10-1-2010

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Published in final edited form as:
Exp Clin Psychopharmacol. 2010 October ; 18(5): 409–417. doi:10.1037/a0021053.

Effects of Alcohol on Tests of Executive Functioning in Men and Women: A Dose Response Examination

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Abstract

Alcohol has been shown to affect performance on tasks associated with executive functioning. However, studies in this area have generally been limited to a single dose or gender or have used small sample sizes. The purpose of this study was to provide a more nuanced and systematic examination of alcohol's effects on commonly used tests of executive functioning at multiple dosages in both men and women. Research volunteers (91 women and 94 men) were randomly assigned to one of four drink conditions (alcohol doses associated with target blood alcohol concentrations of .000%, .050%, .075% and .100%). Participants then completed three tasks comprising two domains of executive functioning: two set shifting tasks, the Trail Making Test and a computerized version of the Wisconsin Card Sorting Task, and a response inhibition task, the GoStop Impulsivity Paradigm. Impaired performance on set shifting tasks was found at the .100% and .075% dosages, but alcohol intoxication did not impair performance on the GoStop. No gender effects emerged. Thus, alcohol negatively affects set shifting at moderately high levels of intoxication in both men and women, likely due to alcohol's interference with prefrontal cortex function. Although it is well-established that alcohol negatively affects response inhibition as measured by auditory stop-signal tasks, alcohol does not appear to exert a negative effect on response inhibition as measured by the GoStop, a visual stop-signal task.

Introduction

Executive functioning (EF) broadly defined refers to higher-order cognitive processing involved in the planning, initiation, and regulation of purposeful behavior (Elliott, 2003; Giancola, 2000). Examples of EF include decision making, complex problem solving, abstract reasoning, effective use of working memory representations, and inhibition or adaptation of behavior based on incoming information. A latent variable analysis of three hypothesized executive functions—set shifting (i.e., shifting between mental sets), working memory updating (i.e., monitoring, revising, and manipulating information in working memory), and response inhibition (i.e., suppression of prepotent responses)—revealed that they are clearly separable but moderately correlated processes, supporting their partial independence and reliance on a common underlying construct (Miyake et al., 2000). In regard to neurological underpinnings, EF has been generally attributed to the frontal lobe and its basal ganglia-thalamic connections, although parts of the prefrontal cortex (e.g., the dorsolateral prefrontal cortex and orbitofrontal cortex) have been the most frequently

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implicated brain regions (Royall et al., 2002; Stern & Prohaska, 1996). Thus, EF is a unified yet multifaceted construct dependent both on brain localization and interconnectedness (Godlaski & Giancola, 2009; Stuss & Alexander, 2000).

Commonly used measures of EF include the Trail Making Test (TMT), the Wisconsin Card Sorting Test (WCST), the Halstead Category Test (HCT), and various response inhibition tasks (e.g., go/no-go, stop-signal, and Stroop tasks; Stern & Prohaska, 1996). Although studies using response inhibition tasks in alcohol-dependent individuals have been scarce (Dom, De Wilde, Hulstijn, van den Brink, & Sabbe, 2006), a number of cross-sectional studies have shown impaired TMT performance in alcohol-dependent individuals with 2-7 weeks of abstinence compared to non-dependent controls (Fitzhugh, Fitzhugh, & Reitan, 1965; Long & McLachlan, 1974; Noel et al., 2001; O'Leary, Radford, Chaney, & Schau, 1977; Parsons, 1983; Ratti, Bo, Giardini, & Soragna, 2002), and similar results have been obtained with the WCST (Parsons, 1983; Ratti et al., 2002; Schwartz et al., 2002; Tarter, 1973) and HCT (Braun & Richer, 1993; Fitzhugh et al., 1965; Jones & Parsons, 1971; Long & McLachlan, 1974), which may be due to the long-term effects of alcohol on EF. Serial cross-sectional and longitudinal studies have also shown improved TMT and HCT performance in alcohol-dependent individuals with prolonged abstinence (Johnson-Greene et al., 1997; Kish, Hagen, Woody, & Harvey, 1980; Long & McLachlan, 1974; Page & Linden, 1974), suggesting that the long-term effects of alcohol on EF remit to some extent with abstinence. In accord with the neuropsychological data, cross-sectional autopsy and neuroimaging studies of alcohol-dependent individuals have revealed a lower density of neurons in the superior frontal cortex (Harper, Kril, & Daly, 1987; Kril, Halliday, Svoboda, & Cartwright, 1997) and a lower level of brain glucose metabolism and regional cerebral blood flow in the frontal cortex (Adams et al., 1993; Dao-Castellana et al., 1998; Goldstein et al., 2004; Kuruoglu et al., 1996; Volkow et al., 1992) in comparison to non-dependent controls. Moreover, longitudinal neuroimaging studies of alcohol-dependent individuals have revealed increased brain glucose metabolism in the frontal cortex with continued abstinence (Johnson-Greene et al., 1997; Volkow et al., 1994). In summary, it appears that chronic, excessive alcohol use causes a long-term disruption in EF via its toxic effects on the frontal lobe.

