COGNITIVE AND BEHAVIOURAL ASPECTS

Conditioned Tolerance to the Effects of Alcohol on Inhibitory Control in Humans

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INTRODUCTION

There is considerable evidence that alcohol reduces the ability to inhibit inappropriate behaviour (e.g. Marczinski and Fillmore, 2003, 2005; Fillmore and Weafer, 2004) and that this mechanism may underlie some of the socially undesirable effects of alcohol, such as increased aggression and risky decision-making (Jentsch and Taylor, 1999; Lane et al., 2004; Rose and Duka, 2007). Moreover, disinhibition after consuming a small amount of alcohol may facilitate further intake of alcohol and contribute to binge drinking (Weafer and Fillmore, 2008).

The impairing effects of an acute dose of alcohol on inhibitory control have been well documented but little is known about how these effects might be modulated by the drinking context. Previous research, predominantly on laboratory animals, has established that learning plays an important role in modulating the effects of drugs according to the context in which a drug is regularly administered. Repeated administration of drugs over time often produces tolerance, whereby a larger dose of the drug may be required to elicit the same magnitude of effect as was initially produced: this tolerance may be more pronounced in those contexts in which the drug is usually administered than in different contexts (Siegell, 1975, 1976, 1977; Lé et al., 1979; Crowell et al., 1981; Dafters and Anderson, 1982; Rozin et al., 1984; White et al., 2002). Such processes might have important implications outside the laboratory. For example, Siegel et al. (1982) argued that conditioned tolerance to the effects of opiates might explain some cases of overdose toxicity among opiate abusers. Thus, heroin addicts might be at risk of ‘overdose’ if they take the drug in an environment different from the one in which they normally take it: the novel environment would fail to elicit the conditioned compensatory responses (CCRs) that would have emerged to counter heroin’s effects in the usual context of administration.

However, not all drug effects show such context-specific conditioned tolerance (Staiger and White, 1988). Here, we ask whether the place in which alcohol is repeatedly consumed can moderate the effect of alcohol on response inhibition through the development of conditioned tolerance in people. A few studies have examined the conditioned effects of alcohol on other aspects of cognitive function such as reaction time and vigilance (Shapiro and Nathan, 1986; McCusker and Brown, 1990; Remington et al., 1997; Birak et al., 2010). All but one employed an opportunistic design that takes advantage of natural associations that can arise between culturally defined drinking contexts and the taste and smell of alcohol. In one study, participants who consumed alcohol in an unusual context (an office) showed greater cognitive impairment than participants given the same dose of alcohol in a familiar context (a bar) (McCusker and Brown, 1990). Similarly, consumption of a novel alcoholic drink which has few prior associations with alcohol leads to greater impairment of cognitive function than is produced by consumption of a familiar alcoholic drink (Remington et al., 1997; Birak et al., 2010).

Shapiro and Nathan (1986) attempted to establish a conditioned association between alcohol’s effects and the drinking context by asking one group of participants to consume alcohol repeatedly in a ‘distinct’ setting and tonic in a ‘home’ environment (a second group were given the reverse pairings). On the test day, all participants were given alcohol in the ‘distinct’ setting. Alcohol given in the context previously associated with the non-alcoholic drink impaired vigilance performance more than when it was given in the alcohol-associated context. However, because participants received very different drinks in the two contexts and no attempt was made to disguise the presence of alcohol, the outcome may have been influenced by beliefs about the effects of alcohol. In addition, there was no evidence that alcohol produced an unconditioned effect to impair performance because prior to the test day the cognitive
tests had only been completed under the influence of alcohol in the alcohol-paired context.

