



THE EFFECT OF DRINK FAMILIARITY ON TOLERANCE TO ALCOHOL

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Abstract — Cues associated with familiar alcoholic drinks such as beer may, through repeated association with the unconditioned stimulus properties of alcohol, acquire the status of classically conditioned stimuli. It has been proposed that such drug-related conditioned stimuli mediate drug tolerance. Thus, the aim of the present experiment was to test this proposition on cognitive, subjective, and psychophysiological indicators of alcohol tolerance using human subjects. Two groups of subjects received alcohol in the form of a familiar drink (beer) or an unfamiliar drink (blue peppermint mixture). Both drinks contained the same dose of alcohol and were consumed at the same rate. Although conditioned heart rate and skin conductance responses occurring while subjects looked at and tasted the test drinks were weak, there were strong indicators of conditioned tolerance on the performance measures following consumption. Subjects who consumed the unfamiliar drink were significantly poorer on cognitive and motor tasks, and they rated themselves more intoxicated than did those who consumed the familiar drink. *Copyright © 1996 Elsevier Science Ltd*

INTRODUCTION

Because many drugs have powerful discriminative and hedonic effects, they have the capacity to act as Pavlovian unconditioned stimuli (US). Thus, any stimulus that is a reliable predictor of such a drug has the potential to act as a Pavlovian conditioned stimulus (CS). Once such a stimulus is established as a CS, its presentation will result in conditioned responses (CR). This process of classical conditioning may have implications for the regulation of drug intake, and there are three general theoretical positions with respect to the ways that intake might be mediated. The first proposes that a drug-based CR in some way directly alters the motivation for the drug on which it is based (e.g., Stewart, de Wit, & Eikelboom, 1984; Wikler, 1948). The second suggests that the presence of a drug CS can increase tolerance to a drug's effects (e.g., Baker & Tiffany, 1985), and there is evidence that raised tolerance to the effects of a drug is associated with increased risk of drug use and dependence (Schukit, 1984, 1985). Third, Siegel (1975; see Siegel, 1989, for review) has argued that a single classical conditioning process may underlie both increases in drug use motivation and tolerance to a drug in the presence of a drug's CS. Siegel proposed that the CR elicited by a drug CS acts to oppose the drug's effects, and this opponent process resembles a state in which drug use motivation is enhanced. For example, the opponent process may resemble a drug-withdrawal state (Hinson & Siegel, 1980).

A number of studies have investigated the role of classical conditioning processes in human subject's tolerance to alcohol (see Goudi and Demellweek, 1986, for a review). Of these, some have examined subject's responses to alcohol cues with the aim of detecting the occurrence of conditioned opponent processes as putative mediators of alcohol tolerance. To study the role classical conditioning plays in mediating tolerance

to alcohol, both Dafters and Anderson (1982) and Shapiro and Nathan (1986) devised studies in which subjects repeatedly consumed both alcoholic and soft drinks. Alcohol was always consumed in one distinctive physical environment, and the soft drink was consumed in a noticeably different environment. It was hypothesised that these different contexts would act as CSs supporting differential conditioning. Following the conditioning procedure, tolerance to alcohol was tested in the soft drink context (i.e., in the absence of the usual environmental cues). Similar effects were observed in both studies.

In Dafters and Anderson's experiment, alcohol caused greater increases in subject's heart rate (HR) when it was administered in the soft-drink context. Increased HR is a drug-like effect, which can be presumed to be reduced by a conditioned opponent process present in the alcohol-related context. Shapiro and Nathan found a similar pattern but with behavioural measures. Alcohol administered in a soft-drink context impaired subject's performance on a cognitive vigilance task more than did alcohol administered in the context where it had previously been experienced.

Shapiro and Nathan also carried out a second test session in which a soft drink was given in alcohol-related and neutral contexts. Under these conditions, subjects performed better on the cognitive vigilance task in the alcohol-related context than when the soft drink was given in its usual environment. These data provide some support for hypothesising a conditioned opponent process, mediating tolerance to both the physiological effects and the cognitive performance-impairing effects of alcohol.

