

*Review***Learning alcohol tolerance:  
the contribution of response expectancies\***

M. Vogel-Sprott and K. Sdao-Jarvie

Department of Psychology, University of Waterloo, Waterloo, Ontario, Canada, N2L 3G1

**Abstract.** This paper reviews research on tolerance developed by task practice under alcohol, and concludes that tolerance in such a situation is influenced by the environmental consequence of drug-compensatory performance. Analysis of the evidence proposes that a learned association between the response and its consequence results in a response expectancy. When the consequence of drug-compensatory performance is more valuable, more tolerance is displayed. Support for this learning analysis is provided by some recent alcohol research indicating that response expectancies affecting tolerance can also be acquired by mental rehearsal of performance and its outcome under drug. Further, these response expectancies may be acquired during the course of a single drug dose, and may alter the display of acute tolerance to alcohol. Additional theoretical predictions are discussed, and the possible social and clinical relevance of the evidence is considered.

**Key words:** Tolerance – Alcohol – Response expectancy

Social drinkers and alcoholics often recount suddenly sobering up during some emergency. This phenomenon has also been noted by Goldberg and Havard (1968) in their discussion of the development of tests to determine blood alcohol concentrations (BAC). Before such tests were available, a medical examination of suspected impaired drivers was required to support the charge. These clinical assessments of suspects proved “unreliable and insensitive as a method of detecting alcohol impairment... Suspects faced with an examination by a doctor called in by the police are often able to pull themselves together sufficiently to pass clinical tests as a result of the physiological and psychological ‘alarm’ reaction induced by the crisis in which they find themselves. Indeed, it is not unknown for a driver to satisfy the police surgeon only to have to be assisted from the police station after the crisis has passed and the symptoms of intoxication have re-asserted themselves” (Goldberg and Havard 1968, p 8). The comparatively sudden occurrence of tolerance to the impairing effect of alcohol appears somehow related to behavioral events after the

dose is administered. This paper reviews research on factors governing tolerance in such situations, offers a learning interpretation of the phenomenon, and considers its possible social and clinical relevance.

The occurrence of tolerance is inferred when the readministration of a drug dose yields a weaker effect, or when a higher dose is required to reinstate the initial effect. Numerous potentially adverse consequences of alcohol tolerance have been suggested. It may contribute to withdrawal symptoms (Hinson and Siegel 1980) and may encourage an escalation of voluntary consumption, posing a risk of drug abuse (Cappell and LeBlanc 1979).

There is good agreement among researchers on the observation required to demonstrate tolerance, and on the assumption tolerance results from some adaptive, compensatory reaction that serves to counteract the drug effect. But the necessary and sufficient conditions for the development of this compensatory reaction remain debatable (Krasnegor 1978). Historically, theories of tolerance stressed the physiological effects of drug exposure, and possible altered absorption, distribution, inactivation or excretion of the drug (Kalant et al. 1971). However, more recent research has held drug exposure constant, and demonstrated that environmental factors which influence learning also can affect drug tolerance.

Much research implicating learning processes in drug tolerance has used Pavlovian training procedures to manipulate events associated with the administration of a drug (e.g., Le et al. 1979; Mansfield and Cunningham 1980; Cappell et al. 1981; Crowell et al. 1981; Dafters and Anderson 1982; Shapiro and Nathan 1986; Siegel and Sdao-Jarvie 1986, Staiger and White 1988). This evidence implies that responses compensating for drug effects may become associated with environmental stimuli predicting drug administration. Thus, the resulting tolerance may reflect the algebraic summation of the agonistic drug effects and the learned compensatory responses to stimulus cues for drug. These studies are consistent with the view that the learning influencing tolerance depends upon an acquired association between cues for drug and the drug stimulus (Hinson and Siegel 1980). Yet such an association apparently cannot explain the variation in drug tolerance observed when stimuli predicting drug are held constant, and the consequence of performance is manipulated after a drug is administered. Much of this evidence is derived from studies of task practice under alcohol, and implies that some learned association between a response and its outcome may also influence

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drug tolerance. Since these findings have received little systematic consideration to date, the present paper provides a review and analysis of this evidence.

### Instrumental training

Investigators have long speculated that practicing a task while under the influence of alcohol results in some learning that may enhance tolerance (Mellanby 1919; Goldberg 1943). However, interest in testing this hypothesis has been slow to develop, and an adequate experimental design that provides clear evidence has been difficult to devise. The next section reviews this early work and the interpretive problems encountered.

*Before-after designs.* Chen (1968, 1972) appears to be the first to attempt to test the task practice hypothesis. In his studies, two groups of rats were trained to criterion on a circular food maze. The groups then received a 1.2 g/kg dose of alcohol on each of 4 days. One group received alcohol *before* running the maze while the other group received alcohol *after* running the maze. Tolerance was subsequently tested by administering alcohol to both groups prior to task performance. The alcohol-before group displayed significantly less behavioral disruption to alcohol (i.e., more tolerance) than the alcohol-after group. Since the groups were equated for drug exposure, and only differed with respect to performance under alcohol, Chen concluded that learning occurring during task practice under alcohol, must contribute to the development of tolerance.