We test for the first time whether tolerance to the effects of alcohol on response inhibition can be conditioned to contextual cues that have never previously been associated with alcohol. We chose to assess performance on two measures of response inhibition: a go/no-go task and a stop-signal task (SST). The conditioning contexts comprised test cubicles that were made distinct with the addition of visual and olfactory cues. Participants alternated between consuming alcohol in one context and placebo in another context over six conditioning sessions (three alcohol and three placebo sessions). At test, half of the participants consumed alcohol in a novel drink in the context previously associated with alcohol and the other half consumed an equivalent dose of alcohol in the context previously associated with placebo. Participants were tested on the same measures of response inhibition at each session to ensure that these procedures were not novel at test, and both groups were given alcohol in a completely novel beverage on the test day.

We predicted that alcohol would impair inhibitory responding, that tolerance would develop to this effect, and that participants who were given an alcoholic drink on a test session in the alcohol-paired environment would be less impaired than participants given alcohol in the placebo-paired environment.

METHODS

Participants
Twenty-four students (mean age 20.8 years, SD = 2.5 years, male n = 12) from the University of Birmingham were recruited to participate in a study advertised as looking at the effects of alcohol on cognition. Participants were recruited via posters on campus and compensated for their time with £45 cash (approximately $70 US). No participant had a history of alcohol-related problems, as determined by the University of Birmingham, School of Psychology Ethics Committee, and the study was conducted according to the ethical standards of the Declaration of Helsinki 1964.

Drinks
The alcohol drink was one part Tesco’s Imperial vodka (37% alcohol by volume), one part Manzana Verde (a non-alcohol apple schnapps drink, The LoNo drinks company, Cirencester, UK) and three parts Indian tonic water (Schweppes, UK). The placebo was one part Manzana Verde and four parts Indian tonic water. The novel drink given on the test day was one part vodka, four parts sparkling water (Spar, UK) and 10 ml of summer fruits squash drink (Spar, UK). The formulations of the two alcohol drinks were decided after extensive pilot work; the main alcohol drink was chosen because of the effectiveness of the placebo equivalent. The two alcohol drinks were successfully used in a previous study, which showed a good match for perceived presence of alcohol but a difference in terms of novelty (Birak et al., 2010). Alcohol doses were 0.65 g/kg body weight for males and 0.57 g/kg for females. Participants were presented with their drinks in three separate glasses to facilitate evenly paced drinking. The drink volume could vary across participants because of their different body weights; therefore, a number of different glass sizes were used to ensure that each participant drank from glasses that were approximately two-thirds full.

The test environments
The conditioned stimuli were provided by two test cubicles that were configured to be distinct from each other to facilitate discrimination and learning. They were similar in size, but one was painted black and the other white. They smelled differently due to the presence of olfactory cues generated by air fresheners. The fragrance of the air fresheners was chosen based on a pilot study that asked participants (n = 20) to rate four sample odours from the ‘Glade plug-in range’ (Attwood et al., 2010). Ratings were made using 100 mm visual analogue scales (VAS) with the anchors ‘not at all’ (0) and ‘extremely’ (100). The two fragrances chosen for the study were ‘Bamboo and White Fresa’ (added to the white cubicle) and ‘Smells of the Orient’ (black cubicle), on the basis that they were well-matched for pleasantness [t(19) = 0.22; P > 0.05], pungency [t(19) = 0.36; P > 0.05] and novelty [t(19) = 0.85; P > 0.05], yet were also considered relatively distinct (similarity score of 30 mm on a 100 mm VAS). To further differentiate the cubicles, they were furnished differently. The black cubicle contained a small table with a white-and-red checkered tablecloth, whereas the white cubicle had a large table with no cloth. The cubicles also displayed different posters on the wall, also chosen on the basis of a pilot study. The two best-matched but distinct posters were pictures of Neuschwanstein Castle, Germany and Bora Bora Island (91 × 61 cm), placed in the white and black cubicles respectively.