In contrast, the acute effects of alcohol on EF are far less known. Understanding the acute effects of alcohol on EF is important because alcohol intoxication is a phenomenon common both to alcohol-dependent individuals and to individuals who periodically become intoxicated. Although experimental research on the effects of alcohol on complex cognitive processes began more than 70 years ago (Jellinek & McFarland, 1940), well-validated tests of EF have been used to study this relationship mostly in the past two decades (Hoaken, Giancola, & Pihl, 1998). To the best of our knowledge, HCT performance during alcohol intoxication has not been examined thus far, and only two studies have examined WCST performance during alcohol intoxication, which have yielded mixed results: Peterson, Rothfleisch, Zelazo, and Pihl (1990) found that social drinkers with a blood alcohol content (BAC) of about .095% or .040% performed similarly to a placebo group on the WCST, whereas Lyvers and Maltzman (1991) found that social drinkers with a BAC of approximately .050% performed worse than a placebo group on the WCST. In addition, only two studies have examined TMT performance during alcohol intoxication, which have also yielded mixed results: Duning, Kugel, Menke, and Knecht (2008) found impaired TMT performance in social drinkers with a BAC of approximately .110%, but not in social drinkers with a BAC of approximately .030% or .065%, relative to their own baseline performance, whereas Gilbertson, Ceballos, Prather, and Nixon (2009) found impaired TMT performance only in older social drinkers with a BAC of approximately .040% relative to their own baseline performance.

Most studies that have measured EF during alcohol intoxication have used a response inhibition task. Several studies have found that alcohol (BACs of approximately .060% to .100%) exerts a negative effect on response inhibition as measured by the Stroop task (Curtin & Fairchild, 2003; Fillmore, Dixon, & Schweizer, 2000a, 2000b; Gustafson & Kallmen, 1990a), although some earlier studies failed to find such an effect (Gustafson & Kallmen, 1990b; Lewis, Dustman, & Beck, 1969; Tarter, Jones, Simpson, & Vega, 1971). Finally, studies using stop-signal or go/no-go tasks have consistently found that alcohol (BACs of approximately .055% to .090%) interferes with response inhibition (Abroms, Fillmore, & Marczinski, 2003; Fillmore & Vogel-Sprott, 1999, 2000; Fillmore & Weafer, 2004; Marczinski & Fillmore, 2003a, 2003b; Mulvihill, Skilling, & Vogel-Sprott, 1997), with the exception of one study that used the GoStop, a recently developed stop-signal task (Dougherty, Marsh-Richard, Hatzis, Nouvion, & Mathias, 2008).

Although various doses of alcohol have been used across the previously reviewed studies, few studies have examined the effects of several doses of alcohol on multiple measures of EF within the same study. Peterson et al. (1990) administered five EF tasks to social drinkers at three different levels of alcohol intoxication; however, BAC measurement was limited (measured before and after the full battery of tests, with only one additional BAC in the middle of testing); sample sizes were small (n = 12); and only men were included. Dougherty et al. (2008) administered three EF tasks to male and female social drinkers at five different levels of alcohol intoxication; however, control of behavioral impulsivity (of which response inhibition is one component) was the only domain of EF measured. Therefore, whether men and women exhibit similar deficits across EF domains during alcohol intoxication has yet to be examined in a single study.

The purpose of the current study was to examine the effects of four doses of alcohol on multiple measures of EF in men and women. We administered three tasks comprising two domains of EF (two set shifting tasks, the TMT and WCST, and a response inhibition task, the GoStop) to male and female social drinkers (N = 185). Participants were randomly assigned to one of four doses of alcohol (alcohol doses associated with target blood alcohol concentrations of .000%, .050%, .075% and .100%), and we also measured BAC before and after individual tasks. Based on previous research, we hypothesized that the two higher alcohol doses will result in impairments in EF across all measures and that men and women will not differ in respect to their response to alcohol.

