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Effects of Alcohol on Performance on a Distraction Task During Simulated Driving

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Abstract

Background—Prior studies report that accidents involving intoxicated drivers are more likely to occur during performance of secondary tasks. We studied this phenomenon, using a dual-task paradigm, involving performance of a visual oddball (VO) task while driving in an alcohol challenge paradigm. Previous functional MRI (fMRI) studies of the VO task have shown activation in the anterior cingulate, hippocampus, and prefrontal cortex. Thus, we predicted dose-dependent decreases in activation of these areas during VO performance.

Methods—Forty healthy social drinkers were administered 3 different doses of alcohol, individually tailored to their gender and weight. Participants performed a VO task while operating a virtual reality driving simulator in a 3T fMRI scanner.

Results—Analysis showed a dose-dependent linear decrease in Blood Oxygen Level Dependent activation during task performance, primarily in hippocampus, anterior cingulate, and dorsolateral prefrontal areas, with the least activation occurring during the high dose. Behavioral analysis showed a dose-dependent linear increase in reaction time, with no effects associated with either correct hits or false alarms. In all dose conditions, driving speed decreased significantly after a VO stimulus. However, at the high dose this decrease was significantly less. Passenger-side line crossings significantly increased at the high dose.

Conclusions—These results suggest that driving impairment during secondary task performance may be associated with alcohol-related effects on the above brain regions, which are involved with attentional processing/decision-making. Drivers with high blood alcohol concentrations may be less able to orient or detect novel or sudden stimuli during driving.

Keywords

Functional Magnetic Resonance Imaging; Alcohol; Visual Oddball; Driving While Intoxicated; Driving

A comprehensive analysis of traffic accidents involving alcohol showed that accidents were more likely to occur when drivers with a high blood alcohol concentration (BAC) were performing a secondary task shortly before the accident; alcohol exacerbated the negative effects of such distraction (Brewer and Sandow, 1980). However, the brain mechanisms underlying this phenomenon have not been thoroughly studied. The use of virtual reality

driving paired with a secondary attention task during a functional magnetic resonance imaging (fMRI) scan, as was used in this study, may help elucidate the neural mechanisms behind this observation.

Visual oddball (VO) paradigms are often used to measure attention. The “classic” format of a VO task consists of stimuli presented visually to a subject at a constant interval. The stimuli are either standard stimuli (occurring frequently) or target stimuli (occurring infrequently); subjects respond when the target stimuli appear (Ardekani et al., 2002). The VO task used in this study is similar to the classic format, except that it was performed while subjects drove in a naturalistic custom built simulator.

Previous fMRI studies using VO tasks have identified many regions of brain activation while attending to target stimuli. Most consistently, studies have reported activations in the bilateral supramarginal gyri (Ardekani et al., 2002; Brazdil et al., 2007; Clark et al., 2000; Kiehl and Liddle, 2001; Linden et al., 1999; McCarthy et al., 1997; Menon et al., 1997; Rangaswamy et al., 2004; Yoshiura et al., 1999) and anterior cingulate cortex (Ardekani et al., 2002; Brazdil et al., 2007; Clark et al., 2000; Crottaz-Herbette and Menon, 2006; Fichtenholtz et al., 2004; Kiehl and Liddle, 2001; Linden et al., 1999; McCarthy et al., 1997). Activations are also reported in the thalamus (Ardekani et al., 2002; Benar et al., 2007; Clark et al., 2000; Linden et al., 1999; Menon et al., 1997; Rangaswamy et al., 2004; Yoshiura et al., 1999), insula (Ardekani et al., 2002; Benar et al., 2007; Rangaswamy et al., 2004), and inconsistently among, cerebellum (Brazdil et al., 2007; Clark et al., 2000), prefrontal cortex (Brazdil et al., 2007; Corbetta et al., 1991), and hippocampus (Crottaz-Herbette et al., 2005). Although there is no clear consensus in previous fMRI studies as to which brain areas are activated by VO tasks, certain areas were noted in most studies. These areas include the bilateral supramarginal gyri and the anterior cingulate cortex, 2 regions that are commonly linked to attention, with the supramarginal gyrus more specifically linked to spatial orientation (Lacquaniti et al., 1997). Although this study did not use a “classic” VO paradigm, the above mentioned previous research provided the basis for brain areas we looked at in our analysis.