Cognitive tasks
CANTAB AGN
Participants were presented with a series of positive words (e.g. ‘joyful’, ‘warmth’ and ‘courage’) or negative words (e.g. ‘mistake’, ‘hopeless’ and ‘burden’) in the centre of the screen. Individual words were presented for 300 ms, with 900 ms between words. At the beginning of each block, participants were informed of the target valence for that block, either positive or negative, and told that they should respond to words of the target valence by pressing the right button of the press pad and that they should make no response to words of the distracter valence. Single words appeared on a computer screen, and participants were initially instructed to
respond to ‘happy words’ but not to ‘sad words’. After two word blocks requiring responses to happy (positive) words, the instructions changed so that the button was pressed after sad (negative) words. There were nine target items and nine distracter items within each block. Conditions were alternated in a PPNPNNPP pattern to create shift and non-shift response blocks. There were 10 blocks of 18 words, with a 900-ms pause between blocks. On each presentation of the task, the first two blocks were practice and not scored. The number of false alarms (incorrect responses) and misses (no response when one is required) were recorded along with the mean correct response times.

The CANTAB SST

First, participants carried out a simple choice reaction time task that served as a practice block. They were told that whenever a circle containing an arrow pointing to the left appeared in the centre of the monitor, they should press the left press pad button as quickly as possible with their left hand. Whenever the arrow inside the circle pointed to the right, they should press the right button as quickly as possible. There were 16 trials for the practice block; results for these were not analysed. In the second part of the task, participants were once again presented with the arrows pointing left or right, and they were instructed to press the relevant button as quickly as possible for each presentation unless there was an audible tone. They were informed that the tone was a stop signal, and that they had to prevent themselves from responding to the on-screen stimulus if it occurred. There were five assessed blocks of trials and each block contained four sub-blocks of 16 trials each. There were therefore 64 trials per block, and 320 in total. Within each test block, there were twelve ‘go’ trials and four ‘stop’ trials. The timing of each of the four auditory stop signals varied within each block to produce four levels of difficulty: greater difficulty reflected an increase in the interval between the ‘go’ and the ‘stop’ signal. The presentation order of trials at different levels of difficulty was pseudo-randomized to avoid anticipatory responding. Participants were told before they began not to wait for the tone but to respond as quickly as possible on the ‘go’ stimuli and to try to stop when they heard the ‘stop’ tone. They were given feedback after each block, and encouraged to be as accurate and fast as possible when pressing the buttons. Measures included correct choices for all ‘go’ stimuli and their reaction times, as well as the number of responses that participants failed to inhibit on the ‘stop’ signals and their reaction times.

Assessment of drink properties and beliefs about drinks

Participants completed sensory evaluations of the drinks to determine whether these variables were related to any of the effects that might arise. The taste properties ‘strength’, ‘pleasantness’, ‘sweetness’, ‘novelty’ and ‘bitterness’ were each rated using a 100-mm VAS with anchor points ‘low’ and ‘high’. At the end of the session, participants were asked whether they thought they had consumed alcohol or something else, and were asked to indicate how sure they were of this judgement by marking their level of confidence on a VAS (0 = ‘not at all confident’ and 100 = ‘extremely confident’).

Procedure

Conditioning sessions

Participants attended six conditioning sessions scheduled between 13:00 and 19:00 h on weekdays. All participants gave written consent to take part and were weighed so that alcohol doses could be calculated. Participants were asked to abstain from alcohol and any other drugs with sedative properties for at least 24 h before each session; they were also asked to abstain from eating for at least 3 h before the sessions. A breathalyser reading was taken to ensure that no alcohol had been taken recently. On the first session only, participants were given instruction on how to perform the cognitive task and allowed 10 min to familiarize themselves with the tasks by trying them for 5 min each. After this 10 min period, participants completed the two tasks in full: this comprised the pre-drink baseline performance test, and was repeated for each session. The two tasks took around 18 min to complete. After the baseline test, the researcher returned and presented the drinks. Participants were asked to take a sip from one of the three glasses and to rate the drink for taste. Participants were then asked to drink each glass over 7 min and to finish all of the drinks within 21 min. If the drinks had not been fully consumed, participants were asked to finish any remaining drink as quickly as possible. At 8 min post-consumption, participants began the cognitive tasks once more. The questionnaire asking about the participant’s beliefs about the drink type and its effects on the test variables was then completed. Each of the subsequent five sessions followed a similar procedure (without the initial 10 min familiarization period) but participants alternated between alcohol and placebo sessions. The orders of drug and test room were fully counterbalanced across the two groups as defined on the test session.