Method

Participants

Participants were 185 (91 women and 94 men) healthy social drinkers between the ages of 21 and 55 (M = 25.6; SD = 6.5). Most of the sample (63.2%) self-identified as “Caucasian;” 24.3% self-identified as “African American;” 4.3% self-identified as “Hispanic;” 6.5% self-identified as “Other;” and 1.6% chose not to answer. The average participant consumed alcohol 2 to 4 times per month, drank 3 or 4 drinks on a typical drinking day, and consumed 6 or more drinks during a single occasion less than monthly. Participants were recruited from the university and surrounding community through fliers, university-based emails, and newspaper and online advertisements calling for volunteers for a paid study ($10 per hour) on “the effects of alcohol on motor skills”. All potential participants were initially screened via telephone interview and were excluded if they reported that they had previously participated in alcohol research, had never consumed alcohol, were currently taking any medication with which alcohol is contraindicated, had any current mental disorder or problem for which they were engaged in treatment, or had any significant medical condition, such as kidney or liver problems. The Alcohol Use Disorders Identification Test (AUDIT; Babor, Higgins-Biddle, Saunders, & Monteiro, 2001) was also administered over the phone,

and a cut-score of 9 was used to exclude potential problem drinkers. Participants scoring in the borderline range (a score of 7 or 8) were administered the Short Michigan Alcohol Screening Test (SMAST; Selzer, Vinokur, & van Rooijen, 1975), on which a score of 3 or more was exclusionary. All participants were also later administered the SMAST and were excluded if they scored 3 or higher. In order to prevent the administration of high doses of alcohol to physically unhealthy individuals, participants with a body mass index of 35 or greater (suggestive of severe obesity) were excluded. Women could not participate if they were pregnant or nursing. This study is part of a larger research program aimed at examining the effects of alcohol on self-injurious behavior. The overall study was approved by The University of Southern Mississippi Human Subjects Protection Review Committee.

EF Measures

Wisconsin Card Sorting Test (WCST)—The WCST is a well-validated test of EF (Royall et al., 2002). In the current study, participants were administered a computerized version of the WCST (Heaton & Goldin, 2005). During each task trial, four stimulus cards and a response card appear on the computer screen, and the participant is asked to match the response card with one of four stimulus cards using the characteristics of color, shape, and number. In order to match two cards, the participant moves the cursor using a mouse and clicks on the stimulus card that he or she believes is a correct match for the response card. The participant then receives visual and auditory feedback indicating that a correct or an incorrect match was made. If the participant receives feedback indicating a correct match was made, then he or she is expected to make the subsequent match attempt based on the same sorting principle (according to the same color, shape, or number), but if the participant receives feedback indicating an incorrect match was made, then he or she is expected to adjust the subsequent match attempt by selecting a different sorting principle. After 10 consecutive correct matches, the computer changes the sorting principle without alerting the participant, and the test continues until six sorting categories are achieved or until 128 response cards are used. The duration of the task was approximately 10-15 minutes, which was partially dependent on how quickly each participant sorted through categories. Categories achieved and perserverative errors (i.e., the number of times an attempt is made to match cards according to the previous sorting principle after feedback has been given that the sorting principle has changed) were chosen as variables of interest due to their association with set shifting ability (Miyake et al., 2000) and sensitivity to frontal lobe damage (Demakis, 2003). Nonperseverative errors (i.e., the number of errors made that are not perseverative in nature) was included as a variable of interest due to its lack of having been examined at higher alcohol doses in the literature. Finally, total errors (i.e., the sum of perseverative and nonperseverative errors) was included as a variable of interest due to its inclusion in past studies of alcohol intoxication (Lyvers & Maltzman, 1991; Peterson et al., 1990).

Trail Making Test (TMT)—The TMT is a widely used test of EF composed of two parts on separate sheets of paper (Stern & Prohaska, 1996). On Part A of the TMT (TMT-A), the participant is instructed to use a pencil to connect 25 randomly arranged numbers in order (1-2-3-4…), and on Part B of the TMT (TMT-B) the participant is instructed to use a pencil to connect 25 randomly arranged numbers and letters in alternating numerical and alphabetical order (1-A-2-B…). The participant is also instructed that erasing is not allowed, and if an error is made (which is quickly pointed out to the participant), then he or she should return to the last correct circle to continue performing the task. Performance on TMT-A mostly requires psychomotor speed, whereas performance on TMT-B also requires flexibility in response set, or set shifting. Although it is intuitive that TMT-B, a set shifting task, would be more appropriate for measuring EF than TMT-A, results of a meta-analysis support the notion that only TMT-A is sensitive to frontal lobe damage (Demakis, 2004).