Chen's (1968) "before-after" design has been adopted to examine the development of alcohol tolerance during the performance of a variety of tasks (Chen 1979; de Souza Moreira et al. 1981; Mansfield et al. 1983). Although evidence from this research is consistent with the phenomenon initially reported by Chen (1968), his interpretation of the evidence has been controversial. Some investigators completely rejected a learning interpretation. Even those who favoured a learning explanation disputed Chen's view, and argued that an acquired association between cues for drug and the administration of the drug could account for the effects of task practice in research using a before-after design.

The denial of Chen's learning interpretation derived from a "functional demand" hypothesis that proposed performance just places greater demand on neuronal functioning, and greater neuronal activity hastens the physiological process of adaptation to drug effects (Kalant et al. 1971). Thus, it was argued that intoxicated practice required of an alcohol-before group simply accelerated the rate of physiological adaptation to drug, and involved no learning. Tolerance merely developed more quickly with the greater functional demand posed by intoxicated practice. This proposal led to other studies examining the amount of tolerance resulting from repeated physiological exposures to alcohol, and from daily intoxicated task practice (Leblanc et al. 1973, 1976). These studies included a physiological group whose tolerance was tested by task practice under alcohol at 4-day intervals. On the basis of these experiments, the authors concluded that intoxicated task practice was not necessary for the development of tolerance. Practice just hastened the development of tolerance, but added nothing to the ultimate degree of tolerance observed. But this interpretation has also been challenged. Wenger et al. (1980,

1981) pointed out that a physiological drug exposure group having tolerance tests at 4-day intervals essentially receives intermittent task practice under alcohol, and this introduces the potential for learning. Wenger et al. (1980, 1981) demonstrated that groups receiving drugged task practice (daily or intermittently) became tolerant, whereas a physiological control group receiving only a single tolerance test at the end of the experiment displayed no tolerance. Since these results indicated that an animal must perform the task under drug to become tolerant, the evidence clearly supported Chen's learning interpretation of tolerance. But Chen attributed the learning to task practice under drug, whereas others offered a different learning interpretation.

Hinson and Siegel (1980) pointed out that classical conditioning effects may account for the results of studies using a before-after design. In the case of Chen (1968), the alcohol-before group had the drug administration and the task consistently associated with drug effects during all tolerance acquisition and tolerance test sessions. Thus, the task as well as other environmental cues may have come to signal drug effects, and to evoke a drug-compensatory response that would be observed as tolerance. In contrast, the alcohol-after group had no opportunity to associate the task with the drug during the tolerance acquisition phase because they performed the task and then received the drug at some later time in the colony room. The subsequent tolerance test administered drug in the task environment, and this uniquely novel situation for the alcohol-after group could explain their lack of tolerance.

Drug state-dependent learning (Overton 1984) has not commonly been offered as an explanation of the results of studies using a before-after design to investigate tolerance. Yet the findings might also be attributed to state-dependent learning because the before group has its training and test in the same drug state, whereas the after group is trained drug-free, and then tested under drug.

In summary, a large number of studies using a before-after design have demonstrated a tolerance facilitating effect of task practice under alcohol. But this experimental design clouds the interpretation of the results. The before group, which typically shows most tolerance, also has greater functional demands under drug. As a consequence, the functional demand hypothesis cannot be unequivocally dismissed. Even if a learning interpretation of the evidence is favoured, stimuli predicting drug or state-dependent learning may account for the enhanced tolerance displayed by the before group. Before-after designs cannot clearly demonstrate that tolerance can be influenced by some additional learning process associated with task practice under drug. However, the problem in interpreting the results of these studies serves to indicate that an adequate test of the hypothesis requires conditions that only manipulate the consequences of performance under drug. Drug state during training and test, functional demand, and learned cues predicting drug must all be held constant. Some research meeting these requirements have employed within- and between-group designs.

*Within-subject designs.* One strategy that only manipulates the consequences of drugged performance is illustrated by studies of drug effects when a subject performs a task under multiple schedules of reinforcement. The use of a within-subject design allows the same environmental cues for drug to be associated with the drug effect during all reinforce-

ment schedules. In addition, the subject performs the same task under drug during all reinforcement schedules, so the drug state and the functional demand are also held constant. Thus, if the tolerance displayed by a subject varies when the reinforcement schedule changes, it may be attributed to the manipulation of the reinforcement for the response under drug.

An early example of such research was provided by Schuster et al. (1966). These researchers trained rats to bar press for food under alternating schedules, fixed interval (FI) and differential low rate of response (DRL). After baseline training, *d*-amphetamine was administered before each bar pressing session. After 30 days of treatment, tolerance to the behavioral effects of *d*-amphetamine was observed only when animals performed under the DRL schedule. Drug effects showed no decrease (i.e., no tolerance) under the FI schedule. Schuster et al. (1966) noted that the initial stimulant effect of the drug disrupted performance under the DRL schedule so that food reinforcement was lost. In contrast, the initial drug effect did not alter the rate of reinforcement under the FI schedule.

The response-reinforcement relationship was further examined (Schuster et al. 1966) using a shock avoidance task where the initial effect of amphetamine increased the number of responses and resulted in fewer shocks being received. After baseline training, *d*-amphetamine was administered for 35 days. Tolerance failed to develop in any rat during this period. These findings led Schuster et al. (1966) to propose a "loss of reinforcement" principle predicting that behavioral tolerance will develop when the action of a drug disrupts the behavior required to meet the environmental requirements for reinforcement. Conversely, if the behavioral effect of a drug either enhances or does not change density of reinforcement, then tolerance is unlikely to be observed.