Test session

The procedure was exactly the same as for the conditioning sessions except that half of the participants were tested in their alcohol-paired room and the other half in their placebo-paired room, and they were given alcohol in a novel drink. Finally, participants were asked to complete a questionnaire asking what they believed the study to have been about, and asking if anything may have affected their performance. Participants were then given feedback about the study’s purpose before being paid and thanked for their time.

Analyses

Data from the conditioning sessions were analysed by repeated-measures two-way analysis of variance with Drink (alcohol/placebo) and Sessions (1, 2, 3; repeated for each drink type) as factors. Independent t-tests were used to test for differences between the group tested in the alcohol-paired context versus the group tested in the placebo-paired context. Independent t-tests were used to test for between-group differences in age, weight and drinking history. Where analyses of the session effect or interaction are not reported there were no significant or near-significant outcomes. Baseline performance scores were analysed in the same way as post-drink performance scores (despite being recorded before the drink manipulation) in order to check for any baseline effects that might contribute to the outcomes.
RESULTS

Participant characteristics

There were six men and six women in each test group. The group tested in the alcohol-paired context did not differ significantly from the group tested in the placebo-paired context in terms of age, weight or drinking history (Table 1). Similarly, breath alcohol levels did not differ significantly between the two groups, either over the conditioning sessions \[F(1,22) = 0.23; P > 0.05\] or on the final test session \([t(22) = 0.98; P > 0.05; \text{Table 1}]\).

Go/no-go task

Conditioning sessions

The number of false alarms recorded at baseline (before the drink was given) declined over sessions \([F(2,46) = 4.95; P < 0.05]\), but baseline performance did not differ between drink conditions, and the drink condition did not interact with session at baseline. However, after drink consumption, there was a significant effect of drink (more false alarms after alcohol than after placebo \([F(1,23) = 8.37; P < 0.01]\)), a significant decline in false alarms over conditioning sessions \([F(2,46) = 8.98; P < 0.01]\), and a significant interaction between drink and session on the ability to withhold responding \([F(2,46) = 4.35; P < 0.05]\): false alarms increased more after alcohol than after placebo, but this effect declined after Session 1 (Fig. 1). Paired-sample \(t\)-tests confirmed a significant difference between alcohol and placebo over the first two sessions \([\text{respectively: } t(23) = 3.08; P < 0.01; t(23) = 2.45; P < 0.05]\), but not on the third session \([t(23) = -0.91; P > 0.05]\). This profile is consistent with the development of tolerance to alcohol’s effects on false alarms. Table 2 summarizes the results for the other two AGN measures that did not show evidence of conditioned tolerance: numbers of ‘misses’ of ‘go’ stimuli, and response latencies for ‘go’ stimuli. Before the drink was consumed, there was a significant decline over sessions in the number of misses \([F(2,46) = 3.53; P < 0.05]\), but no effect of drink or interaction between the factors \((Fs < 1)\). After the drink, there were no significant main effects of alcohol or session \((Fs < 1)\), and although there was an interaction between the factors \([F(2,46) = 3.62; P < 0.05]\), the pattern was not consistent with the emergence specifically of tolerance to alcohol’s effects on misses: the alcohol effect was higher on Session 2 than on Sessions 1 and 3, and performance after placebo was worse on Session 3 than on the 2 previous placebo sessions, yielding an odd interaction profile. For response latency (Table 2), baseline scores showed no effect of session, drink or their interaction \((Fs < 1)\). However, after consumption of the drink, response latencies after alcohol were longer than after placebo \([F(1,23) = 10.54; P < 0.01]\), but there was no effect of session \([F(2,46) = 2.56; P > 0.05]\) and no interaction \([F(2,46) = 0.26; P > 0.05]\), again providing no indication of tolerance (Table 2).