However, neuroimaging studies have consistently revealed greater activation in the prefrontal cortex during performance on TMT-B in comparison to TMT-A (Kubo et al., 2008; Moll, de Oliveira-Souza, Moll, Bramati, & Andreiuolo, 2002; Shibuya-Tayoshi et al., 2007; Zakzanis, Mraz, & Graham, 2005). Therefore, it is important to examine the effects of alcohol on both components of TMT performance. Accordingly, participants were administered both TMT-A and TMT-B before and after alcohol intoxication. Each administration began with TMT-A followed by TMT-B, with a total duration of approximately 5 minutes, and completion time was used as the dependent variable for both TMT-A and TMT-B.

GoStop Impulsivity Paradigm (GoStop)—The GoStop is a recently developed behavioral measure of impulsivity designed to assess response inhibition (Dougherty, Mathias, Marsh, & Jagar, 2005; Dougherty et al., 2008). During the task, the participant is seated at a computer, and a series of black 5-digit numbers are presented rapidly on a white background. Each number is displayed for 500 ms, and there is a 1500 ms interval between number displays. The participant is initially instructed to respond when a number appears on the screen that is exactly the same as the previous number. However, the participant is also told that a matching number may change in color from black to red, which serves as a stop signal. In other words, the participant is told not to respond when a matching number changes in color from black to red. Trials including a stop signal represent stop trials, whereas trials without stop signals are go trials. Stop trials have been conceptualized as trials that require the participant to inhibit an already initiated response because they are indistinguishable from go trials when they first appear on the screen and only reveal themselves to be stop trials (by the number turning red) after a time delay, by which time it is expected that the participant has already initiated a response. Participants completed a total of 80 stop trials and 20 go trials, and a stop-signal delay of 350 ms was used. The duration of the task was approximately 15 minutes. GoStop inhibition percentage (i.e., the percentage of stop trials in which the participant successfully inhibited the response) served as the measure of response inhibition.

Procedure

Participation took place across two days: One day involved alcohol administration and completion of EF measures, and the other day involved completion of the Wechsler Abbreviated Scale of Intelligence (WASI; The Psychological Corporation, 1999) and Barratt Impulsiveness Scale-11 (BIS-11; Patton, Stanford, & Barratt, 1995). The latter two measures were included to ensure that the groups were not different with respect to cognitive abilities or self-ratings of impulsivity when sober. Before participation, written informed consent was obtained. Participants were also instructed to abstain from all medications for one week, alcohol for 48 hours, and food or drink besides water for 4 hours prior to alcohol administration.

On the study day involving alcohol administration, participants were randomly assigned to one of four alcohol doses based on target BAC: placebo (.000% BAC), low dose (.050% BAC), medium dose (.075% BAC), and high dose (.100% BAC). A demographic questionnaire was administered, and all participants provided a urine sample for drug screening. Participants who tested positive for any potential drug of abuse (marijuana, cocaine, amphetamine, methamphetamine, MDMA, benzodiazepines, and opiates) were excluded from alcohol administration. For women, this urine sample was also used to screen for pregnancy, although there were no positive pregnancy test results. An initial BAC estimate was then obtained using an expired breath sample in order to ensure that participants had no alcohol in their system prior to receiving the drink. All BAC estimates were obtained with Alco-Sensor IV (Intoximeters, Inc., St. Louis, MO) hand-held

breathalyzers. The first (sober baseline) administration of the TMT-A and TMT-B was conducted just prior to drink administration.

Participants in the active dose conditions were given a mixture of chilled orange juice and 190-proof grain alcohol (95% ethanol) divided between two cups. The amount of alcoholic drink was based on an equation incorporating weight and gender in order to achieve a target BAC (Watson, Watson, & Batt, 1981). All participants, including those in the placebo condition, were told that the drink could contain alcohol, but no additional information was provided about the drink. For the low, medium, and high doses, men were administered a number of mL of alcohol equivalent to their weight in pounds multiplied by 0.3024, 0.4536, and 0.6046, respectively. To adjust for gender, women received 90% as much alcohol as men. Orange juice was added to the alcohol to achieve a ratio of 5:1 (orange juice to alcohol). For the placebo condition, participants were administered a drink of chilled orange juice equal in volume to a medium dose divided between two cups. In an effort to enhance deception, a few drops of alcohol were floated on top of the drink, and alcohol was also rubbed around the rim of the cups. The deception appears to have been generally successful, with participants in the placebo condition on average estimating that they had received the equivalent of approximately 1.5 shots (1 shot = 1.5 oz.) of 100-proof vodka. Participants were given 15, 22.5, or 30 minutes to consume their drinks in the low, medium, and high doses, respectively. This timing regimen was used so that BACs would peak around the same time across doses in order to minimize dose by peak confounds. Participants in the placebo condition had 22.5 minutes to consume their drinks.