Studies using multiple reinforcement schedules have confirmed that the drug tolerance a subject displays is affected by the reinforcement schedule (e.g., Elsmore 1976; Galbicka et al. 1980; Branch 1983; Brocco et al. 1983). However, the findings do not consistently support a loss of reinforcement principle (Corfield-Sumner and Stolermer 1978). Ferraro and Grilly (1973) have noted a particular reinforcement schedule that induced tolerance in one situation yet failed to do so in another. They speculated that the failure might be due to the fact the latter situation permitted no drug-compensatory response.

The suggestion by Ferraro and Grilly (1973) raises the possibility that the reinforcement schedule for a drug-compensatory response may be the important factor influencing tolerance after a drug is administered. The results of an early experiment examining alcohol tolerance in humans (Vogel-Sprott 1979) is consistent with this notion. This research used a within-subject design in which each subject was trained on a paper and pencil coding task and a motor skill task (pursuit rotor) that required accurate tracking of a rotating target. A trial on each task lasted 3 min. Coding and pursuit rotor performance was assessed by the number of items correctly coded, and the time on target. Following baseline training, four weekly drinking sessions were administered. During these sessions, experimental subjects received alcohol and controls expected alcohol but received a placebo. Both tasks were performed equally often after drinking during each session. The performance of the two tasks under placebo did not change significantly during

these sessions. In contrast, the development of tolerance to the impairing effect of alcohol was evident in a subject's performance on the coding task but not on the pursuit rotor task.

Since the coding and pursuit rotor tasks differed on so many dimensions, the results could not identify the factor causing a subject to display tolerance on only one task. Yet an analysis of the outcomes for drug-compensatory performance on the two tasks indicated that they differed in a fashion that might explain the findings. The coding task conveyed information to a subject about the adequacy of his performance because he could see his work on each trial. Such feedback (i.e., knowledge of results) is found to operate like reinforcement and to enhance learning in humans (Schwartz and Lacey 1982). This outcome for drug-compensatory performance may have been the factor responsible for the development of tolerance on the coding task. When subjects performed a trial on the pursuit rotor task, their scores were not reported. Since subjects could not accurately estimate their scores, information about the adequacy of performance (i.e., knowledge of results) was absent. In this case, tolerance may have failed to develop on the pursuit rotor task because there was no outcome for drug-compensatory performance. This hypothesis has led to several studies examining alcohol tolerance in humans as a function of reinforcement for drug-compensatory performance. This research adopts a between-group design and is reviewed in the next section.

*Between-group designs.* Some studies of alcohol tolerance in humans have manipulated reinforcement for drug-compensatory performance and examined the resulting acquisition, extinction and transfer of alcohol tolerance in humans (Mann and Vogel-Sprott 1981; Beirness and Vogel-Sprott 1984; Rawana and Vogel-Sprott 1985). These experiments used groups that all received the same drug administration ritual. Thus, the association between cues for alcohol and its effect was held constant. Drug state and functional demand were also controlled by requiring all groups to perform the same task equally often under alcohol. Only the consequences of performance under drug differed in each group.

The study by Beirness and Vogel-Sprott (1984) trained four groups of subjects on a tracometer, a complex subject paced tracking task that entails some of the skills involved in driving (Engel et al. 1978). The task presents light targets in one of five positions in a random sequence. Speed and accuracy are required to hit a target, and performance is measured by the time to complete a trial. After baseline training, all groups received a moderate dose of alcohol on repeated sessions and performed the task equally often under drug, but each group received a different outcome for performance under alcohol. Since tolerance is observed as drug-compensatory performance, subjects in one group were paid 25 cents for every test score under alcohol that was as good or better than their drug-free achievement. Since a subject must compensate for the alcohol-induced impairment to obtain the money, this treatment should provide contingent reinforcement of a drug-compensatory response. If this response has some instrumental characteristics, its occurrence should increase to yield enhanced tolerance. This condition was referred to as "R" treatment. Since the subjects could not accurately assess their tracometer performance unless they were informed of their

scores, the R treatment essentially provided both incentive and feedback about performance. The possibility that tolerance develops more slowly when the outcome of drug-compensatory performance has a weaker incentive value was tested by the inclusion of a group receiving information about the adequacy of their performance under drug, but no money (I treatment). Since the interest generated by offering the money might itself, alone, affect behavior under drug, one control group (RR) received 25 cent rewards equal to those earned by the R group, but the money was administered on randomly selected trials, independently of performance. This RR treatment would not be expected to develop much or any tolerance because it provided no systematic consequence for drug-compensatory performance, and no accurate feedback about the adequacy of performance. Another control group (N) received no money, information or other particular outcome for performance under drug. After four alcohol sessions, the R group displayed the most tolerance, and the I group also displayed tolerance to a lesser degree. The two control groups showed the least tolerance. These control treatments were similar in that drug-compensatory performance had no specific consequence, and their impairment remained similarly close to that usually observed under the first dose of alcohol.