Test day

At baseline, false alarm rates did not differ between participants tested in the alcohol-paired context and those tested in the placebo-paired context \([t(22) = 1.32; P > 0.05]\). However, after consuming alcohol, the number of false alarms produced in the placebo-paired context was significantly greater than in the alcohol-paired context \([t(22) = -2.49; P < 0.05; \text{Fig. 1}]\). In order to confirm that the between-group difference on the test session did not reflect pre-existing group

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Table 1. Means (± SD) of participant characteristics for those given alcohol on the test day in the alcohol-paired or the placebo-paired contexts, and breath alcohol levels in micrograms per 100 ml

<table>
<thead>
<tr>
<th>Participant characteristic</th>
<th>Placebo-paired context mean ± SD</th>
<th>Alcohol-paired context mean ± SD</th>
</tr>
</thead>
<tbody>
<tr>
<td>Age (years)</td>
<td>21 ± 2.8</td>
<td>21 ± 2.3</td>
</tr>
<tr>
<td>Height (cm)</td>
<td>174.1 ± 11.5</td>
<td>171.5 ± 9.8</td>
</tr>
<tr>
<td>Weight (kg)</td>
<td>75.4 ± 18.1</td>
<td>65.6 ± 15.6</td>
</tr>
<tr>
<td>Number of years drinking</td>
<td>6 ± 2.9</td>
<td>5 ± 2.9</td>
</tr>
<tr>
<td>Number of alcohol units</td>
<td>22.8 ± 8.3</td>
<td>17.8 ± 7.8</td>
</tr>
<tr>
<td>Breath alcohol level 25</td>
<td>0.47 ± 0.15</td>
<td>0.55 ± 0.21</td>
</tr>
<tr>
<td>min after alcohol</td>
<td></td>
<td></td>
</tr>
<tr>
<td>consumption (µg/100 ml)</td>
<td></td>
<td></td>
</tr>
</tbody>
</table>

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![Fig. 1](image-url) Mean number of false alarms produced on the CANTAB AGN task over three alcohol-paired and three placebo-paired conditioning sessions (left panel) and on the test for conditioned responding (during which all participants were given alcohol; right panel). Bars represent ±1 SEM.
differences in their reactions to alcohol, the two groups were compared for their responses to alcohol on the final conditioning session: there was no significant difference between them in terms of false alarms on the third conditioning session during which alcohol was given [$t(22) = 0.5; P > 0.05$]. Finally, in line with the lack of tolerance effects on the conditioning sessions, no significant effects were found at test for number of stimuli missed or response latency (Table 2).

Stop-signal task

Conditioning sessions

1. Incorrect responses to ‘go’ stimuli: At baseline, before consuming the drink, the number of incorrect responses to ‘go’ stimuli increased over sessions [$F(2,46) = 3.54; P < 0.05$], but there was no effect of drink type and no interaction between the two factors ($Fs < 1$). Alcohol increased the number of incorrect responses to the ‘go’ stimuli compared with placebo [$F(1,23) = 10.58; P < 0.01$], and the number of errors increased over the three sessions in both conditions [$F(2,46) = 0.82; P < 0.01$]. There was no interaction between drink and session [$F(2,46) = 0.28; P > 0.05$] (see Table 2).

2. Reaction times to ‘go’ stimuli: Before drink consumption (baseline), reaction times to ‘go’ stimuli were not significantly influenced by session or drink type, and there were no interactions between these factors (all $Ps > 0.1$). After the drink, reaction times to ‘go’ stimuli decreased over sessions [$F(2,46) = 5.89; P < 0.01$], but there was no significant difference between the alcohol and placebo conditions [$F(1,23) = 1.31; P > 0.05$], and the two factors did not interact significantly [$F(2,46) = 0.72; P > 0.05$] (see Table 2).