Following completion of the drinking phase, participants completed the three EF tasks in the following sequence: (1) the WCST, (2) the second administration of TMT-A and TMT-B, and (3) the GoStop. Breathalyzer readings were obtained before and after each task. Following the completion of all tasks, breathalyzer readings were periodically obtained until the participant's BAC decreased to below .02%, at which point the participant was debriefed and dismissed.

Results

Data were examined for outliers, normality, homoscedasticity, and sphericity. After excluding one participant as an outlier because he inhibited on 100% of Go-Stop trials (indicating a complete lack of responding), 43 placebo participants, 45 low dose participants, 46 medium dose participants, and 51 high dose participants remained. Because of unequal sample sizes and the non-normality and heteroscedasticity of the data, a more conservative alpha level ($p = .025$) was used to test the significance of all parametric tests, which has been shown to be an effective method of correcting for Type-I error inflation due to non-normality and unequal variances when sample sizes are equal or nearly equal (Keppel, 1991; Milligan, Wong, & Thompson, 1987). A series of one-way ANOVAs revealed no significant differences between groups in regard to age, SMAST score, BIS-11 total score, IQ, or years of education. Pearson's chi-square test revealed no significant differences between groups with respect to gender composition ($p > .05$). Demographic data for participants are shown in Table 1.

A series of 4 (alcohol dose) x 2 (gender) ANOVAs revealed that mean BACs were significantly different among the alcohol dose groups at all four points of alcohol intoxication ($p < .001$ for each ANOVA). As expected, however, no significant main effects of gender or interactions between alcohol dose and gender were found. Overall, target BACs were achieved in all alcohol dose conditions. The following peak mean BACs were achieved by participants in each dose group: (1) placebo, $M = .000\%$, $SD = .000\%$; (2) low dose, $M = .053\%$, $SD = .010\%$; (3) medium dose, $M = .073\%$, $SD = .018\%$ (4) high dose, $M = .102\%$,

SD = .020%. Mean BACs in each dose condition at four different points of measurement (prior and subsequent to each test) are shown in Table 2.

Wisconsin Card-Sorting Task (WCST)

A series of two-way ANOVAs was conducted to examine the separate and combined effects of gender and alcohol dose on perseverative errors, nonperseverative errors, total errors, and categories achieved. Alcohol dose was related to perseverative errors ($F_{(3, 177)} = 4.15$, $p = .007$, $\eta_p^2 = .066$) and total errors ($F_{(3,177)} = 3.47$, $p = .017$, $\eta_p^2 = .056$). Post hoc Tukey's tests revealed that participants made significantly more perseverative errors in the medium ($p = .023$, $M = 17.7$, $SD = 12.0$) and high ($p = .009$, $M = 18.2$, $SD = 12.5$) dose groups relative to the placebo group ($M = 11.1$, $SD = 7.2$), whereas participants made significantly more total errors only in the high dose group ($p = .009$, $M = 36.9$, $SD = 22.5$) relative to the placebo group ($M = 24.2$, $SD = 16.5$). No other WCST variables were related to alcohol dose, gender, or their interaction. Means and standard deviations for dependent measures from EF tasks can be found in Table 3.

Part A (TMT-A) and Part B (TMT-B) of the Trail Making Test (TMT)

Separate repeated measures ANOVAs were conducted for TMT-A and TMT-B with alcohol dose and gender as between-subjects factors. For TMT-A, which predominantly measures psychomotor speed, no significant effects of time, alcohol dose, gender, or their interaction were found. For TMT-B, which measures set shifting as well as psychomotor speed, a main effect of time was observed ($F_{(1, 177)} = 13.06$, $p < .001$, $\eta_p^2 = .069$), with participants overall performing more quickly on the second administration ($M_2 = 58.8$, $SD = 22.5$) than the first administration ($M_1 = 64.1$, $SD = 26.3$). An interaction between time and drink condition ($F_{(3, 177)} = 5.31$, $p = .002$, $\eta_p^2 = .083$) was also found. Paired-samples t-tests revealed that this interaction was accounted for by a significant improvement in speed on the second administration in the placebo ($t_{42} = 5.03$, $p < .001$) and low alcohol dose ($t_{44} = 2.59$, $p = .013$) conditions, whereas the medium and high alcohol dose groups did not show improvement. Thus, it appears that moderately high doses of alcohol disrupt set shifting such that any benefits of practice on TMTB are lost.