Other alcohol studies using R treatment to induce tolerance have examined its subsequent extinction and transfer. Tolerance acquired on a pursuit rotor task was subsequently extinguished in spite of continuing alcohol administrations, simply by withholding the expected reward for drug-compensatory performance (Mann and Vogel-Sprott 1981). Tolerance developed on a tracometer task also transferred most readily to a new task (pursuit rotor) when the same reward was maintained for drug-compensatory performance on the new task (Rawana and Vogel-Sprott 1985).

The effects of the treatments employed in this set of alcohol tolerance experiments appear to be in line with the effects such treatments would have on the acquisition, extinction and transfer of an instrumental response. Thus, the findings imply the existence of a drug-compensatory response whose occurrence may be influenced by its consequence. Since the behavioral effect of alcohol tended to impede reactions by slowing performance on the tasks used in these studies, the compensatory response could be expected to be characterized by hyper-reactivity. Although a compensatory response cannot be directly observed when tolerance is tested under drug, it may be revealed when a subject expects alcohol but drinks a placebo. Under these conditions, task performance should be faster than usual.

In order to test for a compensatory response, the study by Beirness and Vogel-Sprott (1984) presented cues for alcohol with a placebo to groups that had received the R, I, RR, and N treatment. Since the groups had all received the same alcohol administration ritual, the cues for drug should evoke a similar compensatory response in all groups. However, if the different amounts of tolerance that the groups had displayed reflected treatment effects on the compensatory response, then group differences that mirrored their tolerance should be observed. When the groups in this study expected alcohol but received a placebo, their subsequent performance revealed a compensatory response (i.e., facilitation of performance above the typical drug-free level). Further, the intensity of this reaction differed among

groups in direct agreement with the degree of tolerance they had previously displayed.

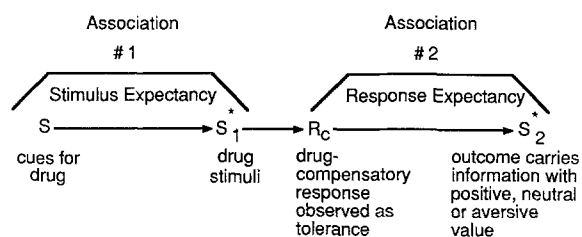
In summary, these between-group studies, like those using a within-subject design, indicate alcohol tolerance is influenced by some learning process occurring after the drug is received that cannot be explained by state dependent learning, functional demand, or stimulus cues for drug. It now seems that some conceptual framework to guide research on the nature of this additional learning process in tolerance is needed. Investigations of tolerance using Pavlovian and instrumental training procedures have developed somewhat independently, and no learning analysis incorporating the evidence from these two sources has yet been proposed.

## Theory

Contemporary views of learning assume that it consists of acquiring information about the environment from the predictable relations between stimulus events. These notions have evolved primarily from research on Pavlovian conditioning. The information hypothesis of Egger and Miller (1962) was a precursor to Rescorla's (1967) proposal that learning under Pavlovian conditioning took place only when a conditional stimulus conveyed reliable information about the occurrence or nonoccurrence of a unconditioned stimulus. Other research on compound conditioning has emphasized expectancies based upon the information value of the stimulus (Kamin 1969; Rescorla and Wagner 1972; Wagner and Rescorla 1972).

Some analyses of learning processes occurring under instrumental training have also emphasized expectancies and information. Bolles' (1972) proposed that a subject learns two kinds of expectancies. The association between environmental stimuli preceding a response is referred to as "stimulus expectancy". A second association between a response and its outcome is termed "response expectancy". The opportunity to learn about predictive relationships between stimuli is afforded under both Pavlovian and instrumental training procedures. However, the instrumental situation adds some predictable consequences for a subject's response and thus, additionally permits the development of response expectancies. Bolles' analysis implies that if a subject has acquired a response expectancy under instrumental training, and then has the outcome devalued, the likelihood of the response should be adversely affected. Recent research testing for learned response-reinforcer associations under instrumental training provides strong support for this prediction (Colwill and Rescorla 1986; Rescorla 1987).

The assumption that instrumental training permits the acquisition of stimulus and response expectancies implies that these two associations may also be acquired during instrumental training of drug tolerance. This is illustrated in Fig. 1. The distinctive stimuli repeatedly accompanying drug administration provide an opportunity to develop stimulus expectancies for drug. This is represented by  $S-S_1^*$ . The drug stimulus ( $S_1^*$ ) evokes a multiplicity of different responses. The one of interest for drug tolerance is compensatory ( $R_c$ ), that is, opposite in direction to the drug effect. When the instrumental procedure provides some systematic consequence for  $R_c$ , the learning of a second association, a response expectancy, is permitted. This is represented as  $R_c-S_2^*$ . When stimulus expectancies are held constant, the probability of observing  $R_c$  depends upon the learned re-



**Fig. 1.** Task practice under drug permits the development of two learned associations

sponse expectancy and the incentive value of  $S_2^*$ . A more valuable  $S_2^*$  should increase the probability of observing  $R_c$  and consequently should increase the display of tolerance.