McCusker and Brown (1990) also assessed tolerance to the effects of alcohol by presenting it in different contexts. Rather than carrying out an explicit conditioning procedure, the design of this study took advantage of subjects' assumed extra-experimental conditioning histories with alcohol. Thus, one group of subjects was given alcohol in a familiar form and situation (lager in a simulated bar), while the other group was administered the same dose of alcohol in a novel form and unusual context (mixed in carbonated water and consumed in an office setting). Subjects in the former group were significantly less impaired by alcohol on subsequent cognitive and motor test tasks than were the latter subjects. Although a third (placebo) group that had received non-alcoholic lager in the bar setting failed to show superior performance on these tests, which might have been considered as further evidence of conditioned opponent processes, some such evidence was found on HR data. Specifically, HR fell following placebo administration, thus replicating previous findings in other opportunistic (e.g., Newlin, 1985) and conditioning (e.g., McCaul, Turkkan, & Stitzer, 1989a; Staiger & White, 1988) studies.

One problem with the opponent process account of tolerance is that there have been many demonstrations of drug-like, rather than drug-opposite, physiological responses to alcohol cues (e.g., see Drummond, Cooper, & Glautier, 1990; Niaura et al., 1988, for recent reviews). Some of these inconsistencies may in part be explicable in terms of the way in which the cues are presented. For example, Staiger and White (1988) found decreases in HR only when an alcohol-associated drink was presented in an alcohol-associated environmental context; the same drink consumed in neutral context produced increases in HR. Similarly, Glautier, Drummond, and Remington (1992) found an effect of the mode of presentation of the cue on the directionality of responses to alcohol cues. When alcohol-associated drinks were held and smelled, skin conductance (SC) increased in comparison to the response to a neutral drink, but the opposite pattern was observed when the comparison drinks were actually consumed.

The aim of the present experiment was to examine further the effect of alcohol-

related cues on tolerance to a dose of alcohol. The study focused on behavioural and subjective indicators of tolerance, as well as on physiological changes. Rather than investigating the role of cues emanating from the physical context (cf. McCusker & Brown, 1990), we examined the role of cues arising directly from the physical properties of the test drinks themselves. The design of the study involved two groups of subjects who were presented with alcohol in the form of a familiar drink (beer or lager) or an unfamiliar drink (a blue peppermint mixture). Both drinks contained the same dose of alcohol and were consumed at the same rate. Following consumption, subjects carried out cognitive and motor tasks and rated their level of intoxication. In addition, because earlier research (Glautier et al., 1992) suggested that the mode of presentation of alcohol-related cues might mediate physiological reactivity to the presentation of the drinks, we monitored subject's HR and SC levels before they consumed their drinks. Responses on looking at and on tasting the drinks were studied. In accordance with a conditioning model of alcohol tolerance, it was predicted that the effects of alcohol would be smaller in those subjects for whom previously established CSs accompanied alcohol consumption.

M A T E R I A L S A N D M E T H O D S

Subjects

Twenty male subjects attending courses at Southampton University (UK) were recruited following their response to a posted notice asking for volunteers to take part in an experiment investigating tolerance to alcohol. Of these 20 subjects, five dropped out before their test session and were replaced by additional respondents. The average age of the 20 subjects who completed the study was 21.75 years (range 18–25), and their average weekly alcohol consumption was 29.5 standard units (range 15–40) (one standard unit = 8 g ethanol). A history of drinking problems, serious physical illness, psychiatric illness, or taking any medications at the time of the experiment were used as exclusion criteria, although no subjects were excluded on these grounds. Subjects were paid £4 (≈\$1.50) on completion of the experiment.

Materials, measures, apparatus, and setting

The experiment was carried out in a sound-insulated psychophysiological recording room measuring approximately 2.5 m × 2.5 m. During the experiment, subjects sat at a table upon which rested an RM Nimbus PC-286 computer, mouse, monitor, and loudspeaker unit, along with the questionnaires and writing materials to be used in the session. A video camera permitted the experimenter to observe the subjects from an adjacent room during the sessions, and a microphone and amplifier allowed instructions to be given to the subject via the loudspeaker.

The experimenter's room housed a Grass Model 7B Polygraph that received inputs from silver/silver chloride SC and electrocardiogram (ECG) electrodes attached to the subject. Commercially available KY jelly was used as the electrolyte, and the subject's skin was cleaned with surgical spirit before attaching the electrodes. Skin conductance was recorded from the palmar surface of the first and second fingers of the subject's non-dominant hand. The ECG was recorded from left calf, and left and right cubital fossae. Heart rate was derived from the ECG signal.