Go-Stop Task

Due to technical difficulties, GoStop data are only available for 141 participants (62 women and 79 men). A two-way ANOVA was conducted to examine the separate and combined effects of gender and alcohol dose on inhibition percentage. No significant effects of alcohol dose, gender, or their interaction were found.

Discussion

As we had hypothesized, high and medium alcohol dose participants (participants with target BACs of .100% and .075%, respectively) displayed impaired performance on the WCST and TMT. Also consistent with our hypotheses, none of the EF measures revealed gender effects. Contrary to our expectations, however, high and medium alcohol dose participants did not display impaired performance on the GoStop.

On the WCST, greater perseverative errors were observed in the high and medium alcohol dose groups in comparison to the placebo group, whereas greater total errors were observed only in the high dose group. Also, the groups did not differ in regard to nonperseverative errors and categories achieved. Consistent with the current study, Lyvers and Maltzman (1991) failed to find differences in total errors, nonperseverative errors, and categories achieved between participants with a BAC of approximately .050% (analogous to our low dose group) and a placebo group. Also similar to the current study, Lyvers and Maltzman

found that alcohol-intoxicated participants made more perseverative errors than the placebo group, although participants in the Lyvers and Maltzman study were found to have impaired WCST performance at a BAC of approximately .050%, which is a finding that was not specifically replicated in the current study. In contrast to the current study, Peterson et al. (1990) failed to find differences in total errors between participants with a BAC of approximately .095% (analogous to our high dose group) and a placebo group. Notably, however, sample sizes in the Peterson et al. study (n = 12) were quite smaller than in the current study (n = 43-51), which may have contributed to this discrepancy.

Because successful WCST performance is largely dependent on the dorsolateral prefrontal cortex (Demakis, 2003; Royall et al., 2002), it is likely that the adverse effects of moderately high doses of alcohol on perseverative errors found in the current study are the result of dorsolateral prefrontal cortex dysfunction caused by alcohol intoxication. Although a meta-analysis revealed that both perseverations and categories achieved are sensitive to frontal lobe damage (Demakis, 2003), perseverative errors may be the most sensitive WCST measure of frontal lobe dysfunction, as has been previously suggested (Miyake et al., 2000). Frontal lobe dysfunction caused by moderately high doses of alcohol is undoubtedly not as severe as frontal lobe dysfunction caused by frontal lobe damage, and deficits in categories achieved may only result from severe frontal lobe dysfunction, such as that resulting from frontal lobe damage or perhaps higher doses of alcohol than used in the current study. The lack of effect on nonperseverative errors found in the current study is consistent with previous studies of frontal lobe damage (Demakis, 2003) and alcohol intoxication (Lyvers & Maltzman, 1991), indicating that nonperseverative errors is not a sensitive measure of frontal lobe dysfunction. Also, the negative effect of high dose alcohol on total errors (i.e., the sum of perseverative and nonperseverative errors) in the current study is likely secondary to its effect on perseverative errors, given the sensitivity of perseverative errors and lack of sensitivity of nonperseverative errors to frontal lobe dysfunction. Thus, the key finding related to the WCST in the current study is that moderately high doses of alcohol impair set shifting, as evidenced by greater perseverative errors among the high and medium alcohol dose groups in comparison to the placebo group.

In regard to the TMT, participants displayed improved performance on TMT-B in the placebo and low alcohol dose conditions (target BACs of .000% and .050%, respectively) compared to their own baseline performance, whereas the medium and high alcohol dose groups did not show improvement, suggesting that moderately high doses of alcohol disrupt set shifting such that any benefits of practice on TMT-B are lost. However, no such effects were found with TMT-A. Similar to the current study, Gilbertson et al. (2009) found that older participants with a BAC of about .040% performed worse on TMT-B, but not TMT-A, compared to a placebo group of a similar age. Although Gilbertson et al. found impaired performance on the TMT-B at a lower BAC than in the current study, evidence of impairment on the TMT-B was found only in older participants (mean age of 57 years), and not in younger participants with a similar mean age to participants in the current study. Therefore, any inconsistencies between the findings of Gilbertson et al. and those of the current study could be due to differences in age among groups. Also similar to the current study, Duning et al. (2008) found that participants with a BAC of approximately .110% were impaired on the TMT compared to their own baseline performance, whereas participants with a BAC of approximately .030% or .065% did not display such impairments. Although Duning et al. gauged TMT performance with total completion time (i.e., the sum of TMT-A and TMT-B completion times), it is possible that a specific negative effect of alcohol dose on TMT-B lead to the differences in total completion time in their study. In summary, it again appears that moderately high doses of alcohol impair set shifting, as evidenced by impaired repeat performance on the TMT-B among the high and medium alcohol dose groups. Because brain activation has consistently been shown to be greater in the prefrontal