This model of learned tolerance identifies two different outcomes.  $S_1^*$  is the drug stimulus, and  $S_2^*$  is a different event. Each may have value for the subject, but these values need not be correlated. The drug may have pleasant or noxious effects, quite independently of whether the drug-compensatory response has an outcome that is pleasant or noxious. The proposed analysis of learned tolerance assumes the Pavlovian procedure provides an opportunity to acquire only stimulus expectancies through the pairing of cues for drug with the drug stimulus. Thus, in a Pavlovian situation the acquisition of tolerance presumably depends solely upon learning this  $S-S_1^*$  association. The instrumental procedure is considered to also permit the development of the  $S-S_1^*$  association, but to introduce an additional association,  $R_c-S_2^*$ . This allows the learning of a drug-compensatory response expectancy that may also influence tolerance.

### Additional evidence

*Learning response expectancies.* If alcohol tolerance can be influenced by the consequence of drug-compensatory performance, then any training technique that provides an opportunity to learn this response expectancy should affect tolerance. One training procedure, which is unique to humans, and which may develop these associations, is "mental rehearsal". Mental rehearsal essentially requires the subject to repeatedly imagine himself performing the task in the absence of any gross muscular movements (Richardson 1967). Reviews of the literature on mental rehearsal indicate that it has been used effectively to develop skill in sports and other psychomotor tasks (Richardson 1967; Feltz and Landers 1983).

Some recent research has examined the effect of mental rehearsal on alcohol tolerance. Vogel-Sprott, Rawana and Webster (1984) trained three groups on a pursuit rotor task, and subsequently administered the same repeated dose of alcohol to all groups. All performed the task with money for drug-compensatory performance on the first alcohol session (i.e., R treatment). On subsequent alcohol sessions, one group mentally rehearsed the task and the outcome of their imaginary performance, while another group actually practiced the task with money for drug-compensatory performance. A control group had the same practice drug-free, before drinking alcohol. A final session testing performance under drug showed mental rehearsal and drugged practice to yield equal and significantly more tolerance than the control condition. Another parallel between mental re-

hearsal and actual practice was indicated by the finding that tolerance is facilitated when subjects either mentally rehearse or practice under drug, but little effect on tolerance is obtained if subjects practice or mentally rehearse drug-free (Sdao-Jarvie and Vogel-Sprott 1986). These findings highlight the potential important contribution of cognitive learning in tolerance; an experience of the consequences of behavior under drug apparently can subsequently be reinstated and cognitively rehearsed to enhance tolerance.

Other research (Annear and Vogel-Sprott 1985) using mental rehearsal has distinguished its effects on alcohol tolerance from those of stimulus expectancy for drug. This study used four groups. Two mentally rehearsed the pursuit rotor task after drinking, in either the same task environment or in a different setting (library). Two control groups performed an auditory detection task after drinking in one or other of these environments. The effect of these treatments on tolerance was tested when all groups subsequently performed the task under alcohol. Since repeated alcohol exposure in the task environment and mental rehearsal of the task each significantly enhanced tolerance, it was concluded that the acquisition of stimulus and of response expectancies each affect the display of behavioral tolerance to alcohol.

*Learning response expectancies during a single dose.* The behavioral effects of a dose of alcohol characteristically abate faster than the blood alcohol concentration (BAC) declines. Thus the effect of a dose of alcohol at a given BAC is usually stronger during the rising than the descending limb of the BAC curve. This phenomenon is referred to as "acute tolerance". Since alcoholics display greater acute tolerance than social drinkers (Goldberg 1943), the factor of drug exposure appears to accelerate recovery of function during declining BAC. But other factors that also may affect acute tolerance have seldom been investigated. One such factor may be the learned consequence of drug-compensatory performance.

Repeated opportunities to associate drug-compensatory performance with some outcome during the course of a single dose should permit the acquisition of a response expectancy as trials accumulate. If the consequence is desirable, the effect of the response expectancy should reduce the effect of the dose. Since more trials necessarily occur later during the course of a single dose, these effects should be strongest during declining BAC and should thus enhance acute tolerance. Some research has tested this prediction by administering a dose of alcohol to groups who repeatedly performed a tracometer task with different outcomes for drug-compensatory performance (Haubenreisser and Vogel-Sprott 1987; Vogel-Sprott et al. 1989). In line with these predictions, accelerated recovery from impairment during the declining limb of the alcohol curve consistently occurred when the drug-compensatory response had a valuable consequence (money or information). Slower recovery at lower declining BACs occurred when groups either received these same outcomes unrelated to compensatory performance, or no outcome whatever.

### Research implications

*Theoretical considerations.* When behavioral tolerance to a drug is measured by a subject's performance under drug, the measure may be influenced by two sources of learning:

**Table 1.** Degree of behavioral tolerance as a function of learned stimulus expectancy for drug and expected consequence of a drug-compensatory response

| Stimulus expectancy | Response expectancy |              |              |
|---------------------|---------------------|--------------|--------------|
|                     | Absent (0)          | Positive (+) | Negative (-) |
| Present (+)         | 0+                  | ++           | -+           |
| Absent (0)          | 00                  | +0           | -0           |

stimulus expectancy for drug, and the expected outcome for drug-compensatory performance. The theoretical model proposed in the present paper provides a means of analyzing the test situation to predict whether and how each source of learning may contribute to the tolerance displayed. These effects are illustrated in Table 1.

