activity during goal-directed visuomotor performance

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The neurophysiological influence of alcohol produces deficits of many cognitive functions, including executive and motor control processes. This study examined the acute effects of alcohol in the context of goal-directed visuomotor performance during functional magnetic resonance imaging (fMRI). Subjects consumed alcohol-laced gelatin during one scan session and non-alcoholic placebo gelatin in another. During each session, subjects performed a visuomotor target capture where they received continuous or terminal positional feedback information. Blood–oxygen level-dependent (BOLD) activity in the cerebellum was suppressed in the presence of alcohol, consistent with the known ethanol sensitivity of the cerebellum. A fronto-parietal network was identified as most affected by alcohol consumption, with differential patterns of BOLD contingent on visual feedback. Results indicate that alcohol selectively suppresses cognitive activity in frontal and posterior parietal brain regions that, in conjunction with cerebellar nuclei, are believed to contribute to the formation of internal cognitive models of motor representation and action.

Introduction

The neurological effects on the motor system characteristic of acute alcohol intoxication in humans are well known—outwardly impaired coordination, resulting in slower, less accurate, and more erratic movements than normal (Solomon and Malloy, 1992). Examinations of the effects of alcohol consumption also implicate a role in higher level cognitive deficits including adverse effects on cognitive control (Curtin and Fairchild, 2003), memory (Kirchner and Sayette, 2003), emotion (Hansenne et al., 2003), response inhibition (Vogel-Sprott et al., 2001), as well as fine motor performance (Zhu et al., 2004). Altered EEG neurophysiological signals in frontal and posterior cortices have been reported following acute alcohol ingestion (Cohen et al., 1993), appearing to alter particular alpha wave signal components (Ehlers et al., 1989), with effects occurring within 35 min after ingestion (Tran et al., 2004). Alcohol-induced reductions in blood oxygenation level-dependent (BOLD)-related signal in primary visual cortex during photic stimulation have also been observed that may have secondary effects on perceptual processes (Calhoun et al., 2004). Automobile driving simulation studies suggest that, in addition to blood alcohol concentration (BAC), measurements of cognitive deficits might be also be used in legally defining intoxication (Brookhuis et al., 2003). However, little is understood about alcohol's influence on the specific cognitive networks involved in the planning, monitoring, updating, integration, and subsequent control of motor output in cognitively demanding, goal-oriented, tasks. These particular systems may be adversely influenced even at concentrations of blood alcohol below the lowest levels considered as legally intoxicated in the U.S. (National Highway Transportation Safety Administration, 2000).

During normal, visually guided, goal-directed movements such as pursuit tracking, a visual representation of a target location must be converted into coordinates appropriate for movement execution (Tong and Flanagan, 2003). Recent studies into the role of movement magnitude (Desmurget et al., 2003), gain (Krakauer et al., 2000), timing (Ivry and Richardson, 2002), and visual feedback (Desmurget et al., 2001) have determined the existence of specific neural subcircuits involved in movement speed, accuracy, and performance tuning. Such studies provide evidence for the notion that the brain constructs and stores internal models of motor control for goal-directed action (Wolpert et al., 1998). Inverse or "forward" models of movement generate sensory or motor consequences for motor actions. These are believed to exist in and be carried out by the cerebellum (Kawato, 1999), which has been supported in part by recent neuroimaging evidence (Miall et al., 2000). These internal representations are essential for predicting the outcomes of movement and making needed online adjustments to maintain movement accuracy (Desmurget and Grafton, 2000).

Visual feedback and its absence, in particular, play central roles in movement monitoring and error detection (Desmurget et al., 2001). Initial learning and the subsequent tuning of forward models require the moment-to-moment assessment and integration of

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proprioceptive components and visual inputs describing performance error (Clower and Boussaoud, 2000). The current state of the system is compared against the desired "goal" and a suitable corrective update to the movement computed, requiring the coordination of a distributed network of activity involving cerebellum, basal ganglia, parietal, as well as frontal cortices. Limited visual feedback, e.g., only at the terminal end of movement trajectory, reduces overall performance speed and delays required corrective actions.