cortex during TMT-B performance in comparison to TMT-A (Kubo et al., 2008; Moll et al., 2002; Shibuya-Tayoshi et al., 2007; Zakzanis et al., 2005), it is reasonable to posit that the adverse effects of moderately high doses of alcohol on TMT-B performance found in the current study are the result of prefrontal cortex dysfunction caused by alcohol intoxication.

Contrary to our expectations, participants did not differ in regard to GoStop performance. Consistent with the current study, however, Dougherty et al. (2008) also found that participants given moderately high doses of alcohol (BACs of approximately .065% and .090%) did not display impaired performance (i.e., greater behavioral impulsivity or response inhibition) on the GoStop. Although the current study used a stop-signal delay of 350 ms, which typically does not discriminate groups as well as the 150 ms delay (Dougherty et al., 2005; Dougherty et al., 2008), Dougherty et al. (2008) did use the 150 ms delay and still failed to find an effect of alcohol on response inhibition as measured by the GoStop. One possible explanation is that the GoStop, a visual stop-signal task, is not as sensitive of an indicator of response inhibition as previous auditory stop-signal tasks. This possibility is made likely by the fact that participants with levels of alcohol intoxication similar to the current study's low and medium dose groups have consistently displayed impaired response inhibition as measured by auditory stop-signal tasks (Fillmore & Vogel-Sprott, 1999, 2000; Mulvihill, Skilling, & Vogel-Sprott, 1997). Another possibility is that the loss of participant data in the current study may have contributed to the lack of a significant finding. This is an unlikely possibility, however, because sample sizes were still adequate (n = 33-38) and data loss was random (i.e., resulted from 350 ms data no longer being collected for all participants beyond a certain point in the study).

None of the EF measures in the current study revealed gender effects, even though men and women remained at a similar level of alcohol intoxication throughout the study. One previous study also failed to reveal gender differences in WCST performance during alcohol intoxication (Lyvers & Maltzman, 1991), although that particular study only examined WCST performance at one level of alcohol intoxication (BAC of approximately .050%). Previous studies of response inhibition task performance during alcohol intoxication have produced mixed results, with one study finding gender differences at a BAC of approximately .080% (Fillmore & Weafer, 2004) and another study failing to find differences at a BAC of approximately .065% (Mulvihill et al., 1997). To the best of our knowledge, no previous studies examined gender differences in TMT performance during alcohol intoxication. Although research conducted thus far has mostly indicated a lack of gender differences in EF during alcohol intoxication, it is still an area that awaits further examination with a greater diversity of EF tests across a wider range of alcohol doses.

Some limitations of the current study should be noted. First, a measure of working memory updating, which is another commonly discussed aspect of EF, was not included. Although prior research has indicated that alcohol adversely affects performance on simple working memory tasks (Saults, Cowan, Sher, & Moreno, 2007), research on the effects of alcohol on more complex working memory tasks appears to be sparse. Second, the inclusion of brain imaging may have allowed for the direct observation of (rather than indirect support for) prefrontal cortex dysfunction caused by alcohol. Third, the order of the administration of EF tasks was not randomized across participants, and such randomization could have helped ease concerns related to the potentially diminishing effects of alcohol on later tasks due to declining BAC. A quick examination of Table 2, however, shows that mean BAC had declined by only about .05% subsequent to TMT administration and by only about .10% subsequent to GoStop administration. Because the decline in mean BAC during later tasks was quite small across all active dose groups, it is unlikely that declining BAC lead to a lack of significant findings, especially in the high dose group (which had a sustained mean BAC of .090% or higher). Fourth, higher doses of alcohol than those used in the current study

may have resulted in impaired GoStop performance. However, the bothersome effects of alcohol intoxication (e.g., nausea) become more prevalent with higher doses. Finally, the inclusion of a told-sober group (i.e., participants who were told they were being administered a non-alcoholic drink) could have allowed us to examine the effects of alcohol expectancies on EF.

In conclusion, alcohol negatively affects set shifting at moderately high levels of intoxication in both men and women. Based on past research, alcohol's deleterious effects on set shifting are likely mediated by prefrontal cortex dysfunction caused by alcohol intoxication. Although alcohol's adverse effects on response inhibition as measured by auditory stop-signal tasks have been well-documented, alcohol does not appear to exert a negative effect on response inhibition as measured by the GoStop, a visual stop-signal task.

