

Alcohol impairment of behavior in men and women

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Submitted 9 December 2003;
initial review completed 10 March 2004;
final version accepted 13 April 2004

ABSTRACT

Aims Studies have shown that alcohol impairs the ability to inhibit behavioral responses in humans and some evidence suggests that men might display greater impairment than women. The present study compared men and women in the degree to which a moderate dose of alcohol impaired their inhibitory control at comparable blood alcohol concentrations.

Design Twelve male and 12 female adult social drinkers received a moderate dose of alcohol (0.65 g/kg) and a placebo in a counterbalanced order and performed a cued go/no-go task that measured the ability to inhibit and execute behavioral responses.

Findings When the behavioral response was pre-potent (i.e. instigated), men displayed greater impairment of inhibitory control under alcohol than women. Men also reported greater levels of subjective stimulation from alcohol compared with women, who reported more sedation from the drug.

Conclusions A gender difference in alcohol impairment of inhibitory control could account for observations that disinhibited and aggressive behaviors under alcohol are more pronounced in men than in women.

KEYWORDS alcohol, behavioral control, gender difference, inhibition.

INTRODUCTION

The association of alcohol use with aggression and other socially inappropriate behaviors has led to considerable research interest in the possibility that alcohol selectively impairs fundamental mechanisms of behavioral control (e.g. Lyvers 2000). Several theories argue that behavioral control can be reduced to conflicting mechanisms: inhibitory and activational (Gray 1976, 1977; Logan & Cowan 1984; Fowles 1987). The relative strength of these systems determines behavioral control. Extreme or disinhibited behavior may arise from either a weakened inhibitory system or a heightened activation system. Research in cognitive neuroscience has focused on inhibitory mechanisms of behavioral control. The ability to withhold or terminate a response is considered to reflect an inhibitory cognitive mechanism of behavioral control (Logan & Cowan 1984). Deficient inhibitory mechanisms have been implicated in disorders characterized by aggressive or impulsive behaviors, such as antisocial personality and

attention deficit/hyperactivity disorders (Barkley 1997; Tannock 1998).

Model-based performance assessments of behavioral control have been used to examine the effects of alcohol in humans (for a review, see Fillmore 2003). Some assessments are based on stop-signal and cued go/no-go tasks that model behavioral control as the ability to activate a response to a go-signal quickly and suddenly inhibit a response when a stop-signal occurs (Logan & Cowan 1984; Miller, Schaffer & Hackley 1991; Logan 1994). These tasks provide independent measures of the countervailing inhibitory and activational aspects of behavioral control. Studies using these models have found that alcohol impairs the ability to inhibit behavior (e.g. Mulvihill, Skilling & Vogel-Sprott 1997; Fillmore & Vogel-Sprott 1999, 2000; de Wit, Crean & Richards 2000; Abroms, Fillmore & Marczynski 2003; Marczynski & Fillmore 2003a, 2003b). Evidence for the reliable impairing effects on inhibitory control in these models is particularly noteworthy given the comparatively mild alcohol doses administered in these studies (e.g. 0.45–0.65 g/kg)

and the relatively simple nature of the inhibitory response tested. Moreover, the findings are important because they identify a basic inhibitory mechanism that is impaired by alcohol which could contribute to the display of aggressive and other socially inappropriate behaviors under the drug (Jentsch & Taylor 1999; Fillmore 2003).

To date, studies based on behavioral control models have not reported gender differences in the degree to which alcohol impairs response inhibition. However, many of these studies examined only men (e.g. Fillmore & Vogel-Sprott 1999, 2000), or involved too few subjects to allow adequate comparisons between gender groups (e.g. de Wit *et al.* 2000; Marcuzinski & Fillmore 2003b). Consequently, little is known about potential gender differences in the impairing effect of alcohol on inhibitory control.

There is some reason to suspect that gender differences might exist. Observations of gender differences in alcohol effects on aggressive behavior suggest that men and women might differ in the degree to which the drug impairs mechanisms of inhibitory control. Several studies have examined the effects of alcohol on aggressive responding in the laboratory (for reviews, see Bushman & Cooper 1990; Taylor & Chermack 1993; Ito, Miller & Pollock 1996). A commonly used laboratory model measures provoked aggression by engaging subjects in competitive tasks against fictitious opponents. Aggressive behavior is inferred by 'retaliatory' responses delivered by a subject against the opponent (e.g. the administration of monetary-point deductions or the delivery of bogus electrical shock). In general, studies have found that individuals who received alcohol displayed more frequent, or more intense, retaliatory responses (i.e. increased aggression) compared with those who received a placebo. These laboratory models also have identified a gender difference wherein men display more intense alcohol-induced aggression than do women (e.g. Giancola & Zeichner 1995; Hoaken & Pihl 2000). In fact, studies report that under some conditions women display no aggressive response following a moderate dose of alcohol (e.g. Giancola *et al.* 2002).