Among its range of cognitive effects, alcohol may inhibit activity in the brain areas most needed for such critical motor transformations to occur. A disruption in the network of cortical and cerebellar areas responsible for the efficient execution of movement programs, putatively contributing to the generally poor reaction times observed in studies of motor response, has been observed in alcohol-dependent subjects (Parks et al., 2003), compatible with motor inefficiency and compensatory alterations of cortical–cerebellar circuitry. This would predict altered physiological response in cerebellar, as well as cortical, regions when subjects have alcohol onboard. However, alcohol-dependent effects in cortical areas would be expected in the context of how visuomotor feedback is processed and integrated into internal models—in particular, when visual information about task performance is restricted or absent. The interaction of cortical and cerebellar systems is critical for successful motor performance monitoring and the integration of information during learning. An altered ability to utilize feedback based on task performance at the cortical level could, along with cerebellar deficits, contribute to the poorer motor performance observed in intoxicated individuals and lead to longer term effects in chronic alcohol use. Apart from its overall depression of CNS activity, alcohol may specifically interfere with motor-cognitive processes responsible for the proper integration of visual feedback, proprioceptive, and top-down cognitive mechanisms needed to inform and guide subsequent movement (Ingram et al., 2000).

To investigate the role of acute alcohol consumption on visuomotor function, we used functional magnetic resonance imaging (fMRI) in two separate scanning sessions to examine BOLD signal changes as a function of continuous or terminal visual feedback during the presence or absence of alcohol levels in the body. We expected that alterations in the degree of visual feedback would alter the pattern of BOLD activity; that subjects would show reduced activity in the presence of alcohol compared to placebo; and that there would be significant interaction effects of feedback-by-treatment in areas of the brain known for their contribution to internal models of motor control.

Methods

Subjects

Study participants were $N = 8$ (4 male, 4 female) healthy, right-handed individuals from the Dartmouth College undergraduate and graduate student community, between 21 and 25 years of age (males: 22.75 ± 0.5 years; females: 22.75 ± 2.2 years), and with weights limited to being between 120 to 180 lbs. (males: 150.75 ± 26.96; females: 156.75 ± 17.69). The mean ± SD years of education of the sample was 16.75 ± 1.49 years across both groups. Subjects were chosen from a pool of volunteers who were screened via questionnaire for abnormal alcohol intake and/or history of alcohol abuse or addiction. Volunteers having extremely high or extremely low alcohol tolerances were excluded from participating as potentially confounding study results. Subject handedness was measured and confirmed to be strongly right handed in all subjects according to the Edinburgh Handedness Inventory (Oldfield, 1971). No extraordinary level of motor skill was required to participate in the experiment other than being comfortable using the dial stimulus input device (see below). The study was approved by the Dartmouth Committee for the Protection of Human Subjects (Protocol #16311). Potential subjects received substantial information regarding the purpose of this study and its procedures prior to being admitted. The applicants who were admitted as subjects were briefed on the purpose of the investigation, asked to provide informed consent, and have their weights taken prior to their scheduled participation. Subjects were also asked to refrain from eating for 4 h before their scheduled participation. Female subjects were tested for pregnancy immediately prior to each scanning session. Once the test was confirmed negative for pregnancy, female subjects were allowed to continue their participation.

fMRI study experimental design

Each subject performed a target capture task while lying in the scanner during functional imaging data collection. The subjects controlled a cursor using a quadrature-encoded, fiber optic, fMRI-compatible dial (Fig. 1A) while laying in the MRI scanner bore. The dial received 5V@1A power via a shielded coaxial cable producing no adverse effects on MR image quality. A single 2.54 cm Mylar quadrature-encoded fiber optic encoder (US Digital Corp.) was used to measure dial position, and this information was transmitted using LED transducers (Agilent Technologies) via fiber optic cable to a receiver box located in the scanner control room. Light impulses were converted to digital signals using a National Instruments DAQPad 6070E multi-purpose data acquisition system and these signals used to map cursor position on a dedicated stimulus presentation/response-recording PC. The dial was positioned on a board secured to the thighs of the subject where subjects grasped the dial using their right (dominant) hand. The visuomotor task consisted of fifteen possible circular targets spread evenly along an arc of 108° (Fig. 1B), displayed to the subject in the scanner bore using a back-projection system (Epson Powerlite 7000). For each event of the task, an outline of a circle would appear on the screen, and the subject would place a cursor within the circle by rotating the screwdriver-like input dial device. When subjects "captured" the target circle, i.e., placed the cursor within the circle's boundaries, the area within the circle would immediately illuminate red. After the cursor remained in the circle for 5 s, another target circle would appear in a different location on the screen, and the subject would rotate the dial in the direction of the target once again, capture it, and so forth. A square green box would appear in the position of the center target in between task trials. The subject would place the cursor within the box for a 30-s rest period, after which the next set of target capture trials would begin (Fig. 2).

Performance of the task consisted of rotating the cursor between the pairs of 15-possible targets as quickly but as accurately as possible. Five periods of target capture were separated by 30 s of rest. Two task conditions were presented to each subject on separate task trials: a "concurrent-feedback" condition (CF), in which the cursor is visible on the screen throughout the duration of