Acknowledgments

This study was supported by funding from the National Institute on Alcohol Abuse and Alcoholism to Mitchell E. Berman (AA14025).

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Table 1

Demographic characteristics of participants

Variable	Placebo (*n* = 43) Mean (SD)	Low Dose (*n* = 45) Mean (SD)	Medium Dose (*n* = 46) Mean (SD)	High Dose (*n* = 51) Mean (SD)
Age in years	24.5 (6.0)	25.6 (6.0)	25.6 (7.0)	26.4 (6.9)
Male/Female ratio	23/20	22/23	26/20	23/28
Years of education[a]	16.8 (2.4)	17.1 (2.3)	16.5 (2.2)	17.3 (3.4)
WASI Full Scale IQ[b]	110.4 (12.8)	105.0 (13.1)	105.4 (11.1)	109.7 (11.9)
BIS-11 total score[b]	60.1 (9.7)	61.1 (11.3)	63.8 (11.0)	61.9 (8.4)
SMAST score[c]	.23 (.53)	.32 (.60)	.35 (.64)	.22 (.46)

Note.

[a] Two participants did not provide information on years of education

[b] six participants failed to complete the WASI and BIS-11

[c] and one participant failed to complete the SMAST.

Table 2

BACs of participants prior and subsequent to each EF test (percentages)

Point of measurement	Placebo (*n* = 43) Mean (SD)	Low Dose (*n* = 45) Mean (SD)	Medium Dose (*n* = 46) Mean (SD)	High Dose (*n* = 51) Mean (SD)
Pre-WCST[a]	.000 (.000)	.053 (.010)	.073 (.018)	.102 (.020)
Post-WCST, Pre-TMT[b]	.000 (.000)	.050 (.010)	.071 (.018)	.100 (.017)
Post-TMT, Pre-GoStop[c]	.000 (.000)	.048 (.010)	.071 (.019)	.098 (.016)
Post-GoStop[d]	.000 (.000)	.040 (.010)	.063 (.017)	.090 (.017)

Note.

[a] Prior to the administration of the WCST

[b] subsequent to the administration of the WCST and prior to the second administration of the TMT

[c] subsequent to the second administration of the TMT and prior to the administration of the GoStop

[d] subsequent to the administration of the GoStop

Table 3

Dependent measures from EF tasks

EF task/measure	Placebo (*n* = 43) Mean (SD)	Low Dose (*n* = 45) Mean (SD)	Medium Dose (*n* = 46) Mean (SD)	High Dose (*n* = 51) Mean (SD)
WCST				
Perseverative errors	11.1 (7.2)[a]	14.9 (10.1)	17.7 (12.0)[a]	18.2 (12.5)[a]
Nonperseverative errors	13.1 (10.4)	14.2 (9.3)	16.3 (10.6)	18.6 (11.9)
Total errors	24.2 (16.5)[b]	29.8 (17.8)	34.0 (21.0)	36.8 (22.4)[b]
Categories achieved	5.6 (1.1)	5.4 (1.3)	5.0 (1.5)	4.8 (1.7)
GoStop				
Inhibition percentage[c]	32.3 (19.7)	42.7 (23.7)	46.9 (28.5)	41.7 (29.0)
TMT (pre-alcohol)				
Part A completion time	31.7 (12.1)	29.8 (7.7)	30.0 (7.7)	30.4 (9.0)
Part B completion time	65.9 (30.7)[d]	70.3 (31.6)[d]	59.2 (14.4)	61.4 (25.0)
TMT (post-alcohol)				
Part A completion time	26.5 (10.5)	24.8 (7.7)	31.1 (29.0)	29.0 (12.9)
Part B completion time	54.7 (27.7)[d]	58.7 (20.1)[d]	57.1 (16.7)	63.9 (23.9)

Note.

[a] Differences in WCST perseverative errors in medium ($p = .020$) and high dose ($p = .007$) groups versus placebo group

[b] differences in WCST total errors in high dose group versus placebo group ($p = .009$)

[c] data are only available for 141 participants ($n = 35$ for the placebo group, $n = 38$ for the low dose group, $n = 35$ for the medium dose group, and $n = 33$ for the high dose group)

[d] differences in post-alcohol TMT-B completion time in placebo ($p < .001$) and low dose ($p = .011$) groups versus their own baseline performance (TMT-B pre-alcohol)