Psychological function was measured using two tests. First, hand-eye coordination was assessed using a computerised version of a pursuit rotor task especially designed for this study. Subjects used the mouse to control the position of a cross displayed on

the monitor. The aim was to keep the cross on a rapidly moving circle. Second, cognitive function was assessed using a word-search task. Subjects were presented with a grid of jumbled letters (16 by 16) that hid 32 common words spelled either forward or backward in horizontal, vertical, or diagonal directions, along with a numbered list of the hidden words. The dependent variable of interest was the number of words found in the sequence listed.

Subjective intoxication was assessed by three questions. Subjects responded on a 5-point scale to the statements: (a) "I feel intoxicated now;" (b) "The alcohol impaired my ability to do the preceding word-search task;" and (c) "The alcohol impaired my ability to do the preceding computer task." The five responses were: strongly agree, agree, don't know, disagree, and strongly disagree. Strongly agree scored 4 and the other responses were scored in a descending sequence such that strongly disagree scored 0. The sum of the scores (maximum 12) on each of these scales was recorded.

Alcohol was given at the single dose of 0.65 g/kg body weight. In the case of the familiar drink (FD), the dose was administered using McKewan's Export Beer (4.5% ethanol by volume) or Carling Black Label lager (4% ethanol by volume), depending on the subject's preference. The unfamiliar drink (UD) was a mixture of Sainsbury's Own Vodka (37.5% ethanol by volume) and tonic water, to which was added 20 drops of Sainsbury's Own peppermint food flavouring and 10 drops of Sainsbury's Own blue food colouring. The volume of tonic water was varied to make up 1300 ml, the approximate volume required to reach the same alcohol dose when the familiar drinks were used. All drinks were served in pint glasses and were brought to subjects hidden in a box placed on the table in front of them.

Procedure

Subjects were screened on initial contact to ensure they met the entry criteria described above, and a preliminary meeting was arranged at which the procedure was explained. Subjects were asked not to smoke, eat, or drink for 1 h before the experimental session, and not to take any alcohol during the whole of the day prior to the session. They were also warned that the drinks they would be given during the session would make them intoxicated and were therefore advised not to drive or undertake any activity that would be dangerous while they were impaired. They were told that the £4 payment was to cover the cost of a taxi fare home after the session. Finally, directions to the laboratory and a summary sheet were given to subjects, and the session date was arranged.

All sessions took place at 1500 h. On arrival at the laboratory, subjects signed a consent form, were weighed without shoes or coat, and were then seated and connected to the physiological recording apparatus. Subjects then completed a single 30-sec practice trial on the computer tracking task and filled out a questionnaire asking about their recent drinking habits. While this was occurring, the experimenter retired to an adjacent room, randomly assigned the subject to either FD or UD conditions, and measured out the required quantity of either drink.

A 10-min stabilization period for physiological recording occurred before the experimenter re-entered the subject's room and placed the box containing the hidden drink on the table beside the subject. The experimenter withdrew again, and a 2-min SC and HR baseline was recorded. At this point, subjects were told to open the box and place the drink on the table in front of them. They were asked to look at and think about the drink while a further 2-min period ensued (the LOOK period), during which additional recording of SC and HR was obtained. Subjects were then told to take four

small sips of the drink, each at 30-sec intervals. Again, SC and HR data were obtained during this 2-min period (the TASTE period). At this point, they were instructed to ingest all of the drink within 15 min. If a subject had not finished the drink within 13 min they were told to finish in the next 2 min.

Immediately following consumption of the drink, subjects were given two 30-sec trials on the tracking task, and average percentage time on target was recorded. This was followed by the word-search task, during which subjects were required to find as many of the hidden words as possible in the order in which they were listed. The number of words found during the 10 min allocated for the task was recorded. Finally, subjects completed the subjective-state questionnaire before being disconnected from the apparatus, debriefed, and escorted to a waiting taxi.