Reasons for a gender difference in alcohol-induced aggression are not certain and some explanations point to social learning that aggressive behavior is more socially acceptable in men than in women (for a review, see Eagly & Steffen 1996). The gender effect might also reflect a more fundamental difference in the degree to which alcohol disrupts basic mechanisms of behavioral control in men and women. Compared with women, men might display a greater reduction of inhibitory control in response to a dose of alcohol. Such a fundamental difference might be evident regardless of situation, and not be specific to those involving aggressive interactions or competition. Furthermore, subtle gender differences in the

operation of basic control mechanisms could have substantial impact on complex behaviors that require impulse control. Many fundamental cognitive processes are considered to operate in a 'bottom-up' fashion to exert increasing influence at each stage of higher-order attentional and cognitive functions (e.g. McClelland & Rumelhart 1981; Barkley 1997). Thus, differences in aggressive responding under alcohol between men and women might reflect a gender difference in the degree to which basic mechanisms of behavioral control are impaired by a dose of alcohol.

The purpose of the present study was to compare men and women in terms of the degree to which a moderate dose of alcohol impairs inhibitory control of behavior. The study measured inhibitory and activational mechanisms of behavioral control with the cued go/no-go task that has been used in other research to study alcohol effects on behavioral control (Abroms *et al.* 2003; Marcuzinski & Fillmore 2003a, 2003b). The task presents go and no-go target stimuli that require a response to be either executed (go) or inhibited (no-go). The task includes a manipulation of response pre-potency by presenting a preliminary go or no-go cue before the actual go or no-go target is displayed. The cues provide information concerning the probability that a go or no-go target will be presented. The cue-target relationship is manipulated so that cues have a high probability of correctly signaling a go or no-go target. Go cues generate response pre-potency which speeds response time to go targets. However, subjects must overcome this response pre-potency in order to inhibit the response if a no-go target is subsequently displayed. Failures to inhibit responses to no-go targets are more frequent following go cues compared with no-go cues, indicating that it is more difficult to inhibit pre-potent responses (Miller *et al.* 1991). The pre-potent response condition also appears to be highly sensitive to alcohol-induced impairment. Studies of alcohol effects on behavioral control using the cued go/no-go task reliably demonstrate a dose-dependent impairing effect on the ability to inhibit responses to no-go targets that are preceded by go cues (Abroms *et al.* 2003; Marcuzinski & Fillmore 2003a, 2003b). The findings indicate that the ability to inhibit a response is particularly vulnerable to alcohol effects in situations where there is a pre-potent tendency to respond.

The present study used the cued go/no-go task to compare men and women in terms of the degree to which a moderate dose of alcohol impairs inhibitory mechanisms of behavioral control. The subjects were adult social drinkers with no history of alcohol or other drug dependence. The study was designed to equate the gender groups on several characteristics to rule out potential confounds. Particular attention was paid to potential gender differences in alcohol pharmacokinetics. Women

tend to achieve a higher blood alcohol concentration (BAC) from a dose of alcohol than men and this is attributed to gender differences in body water volume, alcohol dehydrogenase levels and other factors (Watson, Watson & Batt 1981; Frezza *et al.* 1990; Whitfield & Martin 1994). To control for pharmacokinetic differences the study matched the gender groups in terms of BAC obtained during the period in which behavioral control was tested. The study was designed to test the impairing effect of alcohol during the ascending limb of the blood alcohol curve at average BACs between 75 mg/dl and 85 mg/dl, representing a range reliably associated with impaired response inhibition (e.g. Marcziński & Fillmore 2003a). Thus, it was predicted that alcohol would reduce the ability to inhibit pre-potent responses. Gender differences in this effect were examined to test the possibility that impairment is more pronounced in men than in women.

METHOD

Subjects

Twelve female and 12 male social drinkers participated in this study. The sample ranged in age from 21 to 29 years, with a mean age of 21.9 years ($SD = 1.8$). The racial make-up of the sample was as follows: African American ($n = 4$), Caucasian ($n = 19$) and Asian ($n = 1$). Volunteers completed questionnaires that provided demographic information, drug use history and physical and mental health status. Those who self-reported a substance abuse problem or other psychiatric disorder were excluded from the study, as were those with a score of 5 or higher on the Short Michigan Alcoholism Screening Test (SMAST; Selzer, Vinokur & Van Rooijen 1975). Women who were pregnant or breast-feeding, as determined both by self-report and urine human chorionic gonadotrophin (HCG) levels, were not allowed to participate. All subjects fasted for 4 hours prior to the session and abstained from alcohol for 24 hours prior to the session. Participants were recruited via notices posted on community bulletin boards and local newspaper advertisements. This study was approved by the University of Kentucky Medical Institutional Review Board. All subjects provided informed consent prior to participating, and each received \$60.00 upon completion of the study.