In the absence of a systematic consequence for drug-compensatory performance, learning effects on tolerance may depend solely upon stimulus expectancy acquired by the reliable association of events preceding and accompanying the administration of drug. The usual Pavlovian conditioning situation represents an instance of this type. Column 1 of Table 1 shows more tolerance (0, +) when tests occur in the presence of cues predicting drug than in their absence (0,0) where drug is not expected.

Instrumental training characteristically manipulates the consequences a response. Thus measures of tolerance when a drug is repeatedly administered in an instrumental situation may reflect of the influence of both stimulus and response expectancies. Their possible combinations are illustrated in columns 2 and 3. Clearly most tolerance should be observed when stimuli predict drug, and a rewarding outcome of compensatory performance is expected. This situation is indicated by (+, +) in the top cell of column 2. The lower cell represents tolerance tests in a novel situation where drug has never been received and stimulus expectancy is thus absent. In this (+,0) case, only the expected reward for the drug-compensatory response contributes to tolerance, and so less should be observed.

But what if instrumental training associates compensatory performance with an aversive consequence? The resulting response expectancy should operate to suppress compensatory behavior so little tolerance should be displayed. Drug effects should not abate, and may even intensify. These possibilities are considered in column 3. Even if tolerance is tested in the presence of stimulus expectancy for drug, little tolerance should be displayed because the aversive response expectancy generates a conflicting tendency (+, -). If the consequence of the compensatory response is sufficiently aversive, tolerance may be reversed so that sensitization is observed. However, sensitization is more likely to occur, even with a mildly aversive outcome, when tolerance is tested in the absence of stimulus expectancy for drug (-,0).

Pavlovian conditioning studies have provided considerable evidence for the learning effects on tolerance represented in column 1 of Table 1. Investigations of tolerance in instrumental learning situations have primarily examined the conditions represented in the first row of columns 1 and 2. That is, stimulus expectancy is always present and the outcome of drug compensatory performance is either rewarding or absent. The effects of treatments represented by the other three cells remain to be tested.

Table 1 predicts tolerance when the actual and expected consequence of drug-compensatory performance are the same. In such cases, tolerance reflects the joint influence of the learned expectancy and the incentive value of the outcome. Yet it is possible that learning provides the potential for tolerance, and incentive affects the degree to which tolerance is actually displayed. A distinction between learning and performance of tolerance may be demonstrated by training drug-compensatory performance with one consequence, and subsequently testing tolerance when a different outcome is administered. Studies of this type can test the possibility that drug tolerance requires a learned compensatory response expectancy, but the degree of tolerance subsequently displayed in a situation depends upon the incentive value of the outcome. Some promising support for this hypothesis has been obtained (Sdao-Jarvie 1988). One study using this technique to investigate the extinction of alcohol tolerance by withholding the expected reward for compensatory performance has also been conducted (Mann and Vogel-Sprott 1981). An example of research using a similar strategy in the learning literature has been provided by Rescorla's (1987) studies of goal directed behavior when the reinforcer is devalued.

Pavlovian and instrumental training both depend upon the manipulation of environmental events to develop stimulus and response expectancies. While such procedures may be used to investigate the influence of these two learned expectancies on drug tolerance, it appears that other cognitive training techniques, such as mental rehearsal, may also be used with humans. These findings raise the possibility that a response expectancy might be acquired with only one drug experience, simply by additional cognitive rehearsal of drug-compensatory performance under *imaginary* alcohol effects. Although the notion that such drug-free mental rehearsal without repeated drug exposures may affect tolerance appears counter intuitive, such training bears a parallel to cognitive behavior therapy where a client rehearses coping responses in the presence of some imaginary disturbing stimulus that has previously been experienced (Meichenbaum 1977).

It may be that other procedures that do not involve repeated alcohol exposure can also develop the response expectancies that affect behavioral tolerance. Allowing a subject to observe a rewarding consequence for the drug-compensatory performance of another individual, or providing specific verbal instruction about this contingency are two examples. If such treatments are found to induce tolerance in humans, such evidence would challenge the assumption that repeated drug exposures are essential for the development of tolerance. The possibility that the appropriate response expectancy can be acquired without repeatedly administering drug to a subject, and that this expectancy may subsequently enhance behavioral tolerance would not be predicted by any physiological or other theory assuming that repeated drug exposures are essential for tolerance development. This hypothesis would also suggest a reconsideration of the current theoretical explanation of the tolerance-inducing effect of stimulus expectancy for drug. To date, stimulus expectancies have been acquired by the repeated pairing of events preceding and associated with actual administrations of a drug. However, it may be that stimulus expectancies can be acquired by repeatedly pairing cues for drug with *imagined* alcohol effects. If this proves to be the case, then both stimulus and response expectancies which

affect tolerance in humans may be learned without multiple exposure to alcohol.

*Clinical and social considerations.* Alcohol tolerance has traditionally been considered to be disadvantageous. It may contribute to withdrawal symptoms and relapse to drug abuse. Yet alcohol tolerance occasioned by an expected rewarding outcome of drug-compensatory performance would appear to play quite a different role. This learned response expectancy appears likely to enhance tolerance only when it yields a desirable consequence. In addition, its development may not even require extensive drug use, so it may be acquired by social drinkers, however slight their drug use. Since individuals perform a variety of tasks after drinking, the tolerance-inducing effect of response expectancies could be advantageous, conferring a degree of safety and protection from potentially hazardous consequences of behavioral impairment by alcohol.