To our knowledge, no prior study has examined the effects of alcohol intoxication on functional and behavioral performance of the VO task. However, a few studies have measured alcohol effects on the P300 component (Colrain et al., 1993; Zuzewicz, 1981; Rohrbaugh et al., 1987; Wester et al., 2007), the endogenous component of evoked potential previously shown to be linked with the cerebral information processing neural mechanisms (Pritchard, 1981) of the visual evoked potential. Electrophysiologically, these studies showed increased P300 latency with increased alcohol dosage, while behaviorally showing reaction time (RT) increases with increased alcohol dosage but no significant change in errors (Colrain et al., 1993; Rohrbaugh et al., 1987). In addition, a recent study (Wester et al., 2008) examined the effects of a secondary task during simulated driving and found no differences in errors, but increases in RT. Also, Fillmore and Selst Van (2002) found increased RT, with increased alcohol dose, in a dual-task performance under alcohol challenge.

In addition, there have been studies on effects of acute alcohol intoxication on divided attention (Schreckenberger et al., 2004; Schulte et al., 2001). Similar to the studies on VO distraction tasks, Schulte et al. (2001) showed slower RTs with increased intoxication. Schreckenberger et al. (2004) also showed activations in bilateral striatum and frontal cortex, with deactivations in the occipital cortex.

The purpose of this study was to examine the neural correlates of acute alcohol effects on driving performance under divided attention conditions. Functionally, based on previous findings in the above-mentioned P300 studies, we hypothesized that there would be dose-related activation decreases in all variables measured (oddball vs. standard, oddballs only, and

standards only), in brain areas previously shown to activate during VO tasks. We particularly expect to find this pattern in regions that are involved with attentional processes such as the anterior cingulate cortex, which is specifically involved in error detection (Bush et al., 2000). Also, we expected to find the same activation patterns in additional brain regions not identified in the “classic” VO tasks, such as those found by Schreckenberger et al. (2004) as our paradigm involved additional complex processing skills (e.g., driving, divided attention).

Behaviorally, based on the previous literature, we predicted increased RT during VO performance, following the same linear trend as the functional data. Because the VO task was not the primary task in our paradigm, we predicted increasing errors with increasing alcohol dose although previous literature (Colrain et al., 1993; Rohrbaugh et al., 1987) reports the contrary outcome. In addition, we predicted an increase in driving errors shortly after target stimulus presentation as compared to standard stimuli.

SUBJECTS AND METHODS

Subjects

Forty male ($n = 20$) and female healthy, right-handed, subjects participated in the study; mean age was 24.75 ± 4.7 years. The subjects' estimated short form IQ was 114 ± 13 (as measured by Wechsler Adult Intelligence Scale III: Information and Block Design subtests; Harcourt Assessment, Inc.). Potential participants were excluded for a positive urine screen for recent drug use and for pregnancy in females. They were also given an extensive psychological interview (SCID-I/NP; Biometrics Research) to screen out any participant with DSM IV-TR Axis I psychological disorders (First et al., 2002). Failure to pass any of the above tests resulted in exclusion from the study. All subjects had good visual acuity without correction, a valid driver's license, at least 3 years of recent highway-driving experience, drove several times per week and had good driving histories (assessed by self-report). Subjects were light-to-moderate drinkers who reported using alcohol 3 days (± 1 day) and drinking an average of 4 drinks (± 2 drinks) per occasion. Participants had average scores of 7 ± 3 on the Alcohol Use Disorders Identification Test (AUDIT; (Babor et al., 2001).

Procedure

Subjects passing the screening process were invited to participate in the study. They were asked to not consume alcohol for 24 hours prior to each study visit and requested to eat only a light meal, avoiding fatty foods, before arrival. Upon arrival at the Olin Center, participants were given a breathalyzer (Intoximeters, Inc) test to measure baseline alcohol levels (actual = 0.00% g/ml $\pm$ 0.00% g/ml) and a urine screen to test for drugs and pregnancy. Depending on the participant's schedule, they either had 1 study session (placebo, moderate, or high) or 2 study sessions (placebo first, then either moderate or high). All subjects gave written informed consent prior to participation in the study, which was approved by the Hartford Hospital Institutional Review Board.