Measures obtained from the Personal Drinking Habits Questionnaire showed that men reported a significantly higher mean weekly frequency of drinking occasions than women ($t = -2.1$, 22 df, $P = 0.051$). Men reported an average drinking frequency of 2.6 ($SD = 1.2$) occasions per week compared with women who reported 1.6 ($SD = 1.2$) occasions. The customary dose per occasion was greater for men than for women ($t = -2.7$, 22 df,

$P = 0.016$). Men consumed an average of 1.4 ml/kg ($SD = 0.7$) of absolute alcohol per occasion, compared to a mean of 0.8 ml/kg ($SD = 0.27$) absolute alcohol for women. Based on the mean body weight of men in the sample (77.3 kg), their reported average dose would approximate the alcohol content of six beers. Based on the sample mean body weight of women (62.8 kg), their reported average dose would approximate the alcohol content of three beers. No gender differences were observed in the mean hourly duration of a typical drinking occasion ($P = 0.850$). The mean duration of drinking was 3.5 ($SD = 1.0$) hours for the entire sample. There was no gender difference in age ($P = 0.912$). The mean age of men and women was 21.9 years ($SD = 2.2$) and 22.0 years ($SD = 1.2$), respectively.

Apparatus and materials

Cued go/no-go task

Participants performed a cued go/no-go reaction time task that was operated using E-Prime experiment generation software (Schneider, Eschman & Zuccolotto 2002) and was performed on a PC. A trial involved the following sequence of events: (a) presentation of a fixation point (+) for 800 ms; (b) a blank white screen for 500 ms; (c) a cue, displayed for one of five stimulus onset asynchronies (SOAs = 100, 200, 300, 400 and 500 ms); (d) a go or no-go target, which remained visible until a response occurred or 1000 ms had elapsed; and (e) an intertrial interval of 700 ms.

The cue was a rectangle (7.5 cm \times 2.5 cm) framed in a 0.8-mm black outline that was presented in the center of the computer monitor against a white background. The cue was presented in either a horizontal (2.5 cm \times 7.5 cm) or vertical (7.5 cm \times 2.5 cm) orientation. The go and no-go targets were colored green and blue, respectively. They were displayed on the monitor as a solid hue that filled the interior of the rectangle cue. Participants were instructed to press the forward slash (/) key on the keyboard as soon as a go (green) target appeared and to suppress the response when a no-go (blue) target was presented. Key presses were made with the index finger of the preferred hand. The go and no-go targets were presented in hues that were easily distinguishable by all participants.

The orientation of the cue (horizontal or vertical) signaled the probability that a go or no-go target would be displayed. Cues that were presented vertically preceded the go target on 80% of the trials and preceded the no-go target on 20% of the trials. Cues that were presented horizontally preceded the no-go target on 80% of the trials and preceded the go target on 20% of the trials (see Table 1). Therefore, on the basis of cue-

Table 1 Cue–target combination probabilities. Vertical cue predicts go target and horizontal cue predicts no-go target. Total trial $n = 250$.

Target	Cue			
	Vertical		Horizontal	
	Trial Trial n	Proportion	Trial Trial n	Trial Proportion
Go	100	0.8	25	0.2
No-go	25	0.2	100	0.8

target pairings, vertical and horizontal cues operated as go and no-go cues, respectively. The different SOAs (100, 200, 300, 400 and 500 ms) between cues and targets encouraged participants to pay attention to the cues, and the variability and randomness of the SOAs prevented the participants from anticipating the exact onset of the targets.

A test consisted of 250 trials that presented the four possible cue–target combinations (see Table 1). An equal number of vertical (125) and horizontal (125) cues were presented before an equal number of go (125) and no-go (125) target stimuli. Each cue–target combination was presented at each of the five SOAs, and an equal number of SOAs separated each cue–target combination. The presentation of cue–target combinations and SOAs was random. For each trial, the computer recorded whether a response occurred and, if so, the reaction time (RT) in milliseconds was measured from the onset of the target until the key was pressed. To encourage quick and accurate responding, feedback was presented to the participant during the intertrial interval by displaying the words correct or incorrect along with the RT in milliseconds. A test required approximately 20 minutes to complete.

Personal Drinking Habits Questionnaire (Vogel-Sprott 1992)

This questionnaire yielded three measures of a drinker's current, typical drinking habits: (a) frequency (the number of drinking occasions per week); (b) customary dose (ml of absolute alcohol per kg body weight typically consumed during a single drinking occasion); and (c) duration (time span in hours of a typical drinking occasion).