However, this might also be a mixed blessing. Some investigators have speculated that alcohol tolerance encourages the consumption of larger doses leading to drug abuse (Cappell and LeBlanc 1979). Learned response expectancies may be relevant here, for the protection from unwanted consequences of alcohol impairment afforded by this learning may encourage a drinker to relax constraints on the dose. Higher doses may now be administered and enjoyed without "paying" more. Thus tolerance derived from learned response expectancies may increase an individual's capacity to use higher doses with less risk of undesirable behavioral consequences. In some cases, this could encourage the development of alcohol abuse by permitting an escalation in the consumption of alcohol.

Some degree of tolerance derived from response expectancies may develop in all social drinkers, and most could profit from the resulting protection against the impairing behavioral effect of the drug. Others may use this opportunity as a stepping stone to increase their alcohol use. The conditions under which this latter course is chosen, and the characteristics of individuals likely to choose such a course, provide a fertile and important area for future investigation.

## References

- Annear WC, Vogel-Sprott M (1985) Mental rehearsal and classical conditioning contribute to ethanol tolerance in humans. *Psychopharmacology* 87:90–93
- Beirness DJ, Vogel-Sprott M (1984) Alcohol tolerance in social drinkers: operant and classical conditioning effects. *Psychopharmacology* 84:393–397
- Bolles RC (1972) Reinforcement, expectancy and learning. *Psychol Rev* 79:394–409
- Branch MN (1983) Behavioral tolerance to the stimulating effects of pentobarbital: a within-subject determination. *Pharmacol Biochem Behav* 18:25–30
- Brocco MJ, Rastogi SK, McMillan DE (1983) Effects of chronic phencyclidine (PCP) on the schedule controlled behavior of rats. *J Pharmacol Exp Ther* 226:449–454
- Cappell H, LeBlanc A (1979) Tolerance to, and physical dependence on ethanol: why do we study them? *Drug Alcohol Depend* 4:15–31
- Cappell H, Roach C, Poulos CX (1981) Pavlovian cross-tolerance between pentobarbital and ethanol. *Psychopharmacology* 74:54–57
- Chen CS (1968) A study of the alcohol tolerance effect and an

- introduction of a new behavioral technique. *Psychopharmacologia* 12:433–440
- Chen CS (1972) A further note on studies of acquired behavioral tolerance to alcohol. *Psychopharmacologia* 27:265–274
- Chen CS (1979) Acquisition of behavioral tolerance to ethanol as a function of reinforced practice in rats. *Psychopharmacology* 63:285–288
- Colwill RM, Rescorla RA (1986) Associative structures in instrumental learning. In: Bower GH (ed) *The psychology of learning and motivation*, vol 20. Academic Press, New York, pp 55–104
- Corfield-Sumner PK, Stolerman JP (1978) Behavioral tolerance. In: Blackman D, Sanger D (eds) *Contemporary research in behavioral pharmacology*. Plenum Press, New York, pp 391–448
- Crowell CR, Hinson RE, Siegel S (1981) The role of conditioned drug responses to the hypothermic effects of ethanol. *Psychopharmacology* 73:51–54
- Dafters R, Anderson G (1982) Conditioned tolerance to the tachycardia effect of ethanol in humans. *Psychopharmacology* 78:365–367
- de Souza Moreira LF, Caprioglio MJ, Masur J (1981) Development and reacquisition of tolerance to ethanol administered pre- and post-trials to rats. *Psychopharmacology* 73:165–167
- Egger MD, Miller NE (1962) Secondary reinforcement in rats as a function of information value and reliability of the stimulus. *J Exp Psychol* 64:97–104
- Elsmore TF (1976) The role of reinforcement loss in tolerance to chronic THC effects on the operant behavior of rhesus monkeys. *Pharmacol Biochem Behav* 5:123–128
- Engel R, Paskaruk S, Green N (1978) Driver education evaluation tests: summary report. Ministry of Transport, Ontario, Canada
- Feltz DL, Landers DM (1983) The effect of mental practice on motor skill learning and performance: a meta-analysis. *J Sport Psychol* 5:25–57
- Ferraro DP, Grilly DM (1973) Lack of tolerance to delta-9-THC in chimpanzees. *Science* 179:490
- Galbicka G, Lee DM, Branch MN (1980) Schedule-dependent tolerance to behavioral effects of delta-9-THC when reinforcement frequencies are matched. *Pharmacol Biochem Behav* 1:85–91
- Goldberg L (1943) Quantitative studies of alcohol tolerance in man. The influence of ethyl alcohol on sensory, motor and psychological functions referred to blood alcohol in normal and habituated individuals. *Acta Physiol Scand [Suppl 16]* 5:1–128
- Goldberg L, Havard JDJ (1968) Research on the effects of alcohol and drugs on driver behaviour and their importance as a cause of road accidents. Organization for Economic Cooperation and Development, Paris
- Haubenreisser T, Vogel-Sprott M (1987) Reinforcement reduces behavioral impairment under an acute dose of alcohol. *Pharmacol Biochem Behav* 26:29–33
- Hinson RE, Siegel S (1980) Contribution of Pavlovian conditioning to ethanol tolerance and dependency. In: Rigter H, Crabbe JC (eds) *Alcohol tolerance and dependence*. Elsevier/North Holland Biomedical Press, Amsterdam, pp 181–199
- Kalant H, LeBlanc AE, Gibbins RJ (1971) Tolerance to, and dependence on, some non-opiate psychotropic drugs. *Pharmacol Rev* 23:135–191
- Kamin LJ (1969) Predictability, surprise, attention, and conditioning. In: Campbell BA, Church RM (eds) *Punishment and aversive behavior*. Appleton-Century-Crofts, New York, pp 279–298
- Krasnegor NA (1978) Introduction. In: Krasnegor NA (ed) *Behavioral tolerance: research and treatment implications* (Nat Inst Drug Abuse Res Monogr No 18). US Government Printing Office, Washington DC, pp 1–3
- Le AD, Poulos CX, Cappell H (1979) Conditioned tolerance to the hypothermic effect of ethyl alcohol. *Science* 206:1109–1110
- LeBlanc AE, Gibbins R, Kalant H (1973) Behavioral augmentation of tolerance to ethanol in the rat. *Psychopharmacologia* 30:117–122