Data analysis

Subjects in the FD and UD conditions were compared with each other in terms of age and weekly alcohol consumption using independent *t*-tests. For both physiological variables, average change from baseline was calculated for the 2-min LOOK and TASTE periods. In addition, peak changes during each 30-sec period following a sip of the drink were computed. These change scores in FD and UD conditions were analysed using two mixed-design analyses of variance (ANOVAs). The FD and UD was a between-subjects factor in both analyses, but the repeated measures within-subjects factors differed. In the first analysis, sight versus taste was the within-subjects factor, whereas in the second analysis the peak change in response to each of the four sips was the within-subjects factor. A significant interaction in the analysis of peak changes was followed up using independent *t*-tests. Measures of psychological function (tracking and word search) and subjective state were compared in FD and UD conditions using independent *t*-tests.

RESULTS

There were no differences between FD and UD conditions in terms of subjects' age and weekly alcohol consumption. The data are shown in Table 1.

Averaging over the LOOK and TASTE periods both SC and HR increased (SC: $F(1,18) = 16.84, p < .01$; HR: $F(1,18) = 5.47, p = .03$) but there was no main effect of drink familiarity (SC: $F(1,18) < 1$; HR: $F(1, 18) < 1$). On SC there was no main effect of stimulus period (LOOK 'v' TASTE) on change from baseline ($F(1,18) = 1.93, p = .18$), whereas for HR the change from baseline was much higher during the TASTE

Table 1. Means, SEMs, *t* and *p* values for comparisons of familiar and unfamiliar drink conditions on the different measures of intoxication and on subject intake variables

	FD Mean (SEM)	UD Mean (SEM)	<i>t</i> 18 <i>df</i>	<i>p</i>
Tracking (% time on target)	65.2 (3.35)	43.4 (1.49)	5.97	<.01
Word search (no. words found)	17.0 (1.27)	9.6 (0.93)	4.71	<.01
Intoxication rating	5.0 (0.68)	7.3 (0.47)	2.77	<.02
Age (years)	21.6 (0.54)	21.9 (0.53)	0.40	.70
Weekly alcohol consumption (8-g units)	30 (2.9)	29 (2.7)	0.25	.80

Notes. FD = familiar drink; UD = unfamiliar drink.

period ($F(1,18) = 51.51, p < .01$). There were no significant interactions between drink familiarity and the different stimulus time periods (SC: $F(1,18) < 1$; HR: ($F(1,18) = 1.65, p = .22$).

Turning to peak changes in response to successive sips in the TASTE period, ANOVA revealed that the main effect of drink familiarity failed to reach significance on either SC or HR over the course of the four successive 30-sec epochs (SC: $F(1,18) = 2.40, p = .13$; HR: $F(1,18) = 2.03, p = .17$). There was, however, a main effect of epoch on both measures (SC: $F(3,54) = 25.67, p < .01$; HR: $F(3,54) = 47.10, p < .01$), which was moderated by a significant interaction between epoch and drink familiarity on SC ($F(3,54) = 7.92, p < .01$), and a near significant interaction between epoch and drink familiarity on HR ($F(3,54) = 2.40, p = .08$). These interactions are displayed in Figures 1 and 2. Subjects in the UD condition showed larger SC changes early in the 2-min TASTE period and smaller HR increases during the second 30-sec epoch than did subjects in the FD condition. The interactions were explored further using *t*-tests; for SC, the FD and UD conditions differed significantly during the first 30-sec epoch ($t(18) = 2.27, p < .04$) but not during the remainder (p 's $> .1$). For HR, the FD and UD conditions differed significantly during the second 30-sec epoch ($t(18) = 3.51, p > .01$) but not during the others (p 's $> .1$).

Subjects in the UD condition performed significantly more poorly on both the tracking and word-search tasks, and they reported significantly higher levels of intoxication, than did subjects in the FD condition. Summaries of the analyses of these measures appear in Table 1, which shows the means, standard errors, *t* and *p* values for the UD and FD groups.