3. Response inhibition following ‘stop’ signals: There were no baseline effects of session, drink or their interaction ($Ps > 0.1$). However, after alcohol, participants failed to inhibit responses after the ‘stop’ signal more frequently than after placebo [$F(1,23) = 7.02; P < 0.05$]. There was no significant effect of session [$F(2,46) = 0.08; P > 0.05$] and no significant interaction [$F(2,46) = 0.03; P > 0.05$] for response inhibition (see Table 2).

4. Reaction times following ‘stop’ signals: There were no baseline effects of session, drink or their interaction ($Ps > 0.1$). Post-consumption, there was no significant effect of drink [$F(1,23) = 3.12; P > 0.05$]; reaction times declined significantly over sessions [$F(2,46) = 3.41; P < 0.05$], but there was no interaction between drink and session [$F(2,46) = 0.16; P > 0.05$] (See Table 2).

Test day

No effects were found for any of the four measures (Table 2), either at baseline or after drink consumption [for all comparisons: $ts(22) < 1.3; Ps > 0.1$].

Taste

After the first sip during conditioning, participants rated the alcohol drink stronger than the placebo drink [$t(23) = 3.6; P < 0.05$; mean rating (0–100) for placebo = 54.7 (SD = 24), mean rating for alcohol = 68.8 (SD = 21)]. There were no significant differences between the drinks for ratings of
believed that they had consumed placebo-paired context and two in the alcohol-paired context below 50%.

paired context rated their confidence in their choice just on Sessions 1, 2 and 3, respectively. Typically, those who across conditioning sessions (nine, six and seven participants).

dence was not initially as high. The proportion reporting alcohol on each conditioning session, although their confi-

Our results confirm the robust unconditioned disinhibitory context in which they had not been given alcohol previously.

test contexts (Table 3). None of the participants guessed the beverage they believed they had consumed and their mean ratings (± SD) for how confident they were in their belief (0–100 mm), by group and session.

<table>
<thead>
<tr>
<th>Session</th>
<th>Beverage believed to have been consumed</th>
<th>Placebo-paired context</th>
<th>% Confident mean ± SD</th>
<th>Alcohol-paired context</th>
<th>% Confident mean ± SD</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td></td>
<td></td>
<td>n</td>
<td></td>
<td>n</td>
</tr>
<tr>
<td>Session 1</td>
<td>Alcohol</td>
<td>9</td>
<td>47 ± 27</td>
<td>24</td>
<td>84 ± 16</td>
</tr>
<tr>
<td></td>
<td>Other</td>
<td>15</td>
<td>73 ± 23</td>
<td>0</td>
<td>0</td>
</tr>
<tr>
<td>Session 2</td>
<td>Alcohol</td>
<td>6</td>
<td>29 ± 19</td>
<td>24</td>
<td>78 ± 20</td>
</tr>
<tr>
<td></td>
<td>Other</td>
<td>18</td>
<td>77 ± 19</td>
<td>0</td>
<td>0</td>
</tr>
<tr>
<td>Session 3</td>
<td>Alcohol</td>
<td>7</td>
<td>34 ± 34</td>
<td>24</td>
<td>84 ± 19</td>
</tr>
<tr>
<td></td>
<td>Other</td>
<td>17</td>
<td>89 ± 10</td>
<td>0</td>
<td>0</td>
</tr>
<tr>
<td>Test session</td>
<td>Alcohol</td>
<td>11</td>
<td>91 ± 9</td>
<td>10</td>
<td>91 ± 10</td>
</tr>
<tr>
<td></td>
<td>Other</td>
<td>1</td>
<td>96</td>
<td>2</td>
<td>14 ± 13</td>
</tr>
</tbody>
</table>

‘pleasantness’, ‘sweetness’, ‘novelty’ or ‘bitterness’ [for all: $t(23) < 1.3; P > 0.05]$. On the final test session, there were no significant effects of group on any of the initial-sip taste ratings [for all: $t(22) < 1.47; P > 0.05$].