- LeBlanc AE, Kalant H, Gibbins R (1976) Acquisition and loss of behaviorally augmented tolerance to ethanol in the rat. *Psychopharmacology* 48:153-158
- Mann RE, Vogel-Sprott M (1981) Control of alcohol tolerance by reinforcement in nonalcoholics. *Psychopharmacology* 75:315-320
- Mansfield JG, Cunningham CL (1980) Conditioning and extinction of tolerance to the hypothermic effect of ethanol in rats. *J Comp Physiol Psychol* 94:962-969
- Mansfield JG, Benedict RS, Woods SC (1983) Response specificity of behaviorally augmented tolerance to ethanol supports a learning interpretation. *Psychopharmacology* 79:94-98
- Meichenbaum D (1977) *Cognitive-behavior modification*. Plenum Press, New York
- Mellanby E (1919) Alcohol: its absorption and disappearance from blood under different conditions. Special report series (No 31) Medical Research Committee, London
- Overton DA (1984) State dependent learning and drug discriminations. In: Iverson LL, Iversen SD, Snyder SH (eds) *Handbook of psychopharmacology*, vol 18. Plenum Press, New York, pp 59-127
- Rawana E, Vogel-Sprott M (1985) The transfer of alcohol tolerance, and its relation to reinforcement. *Drug Alcohol Depend* 16:75-83
- Rescorla RA (1967) Pavlovian conditioning and its proper control procedures. *Psychol Rev* 74:71-80
- Rescorla RA (1987) A Pavlovian analysis of goal-directed behavior. *Am Psychol* 42:119-129
- Rescorla RA, Wagner AR (1972) A theory of Pavlovian conditioning: variations in the effectiveness of reinforcement and non-reinforcement. In: Black AH, Prokasy WF (eds) *Classical conditioning*. Appleton-Century-Crofts, New York, pp 64-99
- Richardson A (1967) Mental practice: a review and discussion. Part I. *Res Q* 38:95-107
- Schwartz B, Lacey H (1982) *Behaviorism, science, and human nature*. Norton, New York
- Schuster CR, Dockens W, Woods J (1966) Behavioral variables affecting the development of amphetamine tolerance. *Psychopharmacologia* 9:170-182
- Sdao-Jarvie K (1988) The role of response expectancies in the acquisition and display of alcohol tolerance. Unpublished doctoral dissertation, University of Waterloo, Waterloo, Canada
- Sdao-Jarvie K, Vogel-Sprott M (1986) Mental rehearsal of a task before or after ethanol: tolerance facilitating effects. *Drug Alcohol Depend* 18:23-30
- Shapiro A, Nathan P (1986) Human tolerance to alcohol: the role of Pavlovian conditioning processes. *Psychopharmacology* 88:90-95
- Siegel S, Sdao-Jarvie K (1986) Attenuation of ethanol tolerance by a novel stimulus. *Psychopharmacology* 88:258-261
- Staiger P, White J (1988) Conditioned alcohol-like and alcohol-opposite responses in humans. *Psychopharmacology* 95:87-91
- Vogel-Sprott M (1979) Acute recovery and tolerance to low doses of alcohol: differences in cognitive and motor skill performance. *Psychopharmacology* 61:287-291
- Vogel-Sprott M, Rawana E, Webster R (1984) Mental rehearsal of a task under ethanol facilitates tolerance. *Pharmacol Biochem Behav* 21:329-331
- Vogel-Sprott M, Kartchner W, McConnell D (1989) Impairing effects of an acute dose of alcohol are influenced by the outcome of performance under drug. *Subst Abuse* (in press)
- Wagner AR, Rescorla RA (1972) Inhibition in Pavlovian conditioning: application of a theory. In: Boakes RA, Halliday MS (eds) *Inhibition and learning*. Academic Press, New York, pp 310-337
- Wenger JR, Berlin V, Woods SC (1980) Learned tolerance to the behaviorally disruptive effects of ethanol. *Behav Neural Biol* 28:418-430
- Wenger JR, Tiffany TM, Bombardier C, Nicholls K, Woods SC (1981) Ethanol tolerance in the rat is learned. *Science* 213:575-577

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