Subjects were given an out-of-scanner practice session (~10 minutes) on the same driving simulation program that they would be performing in the scanner, which is sufficient to attain proficiency on the paradigm. They were then administered an individualized beverage designed to target 1 of 3 BAC levels: placebo (target = 0.00% g/ml; actual = 0.00% g/ml $\pm$ 0.00% g/ml), moderate (target = 0.05% g/ml; actual = 0.04% g/ml $\pm$ 0.01% g/ml), and high (target = 0.10% g/ml; actual = 0.09% g/ml $\pm$ 0.01% g/ml). All drinks contained 350 ml of liquid: a level of vodka (40% alcohol) calculated to attain the target BAC, based on the subjects' gender and weight using the algorithm published in (Kapur, 1989). The remainder of the 350 ml beverage consisted of either cranberry juice or orange juice, depending on the subject preference. To help keep subjects blind to the dose of alcohol they were receiving, the drinks were always

served in identical plastic beverage cups with several vodka-soaked gauze sponges secured around the cup with rubber bands. Each beverage also had a small amount of vodka (~10 ml) floating on the top of the drink. Subjects were given 10 minutes to ingest the drink, and were instructed to pace themselves so they would finish in the last 2 minutes of their time limit. After 10 minutes, their BAC was measured using a breathalyzer (Intoximeters, Inc) and subjective ratings of intoxication as well as their ability to perform everyday activities normally, including driving, (on a scale of 1 to 10) were elicited. The subject was then placed in the MRI scanner where they performed the driving task. Each run of the task lasted 10 minutes, with 3 runs in each dose, for a total of 30 minutes of scanning time for each dose.

Equipment Design & Setup

Participants were scanned using a 3 Tesla MRI scanner (Allegra; Siemens, Erlangen, Germany) located at the Olin Neuropsychiatry Research Center at the Institute of Living in Hartford, CT. MRI-compatible driving hardware, including a steering wheel, gas pedal, and brake pedal, were used in the scanner with the driving software (See Fig. 1). The driving software and equipment has been validated and described in detail previously (Carvalho et al., 2006).

Data Acquisition

As a part of the driving paradigm, a light on the simulated dashboard (See Fig. 2) blinked at a random inter-stimulus interval (ISI). The formula used to calculate the ISI was: $ISI = 2 + (\text{random number between 10 and 60}) * 0.63$. The subject was instructed to pay attention to the light. If the light blinked green (standard stimuli), they were told to do nothing, but when the light blinked red (target stimuli), they were instructed to push a button behind the steering wheel as soon as possible. More specifically, each oddball/standard stimuli was treated as an individual event embedded within the “driving” phase of the experiment. Behaviorally, correct responses, errors, and response time were recorded in real time.

Functional imaging data were acquired using an echoplanar sequence using the following imaging parameters; repeat time (TR) = 1,500 ms, echo time (TE) = 27 ms, field of view (FOV) = 22 cm, flip angle = 70°, acquisition matrix = 64 × 64, voxel size = 3.44 × 3.44, slice thickness = 5 mm, number of slices = 29, ascending acquisition. The scanner was equipped with 40 mT/m gradients and a standard quadrature head coil. To achieve longitudinal equilibrium, 6 dummy scans were performed at the beginning and discarded prior to analysis. Scanning was automatically triggered by the paradigm.

Head movement during scanning was minimized using extra padded cushions. Also, the scanner was a “head only” utility, which served to constrict overall motion compared with a whole body scanner. Additional movement correction was performed using the INRIAAlign toolbox. This software program reduces paradigm correlation bias and provides a more robust realignment for functional data (<http://www-sop.inria.fr/epidaure/Collaborations/IRMf/INRIAAlign.html>).

Data Analysis

Behavioral Analysis—Behavioral analysis was performed in SPSS v15.0

(<http://www.spss.com/spss/>). A repeated measures ANOVA was used to compare performance across all doses. A within-subject design was used to account for individual variances in driving habits. The variables measured for oddball performance included: response time, correct hits, misses, and false alarms. Driving errors were measured both before (the period between the oddball and the previous standard stimulus) and after (the period between the oddball and the next standard stimulus) an oddball. The driving variables assessed were: white line crossings, yellow line crossings, opposite white line crossings, speed, gas/brake pedal pressing, and change in steering.