Biphasic Alcohol Effects Scale (BAES; Martin et al. 1993)

The study also examined subjective stimulant and sedative effects in response to alcohol. The BAES is a 14-adjective rating scale of subjective levels of stimulation and sedation. Seven adjectives described stimulating effects

(e.g. stimulated, elated), and the remaining seven adjectives described sedating effects (e.g. sedated, sluggish). Participants rated the degree to which the dose produced each feeling on an 11-point Likert-type scale ranging from 0 (not at all) to 10 (extremely). The stimulation and sedation item scores were summed separately to provide a total subscale score for stimulation and sedation (score range 0–70).

Beverage rating

Participants completed a beverage rating scale to report the perceived alcoholic content of their beverages in terms of either bottles of beer (5% alcohol) or fluid ounces of liquor. Subjects were informed that a standard drink contains 1.5 ounces of alcohol. Both scales ranged from 0 to 10, in 0.5 increments (e.g. Fillmore & Vogel-Sprott 2000).

Blood alcohol concentrations

Blood alcohol concentrations (BACs) were determined from breath samples measured by an Intoxilyzer, Model 400 (CMI, Inc., Owensboro, KY, USA).

Procedure

Individuals who responded to the advertisements called the laboratory and participated in a telephone intake screening interview. Volunteers were told that the purpose of the experiment was to study the effects of alcohol on performance. Interested volunteers then made appointments to participate in two laboratory test sessions. All sessions were conducted in the Human Behavioral Pharmacology Laboratory of the Department of Psychology and began between 12:00 p.m. and 6:00 p.m. The sessions occurred no less than 24 hours apart and no more than 7 days apart. Prior to both sessions, participants provided urine samples which were tested for the presence of drug metabolites (On Trak Teststiks, Roche Diagnostics Corporation, Indianapolis, IN, USA) and HCG (Mainline Confirms HGL, Mainline Technology, Ann Arbor, MI, USA). Breath samples were also provided at the beginning of each session to verify a zero BAC.

Familiarization

During familiarization subjects provided informed consent, were weighed and completed questionnaires. A color vision test required subjects to distinguish between the green and blue colors used as go and no-go targets in the task in order to ensure the ability to discriminate between the stimuli. The task requirements were then explained to the subjects. Subjects were instructed to

press the forward slash key (/) on the keyboard as quickly as possible whenever a go (i.e. green) target appeared and to inhibit this response whenever a no-go (i.e. blue) target appeared. They were encouraged to respond in the fewest milliseconds and were told that the computer would display the reaction time in milliseconds following each response. Subjects then performed a test to familiarize them with the task. A single test is sufficient to produce cue-dependent responding (Marczinski & Fillmore 2003b).

Alcohol test sessions

Performance was tested under two dose conditions: a moderate alcohol dose (0.65 g/kg) and a placebo dose (0.0 g/kg). Doses were administered on separate sessions, and dose order was counterbalanced across subjects. The 0.65 g/kg alcohol dose produces an average peak BAC of 90 mg/dl and was chosen based on prior research showing that the dose impairs response inhibition reliably as measured by the cued go/no-go task (Abroms *et al.* 2003; Marczinski & Fillmore 2003a, 2003b).

Doses were calculated based on body weight and were administered as absolute alcohol divided equally into two drinks, each containing one part alcohol and three parts carbonated mix. Subjects had 1 minute to finish each drink, and the drinks were served 4 minutes apart. This dosing procedure produces the peak BAC at approximately 50–70 minutes from the onset of drinking (Fillmore & Blackburn 2002). The placebo was served in the same manner and consisted of four parts carbonated mix with 3 ml of alcohol floating on the surface. The glasses were sprayed with an alcohol mist that resembled condensation and provided a strong alcoholic scent as the beverages were consumed. Previous research has shown that individuals report that this beverage contains alcohol (e.g. Fillmore & Blackburn 2002).

Subjects were tested on the cued go/no-go task 30 minutes after drinking began. The 20-minute test concluded at 50 minutes post-drinking. Prior research using this dosing procedure indicates that BACs of 75 mg/dl to 85 mg/dl should be evident during this 20-minute test interval (Abroms *et al.* 2003; Marczinski & Fillmore 2003a, 2003b). After the test, subjects completed the BAES and beverage rating scale. Subjects' BACs were measured just prior to the test (i.e. at 30 minutes) and when the test was finished (i.e. at 50 minutes). Breath samples were also obtained at these times during the placebo sessions, ostensibly to measure subjects' BACs. Once the session was complete, subjects remained at leisure in a waiting room until their BAC fell below 40 mg/dl. They were given a meal and read magazines or watched movies. On completing the final session, participants were paid and debriefed.