Beliefs about the drinks consumed

In the post-session questionnaires, all participants reported that they had consumed alcohol each time that they had been given the drink in the alcohol-paired context (Table 3). They were also very confident in their decisions when selecting ‘alcohol’ as the drink given in the alcohol-paired context. In the placebo-paired context, the majority of participants believed that they had consumed something other than alcohol on each conditioning session, although their confidence was not initially as high. The proportion reporting ‘alcohol’ in the placebo-paired context remained similar across conditioning sessions (nine, six and seven participants on Sessions 1, 2 and 3, respectively). Typically, those who thought they had consumed alcohol when in the placebo-paired context rated their confidence in their choice just below 50%.

On the test day, all of the participants except one in the placebo-paired context and two in the alcohol-paired context believed that they had consumed ‘alcohol’ (Table 3). Confidence judgments concerning the administration of alcohol were also very high and very similar across the two test contexts (Table 3). None of the participants guessed the purpose of the study.

**DISCUSSION**

For the first time, we provide evidence for conditioned tolerance to the effects of alcohol on inhibitory control. Responding on a go/no-go task that required the inhibition of a simple behavioural response was initially impaired by alcohol when it was consumed in a novel context, but this effect diminished over subsequent sessions in the same context. On the test day, participants who were given a novel alcoholic drink in the context in which they had prior experience of drinking alcohol were significantly less impaired than participants who consumed the same drink but in a context in which they had not been given alcohol previously. Our results confirm the robust unconditioned disinhibitory effects of alcohol and show for the first time that these effects can be moderated by drinking context.

The most likely explanation for the group difference in response to alcohol on the go/no-go task on the critical test session is that participants learned an association between the context and the effects of alcohol, leading to the development of a CCR (Siegel, 1977). Thus, on the test day, when participants received a novel alcohol drink in the alcohol-associated context, their acquired tolerance countered the effect of alcohol on inhibitory control. On the other hand, as the placebo-paired context was not associated with the effects of alcohol, participants in that context were more susceptible to the alcohol effect because no CCR had been acquired to oppose the effects of alcohol. This interpretation, invoking the emergence of a context-specific CCR through Pavlovian conditioning, would be strengthened if further studies could show that the CCR conforms to the principles of associative learning, such as by demonstrating extinction if the drug-context association is unlearned.

Research has suggested that the cognitive effects of alcohol can be modulated by previously established, alcohol-associated cues (e.g. McCusker and Brown, 1990; Remington et al., 1997; Birak et al., 2010), but few studies have examined how alcohol’s cognitive effects may condition to cues that lack prior associations with alcohol. A previous study by Shapiro and Nathan (1986) indicated that alcohol’s effects on vigilance were weaker in an alcohol-paired context compared with a placebo-paired context, but the influence of expectancy effects cannot be ruled out, and performance over the conditioning sessions was not measured in both pairing groups and so could not indicate the development of conditioned tolerance. Our results provide the clearest evidence to date of context-specific conditioned tolerance to the effects of alcohol on cognition, and they strongly suggest that such tolerance reflects the emergence of a CCR. The effect of context cannot have been due to differences in absorption or metabolism of alcohol because all participants received the same novel alcohol drink at test, and breath alcohol levels were not significantly different in the alcohol-paired context versus placebo-paired context. All participants received exactly the same exposure to the task procedures during training, and all of the participants on the test day were tested in exactly the same way, regardless of group, with the only difference being the room in which they received the novel alcohol drink. An explanation for the response profile in terms of an effect on explicit expectancies is also unlikely for several reasons. First, participants’ beliefs about what they had consumed on each session show that between 6 and 9 of the 24 participants thought that they had been given alcohol on each session in the placebo-paired room. Second, all of the participants believed that the study simply tested performance on cognitive tasks after consuming alcohol. Third, on the critical test day, nearly all of the participants in both groups assumed that they had been given alcohol, and there were no differences between the two test groups in terms of their ratings of the novel drink for strength, pleasantness, sweetness, bitterness or novelty. However, one potentially anomalous finding in relation to the emergence of a CCR is the absence of any observable effect on baseline performance, before alcohol is administered, on the test session and/or on the later conditioning sessions in the alcohol-paired context.
Conventionally, a conditioned response often becomes apparent as an anticipatory response, detected in advance of the US. It may be that the false alarm rate at baseline is simply too low to be able to detect significant improvement by the CCR, and that it is necessary for the error rate to be driven up by alcohol in order that any effect of the CCR be apparent (i.e. there was a ‘floor’ effect). Across baseline sessions (and after placebo) average false alarm rates consistently remained in the range of 4–6; this level of performance may not allow scope for a CCR to be revealed. Alternatively, the CCR may only emerge when the full stimulus complex is present, incorporating the processes involved in the administration of the drink. This issue deserves further examination.