Regions of Interest Analysis—An regions of interest (ROI) analysis was performed using masks created in WFU Pickatlas (version 2.4; <http://www.fmri.wfubmc.edu/cms/software>) for brain regions noted in previous VO fMRI studies. The small volume correction (SVC) function in SPM was used to overlay the masks. This analysis included masks for anterior cingulate cortex, cerebellum, hippocampus, parahippocampus, insula, dorsolateral prefrontal cortex, supramarginal gyri, and thalamus (See Table 1). This analysis was performed comparing all 3 conditions, as well as comparing only sober and high conditions to validate our method. Similar to the behavioral analysis, a within-subject design was used to control for individual variance.

Whole Brain Analysis—As this study encompassed more tasks than VO alone, including driving (Meda et al., in press), a whole-brain analysis was used to determine which neural networks were activated globally during this dual-performance task.

Image analysis was carried out using SPM2 (<http://www.fil.ion.ucl.ac.uk/>). At the subject level, for each dosage, contrasts were generated to examine the following brain activation differences/responses: (i) oddball versus standards, (ii) oddball versus implicit baseline (during driving and without any target or standard stimuli), (iii) standards versus implicit baseline. For the oddball versus standards comparisons and the oddballs versus implicit baseline comparisons, there were only 27 oddball presentations to analyze. Similar to the behavioral and ROI analysis, a within-subject design was used to control for individual variance. To validate our study we performed a one-sample *t*-test for the oddballs versus standards during the sober condition alone. Furthermore, a standard random effects repeated measure analysis was performed to examine dosage-related differences in each of the above contrasts. For reporting purposes, significant regions were converted from MNI to Talairach space using Matthew Brett's nonlinear transformation utilities (<http://imaging.mrc-cbu.cam.ac.uk/imaging/MniTalairach>).

Correlation of Behavioral and Functional Data

To further validate our results, functional response values (sober vs. high condition) for the oddball versus standards contrast were extracted at the peak difference voxel within previously mentioned ROI's used for SVC. A bi-variate correlation analysis was then performed between the functional values and real time behavioral measures (sober—high) acquired during the driving phase of the experiment in SPSS v15.0 (<http://www.spss.com/spss/>).

RESULTS

Behavioral

Oddball Performance—Repeated measures ANOVA showed a dose-dependent linear increase (See Fig. 3) in RT ($p = 0.05$; $F = 3.15$), with no effects on either correct hits or false alarms.

Driving Performance—In all conditions, driving speed decreased (compared to speed before a VO stimulus) after a VO stimulus ($p = 0.03$; $F = 3.63$), however at the high dose this decrease was significantly less (significant at placebo and moderate doses at $p = 0.001$ and insignificantly at high dose at $p = 0.074$; See Fig. 4). Interestingly, speed was slightly slower at the moderate condition. Passenger-side line crossings significantly increased ($p = 0.01$; $F = 4.43$) with dosage after oddball presentation. However, the least amount of errors occurred at the moderate dose ($M_{\text{placebo}} = 10.33 \pm 5.37$; $M_{\text{moderate}} = 7.86 \pm 5.34$; $M_{\text{high}} = 10.97 \pm 5.76$). With the exception of speed and white line errors, there was no difference, regardless of condition, in driving errors before the oddball occurrence versus those after the oddball occurrence.

Functional Imaging

Small Volume Correction—A SVC analysis was performed on the oddballs versus standard comparison by initially thresholding the whole brain results to $p < 0.05$ uncorrected. Upon masking, significant activations ($p < 0.05$ FDR corrected; See Table 2) were found in the following regions: left and right anterior cingulate, right cerebellum, left and right hippocampus, right parahippocampus, right insula, and left prefrontal cortex. Non-significant trends (See Table 2) were noted in the following regions: left cerebellum, left parahippocampus, left insula, right prefrontal cortex, left supramarginal cortex, and left thalamus. Activation in right supramarginal cortex and right thalamus did not survive SVC.