Gender-matching on alcohol pharmacokinetics

Different methods of matching gender on BAC were considered, including gender-based dose adjustments and use of a common 'target' BAC to determine the onset of the behavioral control test. However, these methods are limited in their effectiveness and feasibility. Use of a common target BAC to start testing is problematic because of marked individual differences in the rate at which BAC rises following a dose (Fillmore & Vogel-Sprott 1998). Gender-based dose adjustments involve gender-specific parameters, such as total body water (e.g. Watson *et al.* 1981), for which there is no consensus regarding the exact estimates that should be used to equate gender in BAC (Graham *et al.* 1998). Moreover, considerable individual differences in body characteristics exist within each gender group that can influence BAC at the level of the individual (Fillmore & Vogel-Sprott 1998).

The present study used a matched-pairs method to ensure a comparable average BAC across gender groups. Individual pairs of men and women were selected from the original sample based on the equivalence of their BACs at 30 minutes. The BACs of men and women were compared and pairs of male and female subjects with equivalent BACs were selected. Power estimates based on prior research (Marczinski & Fillmore 2003a) indicated that group sizes of at least 10 subjects were needed to have an 80% likelihood of detecting a significant difference in p-inhibition failures between alcohol and placebo conditions. Thus, pairs of male and female subjects were tested in order to obtain a set of at least 10 male–female pairs that could be matched in terms of their BAC during testing. An original sample of 36 subjects allowed 12 female–male pairs (24 subjects) to be selected on the basis of matched BACs. In seven of these pairs, the male and female subject had an identical BAC. Within the remaining five pairs, the BAC of each member was within 1 mg/dl of each other (within measurement error of the breathalyzer, ± 3 mg/dl). Subjects who did not meet matching criterion displayed BAC differences that exceeded the measurement error of the breathalyzer. The range of BACs in the matched sample comprised the full range of BACs observed in the original sample.

Criterion measures

The two primary measures were subjects' failures to inhibit responses to no-go targets (failures of response inhibition) and their speed of responding to go targets (response execution).

Failure of response inhibition

Failure of response inhibition was measured as the proportion of no-go targets in which a subject failed to inhibit

a response. These p-inhibition failure scores were calculated for each cue condition (go and no-go). The hypothesis that men would fail to inhibit more than women under alcohol was tested by a 2 dose (0.0 g/kg versus 0.65 g/kg) \times 2 cue (go cue versus no-go cue) \times 2 gender (male versus female) mixed-design analysis of variance (ANOVA).

Response execution

Response execution was measured by the RTs to go targets. Shorter RTs indicated greater facilitation of response execution. A mean RT score for a subject was calculated for each cue. Responses with RTs less than 100 ms and greater than 1000 ms were excluded. These outliers were infrequent, occurring on average in less than 2.3% of the trials for which a response was observed. RT scores were analyzed by a 2 (dose) \times 2 (cue) \times 2 (gender) mixed-design ANOVA.

Omission errors were also recorded. These errors occurred when subjects failed to respond to go targets. Omission errors were infrequent and occurred on less than 2% of go target trials (~ two trials per test).

RESULTS

Blood alcohol concentrations

No detectable BACs were observed under the placebo condition. Gender differences in BAC under alcohol at 30 and 50 minutes were examined by a 2 (gender) \times 2 (time) mixed-design ANOVA. No significant main effect of gender ($P=0.759$) or gender-time interaction was obtained ($P=0.319$). A significant main effect of time was obtained ($F=57.6$, 1/22 df, $P<0.001$), owing to the increase in BAC from 30 to 50 minutes post-drinking. At 30 minutes, just prior to the test, the mean BACs

for men and women were 72.4 mg/dl (SD = 15.2) and 72.7 mg/dl (SD = 15.7), respectively. At 50 minutes, just after the test, the mean BACs for men and women rose to 83.2 mg/dl (SD = 15.1) and 86.8 mg/dl (SD = 16.6), respectively.