The SST produced different results from those obtained using the go/no-go task. In line with previous studies, it was sensitive to the unconditioned effects of alcohol (Mulvihill et al., 1997; Ramaekers and Kuypers, 2006). However, there was no obvious tolerance to alcohol’s effects on performance, which explains the absence of a CCR at test: a CCR is only likely to be apparent if prior tolerance is evident. One possible reason for the different effect profiles for the two tasks over conditioning may be their different levels of complexity. While both tasks require participants to respond to stimuli as quickly as possible, the go/no-go task requires participants to concentrate simply on responding or not responding. Thus, participants were required to process whether the words seen on screen matched the target words that they were permitted to respond to (press right button) or were distractor words and inhibit their response (refrain from pressing the right button). On the other hand, the SST requires participants to concentrate on making the correct response to the ‘go’ stimuli (i.e. left or right press pad button) as well as then inhibiting responses upon presentation of the ‘stop’ signal. The results from the SST indicated that participants adopted very different strategies compared with the go/no-go task: gains in response speed were traded off against an increasing numbers of response errors over sessions, and there was no indication that performance measures had stabilized by the time of the test for conditioned responding.

The contrast between the outcomes on the two tasks suggests that although conditioned tolerance to the disinhibitory effects of alcohol can develop, it is not readily observed if complex, demanding tests of inhibitory control are carried out under the influence of alcohol. The different levels of difficulty associated with the two tasks are supported by their different ratios of target to distracter items. The go/no-go task incorporated a 1:1 ratio of target items (‘go’ stimuli) to distracter items (‘no-go’ stimuli). However, the SST effectively utilized a 3:1 ratio of ‘go’ stimuli to ‘stop’-signalled stimuli. The substantially higher proportion of stimuli requiring a response in the SST makes the inhibition of responding much more challenging. Additional conditioning trials might be necessary for conditioned tolerance to emerge in these circumstances. The finding that there was no indication of any decline whatsoever in alcohol’s effects on errors in the SST over three sessions suggests that many more sessions would be necessary to reveal tolerance development (and thus a CCR) for this task. Therefore future studies might more profitably examine the potential for conditioned tolerance in the SST by altering the ratio of target to distracter stimuli rather than by extending the number of conditioning sessions substantially. Other aspects of the procedure that could be amended in a future study include adding a measure of intoxication, and perhaps using the Positive and Negative Affect Schedule (Watson et al., 1988) to test whether any negative affect emerges in the placebo-paired context. The practical difficulties and commitment of time associated with running such studies might also favour the use of a more homogeneous sample, in terms of drinking habits and stricter control of food intake and its timing.

In summary, we have shown that the repeated pairing of alcohol’s effects with a particular context produced conditioned tolerance to alcohol’s effects on a simple test of behavioural inhibition. The results are consistent with the findings of conditioned tolerance to some of the physiological effects of alcohol in humans, such as its effects on heart rate (Dafters and Anderson, 1982) and skin conductivity (McCaul et al., 1989). One implication of conditioned tolerance to alcohol’s effects on inhibitory responding is that consumption of alcohol in a novel context, for example in an unfamiliar place, may disrupt inhibitory control, which might increase the likelihood of undesirable behavioural consequences.

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REFERENCES