Sober Only

Oddball Versus Standard: A GLM analysis of the oddball v standards contrast for the sober dose alone showed activation in all the expected regions ($p < 0.05$, FDR corrected; See Table 3), including anterior cingulate, hippocampus and insula.

Dose-Related Responses

Oddball Versus Standard: Results were initially thresholded at $p < 0.05$ FDR corrected for all 3 comparisons, however to show less robust activations, the threshold was lowered to $p < 0.001$ uncorrected when nothing significant was found at $p < 0.05$ FDR corrected. GLM analysis showed a dose-dependent difference in the insula (Brodmann Area [BA] 13) between the 3 conditions (sober, moderate, high). The least activation occurred at the high dose, while the highest activation occurred at the moderate dose. However, when we removed the moderate dose from the contrast and performed a 2-sample repeated measures t -test, we found a more robust effect (See Fig. 5 and Table 4). Activations were noted bilaterally in the hippocampus (parahippocampal gyrus; BA 19) and anterior cingulate (BA 24). There were also unilateral differences for sober > high contrast in frontal lobe activation: right inferior frontal gyrus (BA 45), left medial frontal gyrus (BA 10) and left superior frontal gyrus (BA 10). These activations are noted as a linear trend, with the highest activation in the sober condition and the least activation in the high condition (see Fig. 6). This is still observed when the moderate dose is included in the analysis, however it is not significant. The frontal regions were activated in the placebo and moderate conditions, but had significantly less activation in the high condition.

Dose-Related Responses

Oddballs Only: There were no differences in brain activation for the oddball condition (at $p < 0.05$, FDR corrected; this threshold is notably low and was only used for exploratory purposes). Because removal of the moderate dose showed a more robust effect for the oddballs versus standards condition, we also removed the moderate dose from the oddballs only analysis. This did not change the results. However, when we lowered the threshold (to $p < 0.01$ uncorrected), we found differences in dorsal anterior cingulate (BA 32), cingulate gyrus (BA 24), and insula (BA 13). These regions, similar to the frontal regions discussed earlier, had similar activation patterns in the sober and moderate conditions, but less activation in the high condition.

Dose-Related Responses

Standards Only: The results of analysis of the standards condition revealed no significant differences in brain activation (at $p < 0.05$ FDR corrected). Similar to the oddballs only condition, this did not change when we removed the moderate dose from the analysis. At a lower threshold ($p < 0.01$ uncorrected), the dorsal anterior cingulate (BA 32) was similarly activated in the sober and moderate conditions, but had less activation at the high dose.

Functional and Behavioral

The results of the correlation analysis between functional results and behavioral results revealed a correlation between Hippocampus ($r = 0.33$; $p = 0.04$), ACC ($r = 0.41$; $p = 0.01$), cerebellum ($r = 0.52$; $p = 0.001$), and insula ($r = 0.33$; $p = 0.04$) and correct hits.

DISCUSSION

This study was the first to examine fMRI brain activation during a VO task with varying levels of alcohol intoxication. It was also the first to combine a VO task with a simulated driving paradigm, providing novel information regarding specific real-life applications of the VO task. Our findings replicate, in part similar, earlier studies on sober performance of the VO task. For example, we found activation in anterior cingulate cortex, also noted in prior papers (Ardekani et al., 2002; Brazdil et al., 2007; Clark et al., 2000). Interestingly, we only found unilateral (left) supramarginal gyrus activation, although activation in supramarginal gyrus is usually bilateral (Ardekani et al., 2002). However, we also report hippocampal activation, which was less commonly detected in studies on sober VO performance, but has been shown to be related to P300 (Ardekani et al., 2002). Therefore findings support earlier studies (Colrain et al., 1993; Wester et al., 2008) that have found decreased P300 response with increased alcohol dosage, particularly when a secondary task is involved (Wester et al., 2008).

Behavioral data on the VO task replicated results from previous studies (Colrain et al., 1993; Wester et al., 2008) that examined alcohol effects on VO performance—slower reaction time, with no increase in VO errors. However, we did find increases in driving errors (e.g., increased passenger-side line crossings) following oddball occurrences.