DISCUSSION

The main result of this experiment is the striking differences in the motor, cognitive, and subjective effects of alcohol given in different vehicle mixtures. When alcohol was

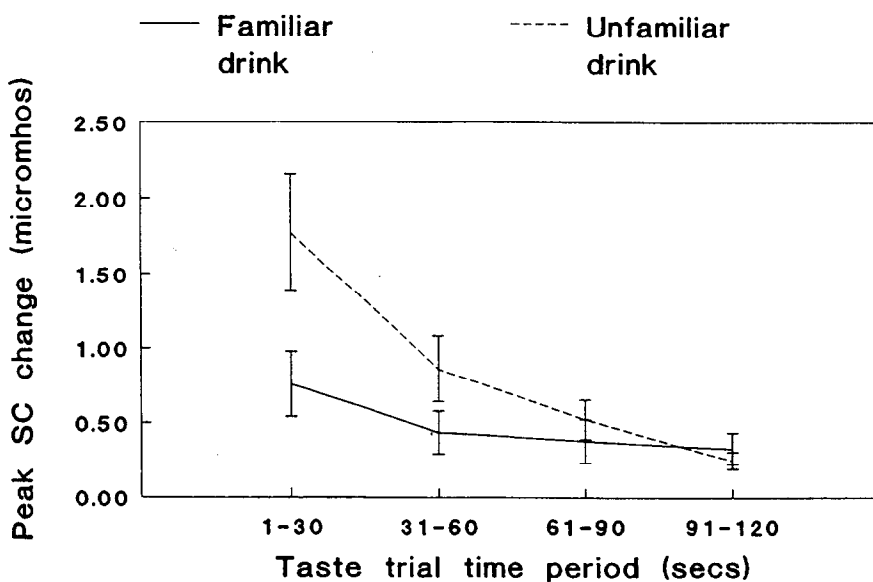


Fig. 1. Changes from baseline on SC during successive 30-sec epochs of the taste periods. Error bars cover 2 SEM units.

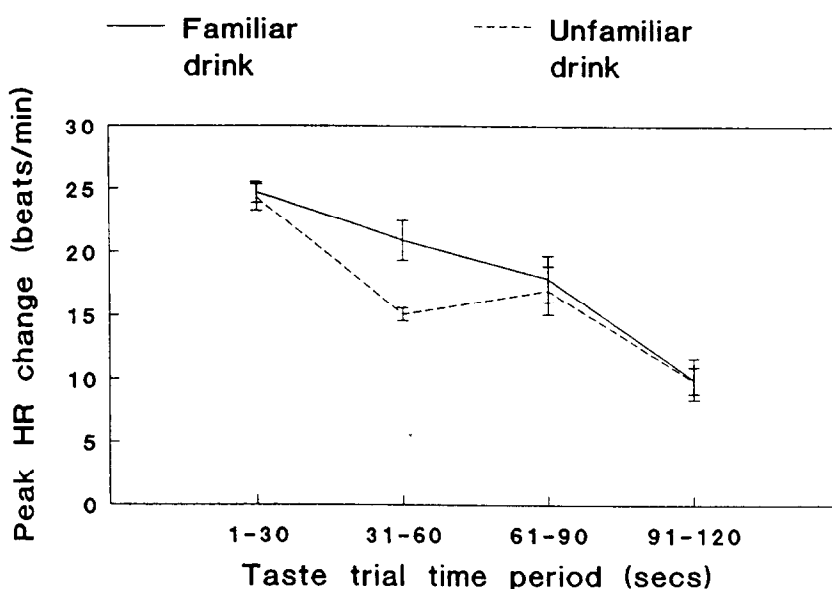


Fig. 2. Changes from baseline on HR during successive 30-sec epochs of the taste periods. Error bars cover 2 SEM units.

given in the form of a familiar drink, the cues present can safely be assumed to have had extensive extra-experimental history of pairing with alcohol. Under these conditions, subjects were less impaired on the motor and cognitive tasks and rated themselves as less intoxicated than when the same dose of alcohol was presented in an unfamiliar drink. Differences between groups was highly reliable owing to the small within-group variances on these measures. The small within-group variances may be characteristic of the particular measures we used, but it is likely that the overall homogeneity of the sample in terms of age, sex, drinking habits, social class, etc., contributed to this effect. The results support the view that cues accompanying alcohol may serve to mediate tolerance to its effects.

Although the present data replicate the results of other studies of this kind (e.g., Dafters & Anderson, 1982; McCusker & Brown, 1990; Shapiro & Nathan, 1986) they also extend them. These earlier experiments indicated that the environmental context of alcohol delivery was important, but our effects did not require a contextual manipulation. In a neutral laboratory setting, differences relating only to the sensory cues associated with the drinks themselves (sight, smell, taste, etc.) were sufficient to produce marked effects on motor and cognitive performance, and on perceived intoxication.