Cued go/no-go task performance

Failure of response inhibition

P-inhibition failures were analyzed by a 2 (dose) \times 2 (cue) \times 2 (gender) mixed-design ANOVA. The ANOVA revealed significant main effects of dose ($F=4.5$, 1/22 df, $P=0.044$) and cue ($F=11.9$, 1/22 df, $P=0.002$). The analysis also obtained a significant three-way interaction ($F=5.1$, 1/22 df, $P=0.034$). Figure 1 shows the mean p-inhibition failures for men and women under alcohol and placebo. The left side of the figure illustrates p-inhibition failures in the go cue condition (i.e. when responses were pre-potent). In this condition, p-inhibition failures were greater under alcohol compared with placebo. The figure also shows that men displayed more p-inhibition failures under alcohol than women. The right side of the figure plots p-inhibition failure scores in the no-go cue condition. In this condition, p-inhibition failures of men and women were infrequent and did not appear to be affected by alcohol. Figure 1 shows that the main effects of dose and cue are due to generally higher p-inhibition failure scores in the go cue condition and in response to alcohol. The interaction is evident in the go cue condition and is due to a gender difference in the degree to which p-inhibition failures increased under alcohol compared with placebo. This was confirmed by follow-up paired samples *t*-tests which compared the mean p-inhibition failures under alcohol and placebo in each gender and cue condition. In the go cue condition, men displayed significantly greater p-inhibition failures under alcohol

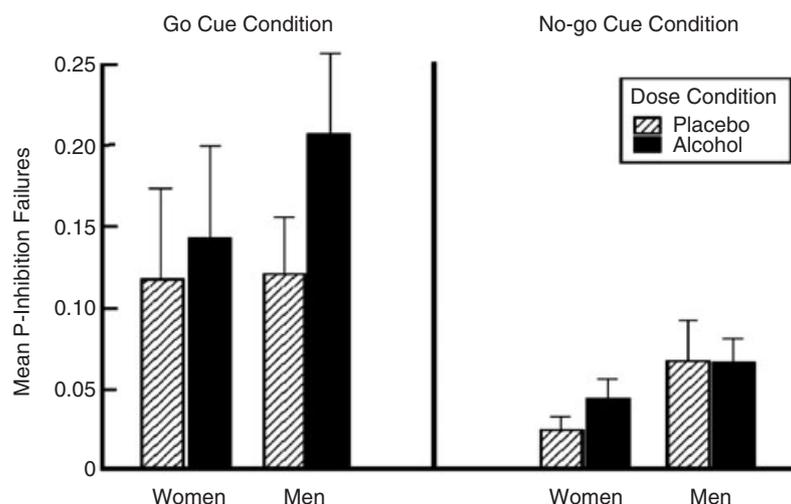


Figure 1 Mean proportion of failures to inhibit responses to no-go targets following go and no-go cues under 0.65 g/kg alcohol and placebo in women and men. Capped vertical lines show standard errors of the mean

compared with placebo ($t = -2.7$, 11 df, $P = 0.015$). The effect size of this comparison was large (0.892). By contrast, women showed no significant difference in p-inhibition failures between alcohol and placebo conditions ($P = 0.400$). In the no-go cue condition, no significant difference in p-inhibition failures were observed between alcohol and placebo conditions for either men ($P = 0.848$) or women ($P = 0.083$).

Given that men and women differed in terms of customary dose and drinking frequency, it was important to determine if either of these drinking habits related to subjects' p-inhibition failure scores observed under alcohol in the go cue condition. Subjects' p-inhibition failure scores were regressed onto their customary dose and frequency of drinking measures in two separate regression analyses. Neither drinking habit measure was significantly related to subjects' p-inhibition failure scores under alcohol ($P_s > 0.529$).

Response execution

RT to go targets was analyzed by a 2 (dose) \times 2 (cue) \times 2 (gender) mixed-design ANOVA. The ANOVA revealed a significant main effect of cue ($F = 25.6$, 1/22 df, $P < 0.001$). No other main effects or interactions were significant ($P_s > 0.119$). Figure 2 shows the mean RTs to go targets for men and women under alcohol and placebo for go and no-go cue conditions. RTs were fastest in the go cue condition and did not appear to be affected by dose or gender.

Subjective effects

Subjective ratings of stimulation and sedation were analyzed by a 2 (dose) \times 2 measure (stimulation versus sedation) \times 2 (gender) mixed-design ANOVA. The ANOVA

revealed a significant three-way interaction ($F = 24.2$, 1/22 df, $P < 0.001$). Figure 3 illustrates the mean subjective ratings of stimulation and sedation reported under alcohol and placebo. The left side of the figure shows that men reported a marked increase in stimulation ratings under alcohol compared with placebo, whereas women reported little difference in stimulation between dose conditions. By contrast, the right side of the figure shows that women displayed a marked increase in sedation ratings under alcohol compared with placebo, whereas men displayed little difference in sedation between dose conditions. Paired samples t -tests of stimulation ratings revealed a significant difference between dose conditions for men ($t = -5.1$, 11 df, $P < 0.001$), but not for women ($P = 0.143$). For sedation ratings, paired samples t -tests revealed a significant difference between dose conditions for women ($t = -3.1$, 11 df, $P = 0.010$), but not for men ($P = 0.465$).