As expected, the specified brain areas had less activation with increased alcohol intoxication (with the exception of the insula, which had increased activation at the moderate dose, although not significantly, but less activation at the high dose). This functional trend may help explain the neural mechanisms associated with the behavioral results. The anterior cingulate and hippocampus, which are commonly linked to target/hazard detection in previous fMRI studies (Ardekani et al., 2002; Clark et al., 2000; Crottaz-Herbette et al., 2005), were positively correlated with correct hits. In addition, these 2 areas exhibited less activation in association with increased alcohol intoxication. This suggests that alcohol intoxication may decrease one's ability to detect targets. In the realm of drinking and driving, a target could represent a salient driving-related stimulus, for example an obstacle in the road that an intoxicated person may have reduced ability to orient to. The findings that correct hits are also positively correlated with the cerebellum, shown to be involved in motor coordination (Clark et al., 2000), and the insula, shown to be involved in selective attention (Ardekani et al., 2002), both of which are decreased in activation during the high dose, further substantiates this claim.

More specifically, the hippocampus has been shown to be involved with visuospatial memory (Burgess et al., 2002). In our task, hippocampal activation could be involved with the ability to remember the vehicle's location on the road before being distracted by the target. The decrease in activation of this region with increased alcohol dose could explain why more driving errors were noted following a target stimulus.

Other brain regions significantly more activated during target presentation, with less activation at the high dose, included multiple frontal lobe regions, specifically the right inferior frontal, right medial frontal, and left superior frontal gyri. These areas are involved in planning and decision-making. Lower activation in these regions may be associated with reduced ability to decide between responding to a target stimulus and focusing on driving-related task information.

A limitation to our study was the number of target stimuli available to analyze. The ratio of targets to standards (1:9) was consistent with most previous studies; however, because of the ISI and length of the tasks, there were only 27 target stimuli to analyze for each dose. Also, it is possible that the distraction task was not difficult enough to induce large effects on driving. Perhaps a more complex or time-consuming task would have produced greater results. In addition, while the use of a within-subject design helped to control for individual variance in driving habits and brain activation, the fact that some participants performed multiple sessions on the same day could have affected the results.

Although we were able to show both decreased driving performance and increased response time for target response at both the moderate and high alcohol dose, we were only able to demonstrate significantly reduced brain activation at the higher dose. However, the insula showed increased activation at the moderate dose. This finding, attributed to compensation for deficits related to intoxication, is similar to that of our previous fMRI and alcohol study (Calhoun et al., 2004). The behavioral results, which showed better driving performance in the moderate condition, support our previous studies (Calhoun et al., 2004; Meda et al., in press).

In these previous studies, as well as in this one, our interpretation was that subjects were mildly subjectively impaired, but capable of (over) correcting driving performance. Our results suggest that the ability to perform a secondary task while driving is impaired at intoxication levels above the legal limit (0.09% g/ml), as measured both by decreased driving performance and increased response time to target stimuli. The functional imaging results may help explain why these impairments may be occurring in association with altered activation in brain regions responsible for task performance, including ACC, hippocampus, and frontal regions.

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Fig. 1.
Photo of “head only” scanner with driving simulator equipment.

Fig. 2.

Screen shots of the driving software, with arrow pointing to: 1. standard presentation; 2. no stimulus presentation; 3. oddball presentation.

Fig. 3.

Graph of mean response times after oddball stimulus presentation with standard error bars. There is a dose-dependent linear increase ($p = 0.018$), with the longest response time occurring in the high dose.

Fig. 4.

Graph of mean speed before and after oddball occurrence with standard error bars. Speed did not decrease as much in the high dose as it did in the sober and moderate doses. The main effect of alcohol on speed pre and post oddball was significant ($p = 0.031$).

Fig. 5. Image showing results of repeated measures ANOVA ($p < 0.001$) for oddball versus standard stimuli for only sober versus high contrast in rendered view (right) and section view (left), showing sub-cortical activation ($p < 0.001$ uncorrected) in anterior cingulate and hippocampus.

Fig. 6. Contrast plots showing the dose-dependent linear trend of the noted brain activations (BA 19, BA 24) in the targets versus standard comparison.