We noted at the beginning of this report that some theoretical models of classical conditioning and drug tolerance held that conditioned opponent processes were responsible for conditioned tolerance (Siegel, 1989), and that some experiments had provided evidence for these opponents on physiological measures (e.g., McCaul et al., 1989a). Analysis of SC responses to individual sips of the different drinks (Fig. 1) raises the possibility of physiological opponent processes because the response to the alcohol-associated drink (FD) was lower than that to the control drink. This stands in contrast to the results on HR where, if anything, the HR response to the taste of the FD was higher.

A further difficulty with the physiological data is the failure to replicate the finding by Glautier et al. (1992) that the directionality of response to an alcohol cue may be

influenced by the modality of cue presentation. There was no evidence of an interaction in the present comparison of responses to visual and taste cues associated with familiar and unfamiliar drinks. However, it should be borne in mind that in the Glautier et al. (1992) study, the comparison was between holding and actually consuming alcohol-associated and neutral drinks. Thus, in the present study we have simply ruled out interactions between taste and visual cues and level of previous alcohol association as an explanation for the Glautier et al. results.

Given this pattern of results, it is necessary to reflect carefully on what these results tell us about the mechanisms involved. The design of the experiment was opportunistic in that it did not employ conditioning procedures but, instead, relied upon subjects' extra-experimental conditioning histories. Therefore, any interpretation of results in terms of conditioning mechanisms must be tentative. For example, in this study physiological responses to the different tastes of the drinks necessarily confounded the unconditioned properties of the drinks with any conditioned properties. In addition, the mere fact of drink familiarity could be sufficient to produce the effects we recorded. Unless the drinks serving different cueing functions are counterbalanced or can be shown to have equivalent physiological response-eliciting capacities at the outset, we cannot be sure whether conditioned or unconditioned effects prevail (e.g., Glautier et al., 1992; McCaul, Turkkan, & Stitzer, 1989b). Given the reactivity of the autonomic nervous system to sensory stimuli such as drink flavours, this issue raises serious questions about the interpretation of the physiological data in studies of this kind. It is, however, much harder to see how any unconditioned differences between the drink cues could have led to such marked differences on the behavioural and subjective measures. Nevertheless, caution is still needed because although we randomised subjects to FD and UD conditions we cannot rule out the possibility that these two groups differed at intake on some important variables (e.g., IQ, motor skill, etc.); they did not, however, differ on age or weekly alcohol consumption.

Even if it is correct to assume that the observed data are dependent on the conditioned rather than the unconditioned effects of the different drinks, we still need to know more about the nature of the conditioning process. Apart from the opponent-process mechanism already discussed, several possibilities need to be explored. Baker and Tiffany (1985) have proposed that Wagner's (1976) memorial model of classical conditioning provides an adequate account of conditioned drug tolerance. They proposed that an expected dose of a drug is less effective as an unconditioned stimulus (US) because a representation of the US is "primed" in short-term memory prior to its appearance. Thus, when alcohol is effectively predicted by cues arising from its vehicle drink, it should have a smaller effect. Although no opponent processes were hypothesised by Baker and Tiffany, it should be noted that refinements of Wagner's original conditioning model (e.g., Wagner, 1981) have explicitly incorporated the concept of an opponent process. Another possibility is that either the absorption or metabolism of alcohol is affected by the vehicle, either because of the physical properties of the drink mixtures or, again, through the operation of conditioning processes (e.g., Melchior & Tabakoff, 1984). Given that blood alcohol levels were not measured in this study, this possibility cannot be ruled out. However, the ease with which blood alcohol can be measured should make it a good candidate for useful incorporation in future studies of this sort.

In conclusion, it seems clear that the role of classical conditioning mechanisms in human tolerance to alcohol is an area ripe for exploration. A number of studies, using quite elaborate conditioning paradigms or more opportunistic designs, already appear

to have demonstrated conditioning effects, although at present we have little information concerning which of several conditioning mechanisms may be at work. However, with procedures of the kind used in this experiment available, it should now be possible to begin to explore this issue in more detail in studies with human subjects.

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