Beverage ratings were analyzed by a 2 (dose) \times 2 (gender) ANOVA. A significant main effect of dose was found ($F = 114.7$, 1/22 df, $P < 0.001$). No other effects were significant ($P_s > 0.198$). Subjects rated the alcohol content of the active dose as equivalent to an average of 4.1 (SD = 1.6) standard drinks. The placebo was rated as containing an average of 0.8 (SD = 0.8) standard drinks, which was significantly greater than zero ($t = 4.8$, 23 df, $P < 0.001$), indicating that the placebo was a credible treatment for producing the expectation of alcohol.

DISCUSSION

This research used a cued go/no-go RT task to test the degree to which alcohol impaired response execution and response inhibition in a group of men and a group of women who were matched in terms of their BACs. The study showed that men displayed more failures to inhibit

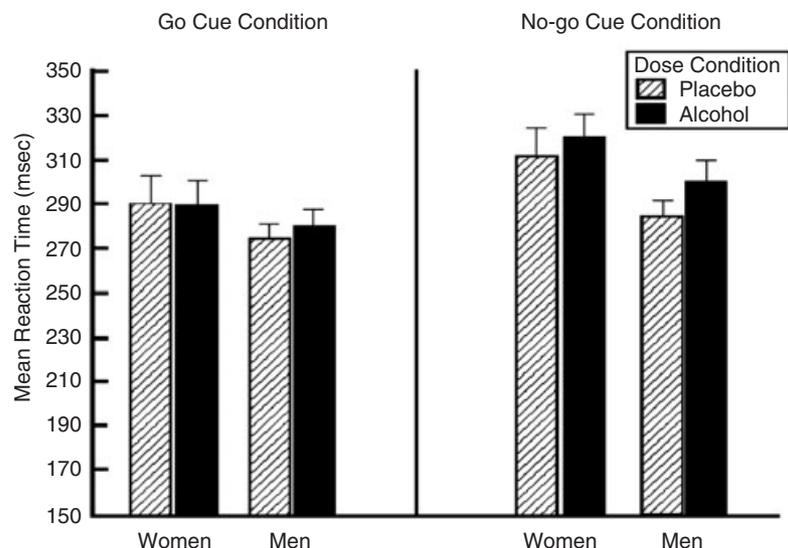


Figure 2 Mean reaction time in milliseconds to respond to go targets following go and no-go cues under 0.65 g/kg alcohol and placebo in women and men. Capped vertical lines show standard errors of the mean

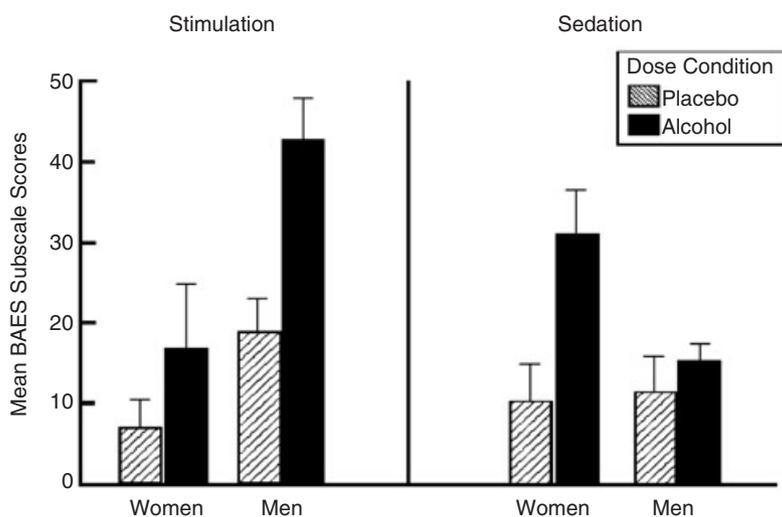


Figure 3 Mean ratings of subjective stimulation and sedation on the BAES under 0.65 g/kg alcohol and placebo in women and men. Capped vertical lines show standard errors of the mean

responses to no-go targets under alcohol than women. This impairing effect was specific to the inhibition of responses that were made pre-potent by the presentation of a go cue. Response inhibition to no-go targets following no-go cues was not impaired under alcohol in either men or women. Measures of reaction time to go targets showed no impairing effect of alcohol on the ability to quickly execute responses in either men or women. Responses to go targets were faster following go cues compared with no-go cues and this effect was evident in both men and women. The study also found gender differences in subjective responses to alcohol. Men reported increased stimulation from alcohol and women reported increased sedation.