Table 1
Regions Used for ROI With Component Processes

Region	Component processes
Anterior cingulate cortex	Target detection; Error detection; Visual stimulus detection ¹
Cerebellum	Motor coordination ²
Hippocampus, Parahippocampus	Working memory ³
Insula	Selective attention ¹
Dorsolateral prefrontal cortex	Target detection; Working memory ¹
Supramarginal Gyri	Visual stimulus detection ¹
Thalamus	Target detection ¹

¹Ardekani et al., 2002

²Clark et al., 2000;

³Crottaz-Herbette et al., 2005;

Table 2

Results of Small Volume Correction Analysis for Oddball > Standard, Sober versus High

Region	Cluster volume	MNI coordinates	T value	p value (FWE)
L ACC**	327	-9,9,24	3.76	0.007
R ACC**	275	3,27,-9	3.59	0.01
L Cerebellum*	912	-3,-81,-18	3.36	0.09
R Cerebellum**	1014	3,-81,-18	3.86	0.02
L Hippocampus**	81	-12,-36,0	2.86	0.05
R Hippocampus**	128	27,-21,-15	3.50	0.01
L Parahippocampus*	41	-24,3,-18	3.00	0.07
R Parahippocampus**	122	27,-21,-15	3.50	0.02
L Insula*	467	-39,-6,15	2.81	0.10
R Insula**	469	39,-9,18	3.07	0.05
L Prefrontal**	240	-27, 51,24	3.52	0.04
R Prefrontal*	14	57,27,21	3.37	0.06
L Supramarginal*	20	-60,-45,36	2.63	0.07
L Thalamus*	21	-3,-6,3	2.74	0.06

Areas with cluster volumes <10 were excluded from results.

* Indicates a non-significant trend ($p < 0.05$ FWE corrected).** Indicates significance ($n = 40$; $p < 0.05$ FWE corrected).

Table 3
Results of Sober Only Analysis for Oddball > Standard ($n = 40$; $p < 0.05$ FDR corrected)

Talairach label	Brodmann area	L Vol in cubic centimeters	R Vol in cubic centimeters	Total Vol in cc cubic centimeters	Talairach coordinates max T left (x,y,z)	Talairach coordinates max T right (x,y,z)
Middle frontal gyrus	10, 46	20.5	22.8	43.3	4.2 (-48,30,23)	4.5 (33,61,2)
Superior frontal gyrus	10	11.6	14.8	26.4	4.4 (-21,59,11)	4.3 (27,64,5)
Precuneus	7, 31	9	13.1	22.1	3.4 (-3,-71,34)	3.7 (3,-62,42)
Medial frontal gyrus	9, 10	11	10.8	21.8	3.4 (-15,56,14)	3.6 (0,45,17)
Inferior frontal gyrus	45, 47	11.4	9.6	21	3.9 (-42,24,15)	3.8 (30,8,-18)
Cuneus	30	10.8	9	19.8	4.1 (-3,-99,10)	4.2 (0,-64,3)
Parahippocampal gyrus	30, 34	8.4	9.6	18	3.7 (-27,2,-15)	3.8 (6,-44,2)
Cingulate gyrus	31, 24	6.1	10.6	16.7	3.6 (-3,-30,37)	4.0 (0,-27,40)
Superior temporal gyrus	38, 22	7.6	8.4	16	3.4 (-50,17,-11)	4.3 (30,8,-23)
Middle temporal gyrus	21, 19	7.6	7.9	15.5	3.9 (-62,-49,2)	3.6 (65,-47,0)
Lingual gyrus	18	6.5	8.4	14.9	4.0 (-3,-67,1)	4.3 (0,-79,-9)
Posterior cingulate	29, 30	5.9	8.1	14	4.2 (-3,-52,14)	4.7 (3,-52,14)
Fusiform gyrus	37	5.6	6.1	11.7	3.3 (-42,-54,-23)	3.9 (45,-59,-22)
Inferior parietal lobule	40, 7	5.9	5.1	11	4.1 (-45,-50,55)	3.5 (45,-53,52)
Anterior cingulate	32	5.3	4.4	9.7	3.6 (-3,44,3)	3.3 (0,47,0)
Precentral gyrus	9, 4	2.9	3.4	6.3	3.0 (-33,22,35)	3.1 (42,25,35)
Paracentral lobule	31, 4	2.1	3.4	5.5	3.5 (-3,-30,43)	3.4 (3,-34,68)
Supramarginal gyrus	40	2.3	2.6	4.9	3.5 (-62,-42,33)	3.0 (39,-48,30)
Caudate	Caudate head, caudate body, caudate tail	2.9	2	4.9	3.1 (-3,3,3)	3.0 (39,-29,-4)
Superior parietal lobule	7	2.8	1.8	4.6	4.2 (-42,-56,53)	4.0 (39,-59,53)
Insula	13, 22	1.8	2.4	4.2	3.6 (-39,21,18)	3.1 (33,21,18)
Postcentral gyrus	5, 2	1.3	1.6	2.9	2.6 (-3,-40,68)	3.9 (6,-40,68)
Lentiform nucleus	Putamen	1.3	0.8	2.1	2.6 (-18,11,-8)	2.6 (21,4,22)
Middle occipital gyrus	18	1.4	0.6	2	3.7 (-9,-92,16)	3.5 (6,-95,16)
Inferior temporal gyrus	37	1.1	0.8	1.9	3.2 (-59,-56,-5)	2.7 (59,-24,-16)
Angular gyrus	39	1.3	0.5	1.8	3.1 (-56,-60,33)	2.4 (50,-62,34)
Thalamus	Anterior nucleus, Pulvinar, Medial geniculum body	0.8	0.8	1.6	2.9 (-3,-3,6)	2.8 (0,-5,9)

Talairach label	Brodmann area	L Vol in cubic centimeters	R Vol in cubic centimeters	Total Vol in cc cubic centimeters	Talairach coordinates max T left (x,y,z)	Talairach coordinates max T right (x,y,z)

Table 4
Whole Brain Results of Oddball Versus Standards (Sober vs. High Only) Analysis ($n = 40$; $p < 0.001$, Uncorrected)

Talairach label	Brodmann area	L Vol in cubic centimeters	R Vol in cubic centimeters	Total volume in cubic centimeters	Talairach coords left max T (x,y,z)	Talairach coords right max T (x,y,z)
Hippocampus	Hippocampus	4.8	6.6	11.4	3.7 (-12,10,22)	3.1 (15,23,-4)
Inferior frontal gyrus	45, 46	4	4.9	8.9	3.0 (-36,31,-12)	3.4 (56,27,18)
Insula	13	4.2	4.5	8.7	2.8 (-39,-5,14)	3.1 (39,-8,17)
Anterior cingulate	33	4.3	3.3	7.6	3.4 (-6,10,22)	3.7 (0,26,-9)
Middle frontal gyrus	46	5.8	1.8	7.6	3.5 (-27,51,20)	2.9 (53,30,18)
Cingulate gyrus	31, 24	3.1	2.9	6	3.2 (-18,-34,27)	2.9 (0,16,30)
Superior frontal gyrus	10	4.7	0.9	5.6	3.4 (-18,62,16)	3.0 (9,6,63)
Parahippocampal gyrus	28, 30	2.4	2	4.4	3.0 (-24,2,-15)	3.5 (27,-21,-12)
Medial frontal gyrus	10, 9	4.1	0.3	4.4	3.1 (-9,62,8)	2.6 (0,45,20)
Lingual gyrus	18	1.2	2.4	3.6	3.3 (0,-79,-6)	3.3 (3,-76,-6)
Posterior cingulate	29, 30	1.9	1.5	3.4	3.3 (-3,-49,8)	2.8 (3,-49,8)
Superior temporal gyrus	38, 22	1.5	1.3	2.8	3.3 (-56,-40,8)	3.2 (62,0,6)
Precentral gyrus	6, 43	1.1	1.3	2.4	2.9 (-48,-11,12)	3.1 (62,3,8)
Middle temporal gyrus	22, 21	0.8	0.6	1.4	3.0 (-56,-38,5)	2.6 (62,-44,-3)
Postcentral gyrus	40, 43	0.3	0.8	1.1	2.5 (-56,-28,18)	2.6 (53,-14,15)
Precuneus	7, 31	0.2	0.8	1	2.4 (-3,-65,34)	2.5 (12,-53,39)