The gender difference in impaired response inhibition under alcohol could not be accounted for by differences in the BACs of men and women during testing. Gender groups displayed identical average BACs at the beginning of the test and nearly identical average BACs at the conclusion of the test. The within-gender variance in BAC was also nearly identical as shown by the standard deviations associated with the means. Men and women were also comparable in terms of age and were regular weekly social drinkers. On average, men reported higher alcohol consumption than women in terms of drinks per occasion and frequency of drinking occasions. This gender difference is common among young adult social drinkers (York & Welte 1994; Fillmore *et al.* 1997). However, it appears unlikely that drinking habits can account for the gender difference in impaired response inhibition under alcohol. Results showed that neither drinking habit measure was related to response inhibition under alcohol.

The gender difference in alcohol impairment also cannot be attributed to differences in drug-free levels of inhibitory control. Under placebo, gender groups were nearly identical in terms of their p-inhibition failures and

differed only when alcohol was administered. Subjects' reaction times are also unlikely to account for the gender difference in p-inhibition failures under alcohol. Faster reaction times allow less time to inhibit a response and thus could increase inhibition failures. However, a speed-accuracy trade-off cannot explain the increased p-inhibition failures under alcohol for men because their reaction times were unaffected by the drug.

Evidence that alcohol impairs the ability to inhibit pre-potent responses on the cued go/no-go task is consistent with other studies that have used this task in our laboratory (Abroms *et al.* 2003; Marczynski & Fillmore 2003a, 2003b). However, the specific mechanisms underlying this impairment remain unclear. Some neuropsychological accounts argue that inhibitory actions mediated by frontal lobe functions are especially sensitive to the disruptive effects of alcohol. (e.g. Jentsch & Taylor 1999; Lyvers 2000). However, others have implicated non-specific alcohol-induced constraints on information processing (Steele & Josephs 1990; Fillmore 2003). These information processing accounts suggest that alcohol reduces the capacity to process information so that increased information, such as that conveyed by conflicting cues, cannot be processed effectively leading to inappropriate responses. This explanation implies that the ability to inhibit a response is not especially vulnerable to the impairing effects of alcohol, but rather alcohol causes a general impairment of the ability to process and react appropriately to all environmental cues (i.e. cues to inhibit and to respond).

The finding of a gender difference in impaired response inhibition is new and is relevant to other research on alcohol effects on behavioral control in men and women. One other study compared alcohol effects on response inhibition in men and women and reported no gender difference (Mulvihill *et al.* 1997). That study differed from the present research in several respects. The

study did not match gender on BAC and assessed impairment across ascending and descending limbs of the blood alcohol curve. Also, response inhibition was measured using a stop-signal task. Like the cued go/no-go task, the stop-signal task measures behavioral control by the ability to execute and inhibit responses. However, unlike the cued go/no-go task, the stop-signal task does not include a cue-induced manipulation to increase response prepotency. Present findings from the cued go/no-go model suggest that gender differences in alcohol impairment of inhibitory control might be most evident in cases where there is a strong prepotency to respond. This finding also could explain why studies of aggressive behavior that involve the instigation of aggressive responses find that alcohol-induced aggression is more pronounced in men than in women (e.g. Giancola & Zeichner 1995; Hoaken & Pihl 2000).

The gender difference in response inhibition could also reflect differences in alcohol-induced arousal in men and women. Men reported increased stimulation and women reported increased sedation in response to alcohol. Studies typically find that alcohol exerts a biphasic effect on subjective states of arousal in which greater stimulant effects are reported during the ascending limb of the blood alcohol curve and increased sedation is reported during the descending limb of the curve (Martin *et al.* 1993). Evidence that men report greater stimulation than women could reflect a basic gender difference in the degree to which alcohol increases arousal that might also contribute to disinhibited behavior. Research on alcohol-induced aggression has shown that men who report greater subjective stimulation from alcohol also display more intense aggression under the drug (Giancola *et al.* 1998). The inhibition-impairing effect of alcohol displayed by men in the present study could be due, in part, to a gender-specific arousal response to alcohol that makes inhibiting a pre-potent response more difficult. A clearer understanding of the potential role of arousal could be gained by research that manipulates subjects' arousal to determine its influence on inhibitory control under alcohol.

The biological and psychological mechanisms underlying the gender difference in the present study are unknown and could involve gender-specific hormonal or other neurochemical effects that interact with alcohol to determine the behavioral response. Social and cultural learning also cannot be ruled out as a causal factor. For example, men and women differ in the types of effects that they expect from alcohol, and such expectations could influence behavior under the drug (Vogel-Sprott & Fillmore 1999). Although the exact causal factors remain unknown, the reductionist approach offered by the present research provides new insights into how alcohol can disrupt behavioral control in men and women at

a more fundamental level that involves basic inhibitory and activational mechanisms.

Acknowledgement

This research was supported by Grant R01 AA12895 from the National Institute on Alcohol Abuse and Alcoholism.

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