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Impairment and Recovery Under Repeated Doses of Alcohol: Effects of Response-Outcomes

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VOGEL-SPROTT, M. AND M. T. FILLMORE. *Impairment and recovery under repeated doses of alcohol: Effects of response-outcomes.* PHARMACOL BIOCHEM BEHAV 45(1) 59-63, 1993.—This research examined the behavioral effect of alcohol during rising and declining blood alcohol concentrations (BACs) when the dose was repeated three times (mean peak BAC = 78 mg/100 ml). A total of 36 male social drinkers learned a complex psychomotor task and subsequently performed it at intervals after alcohol was received. Subjects performed under one of two conditions: an experimental (E) treatment associated drug-compensatory (nonimpaired) task performance with a positively reinforcing outcome or a control (C) treatment associated no environmental consequence with performance. E treatment diminished impairment at all positions on the BAC curve and carried over to result in progressively less impairment when the dose was repeated. In contrast, C treatment tended to increase impairment around the BAC curve with repeated doses. The rate of recovery during declining BACs remained stable across sessions and was not altered by the treatments. The results imply that impairment under a dose of alcohol is governed by two processes: response-outcome associations that determine the amount of impairment displayed under a dose and some adaptive process that determines the rate of recovery with time during exposure to a dose.

Alcohol Tolerance Sensitization Learning Humans

RESEARCH has shown that when animals receive repeated doses of a drug under constant environmental conditions the development of behavioral tolerance depends upon the consequence of performance under the drug (13). More recent evidence leading to a similar conclusion has been obtained from studies of social drinkers (3,11,12,14,15). These experiments have demonstrated that the development of chronic tolerance to repeated doses was enhanced when drug-compensatory (i.e., nonimpaired) performance was positively reinforced by knowledge of results, or money. This conclusion has been obtained using a variety of control treatments, such as administering money randomly with respect to compensatory performance or promising and paying money for compensatory performance at the conclusion of the study or providing no consequence whatever. A learning interpretation of the evidence proposes that information about a reliable relation between a response and an outcome permits the acquisition of a response-outcome expectancy. Thus, training that associates a compensatory response with a favorable outcome allows the acquisition of a drug-compensatory response expectancy that enhances alcohol tolerance (16,18).

To date, research on the chronic tolerance of social drinkers has measured the mean effect of a dose of alcohol based upon the average effect observed on performance at intervals during the rising and declining phases of the blood alcohol curve. Such an average provides a comprehensive measure of changes in the effect of a dose. However, when tolerance is indicated by a decline in the mean effect of the dose the mean score does not reveal where, during the course of the dose, impairment has diminished.

Acute tolerance refers to the observation that the intensity of the effect of a given blood alcohol concentration (BAC) on the rising portion of the blood alcohol curve is greater than that displayed at the same BAC on the descending limb of the curve. Some investigators have speculated that adaptation during exposure to alcohol contributes to acute tolerance during a single dose and chronic tolerance to repeated doses (8). Therefore, a reduction in the mean effect of repeated doses might be explained by a progressively accelerated recovery during the declining limb of the BAC curve. On the other hand, a reduction in impairment might also be attributed to learning as a function of trials associating the response with a positive outcome.

Some research administering a single dose of alcohol has examined the impairment displayed by groups of social drinkers who performed a motor task at intervals either with or

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without a favorable outcome contingent upon drug-compensatory performance (6,17). These studies found the groups that had the opportunity to experience this response-outcome association displayed a briefer duration of impairment owing to recovery at higher declining BACs. This may be due to learning the response-outcome relationship as practice trials accumulate during the course of the dose. However, the accumulation of practice trials was also correlated with duration of exposure to blood alcohol. Thus physiological adaptation as a result of drug exposure time also may explain the effect. Therefore, the evidence from a single-dose experiment cannot differentiate between these two interpretations. An evaluation of the alternative explanations requires an examination of the profile of impairment during rising and declining BACs when doses are repeated.

If the acquisition of the tolerance-enhancing response-outcome association increases with practice, then the first few trials as BAC rises during an initial dose may not yield detectable effects. However, learning occurring during the dose should be retained and operate sooner upon each readministration of the dose. Such carryover of learning should lead to a progressive reduction in impairment on the rising as well as the declining limb of the BAC curve under successive doses. Further, no such effect should be displayed under a control treatment in which performance under doses of alcohol is not associated with any environmental outcome. The present article tests these hypotheses.

METHOD

The data were obtained in two experiments that repeatedly administered equivalent doses of alcohol to social drinkers and tested their performance on the same task at the same intervals after each dose was received (3,14). Both experiments employed the same experimental and control treatments during the first three alcohol sessions, and subsequent doses were administered to test different hypotheses. Although the studies reported the average alcohol effect during the first three sessions, the individual trial scores within sessions were not investigated or reported.

Subjects

In each experiment, 18 male social drinkers, aged 19–25, were randomly assigned to one of three groups containing six subjects each: two experimental (E) groups whose performance under alcohol was positively reinforced either by knowledge of results or by money; one control (C) group whose performance under alcohol had no environmental consequence.

Apparatus

A Tracometer was used to measure psychomotor performance (5). The subject sat in front of a tracking unit and moved a steering wheel to control the movement of a pointer across a vertical display panel on a tracking unit. The display panel contained five 2.4-mm circles, positioned in a semicircle and separated by 41 mm. When a circle was illuminated, it served as a target. The subject was required to center the pointer over the target as quickly and accurately as possible. When this was achieved, a new target was presented in another position. A single trial presented 100 targets. Moderate doses of alcohol depress speed of Tracometer performance and have no reliable effect on errors (2). Therefore, performance was evaluated in terms of total time (seconds) to complete a trial.

Procedure

All subjects received a series of preliminary training trials on the Tracometer to establish a drug-free level of achievement prior to the administration of alcohol. In each alcohol session, subjects performed drug-free trials to provide a baseline measure of achievement prior to drinking a dose of alcohol designed to obtain peak BACs close to 80 mg/100 ml. The dose was divided into three equal drinks, served at 20-min intervals.

During each alcohol session, subjects in both experiments performed nine Tracometer trials at the same times after drinking. Each trial was accompanied by a measure of the subject's BAC based upon a breath sample. The first trial occurred 20 min after drinking commenced, and trials were repeated at 40, 60, 70, 80, 90, 100, 110, and 130 min.

Alcohol sessions. The training administered to the two E groups of both studies associated drug compensatory (i.e., nonimpaired) performance under alcohol with a positively reinforcing outcome. The performance of subjects in the E groups was evaluated with respect to their own drug-free levels of achievement, and subjects were informed of the outcome of their performance in every trial, before and after drinking. Information was provided to one E group by verbal knowledge of results, and the other E group received money (25 cents) contingent upon the display of drug-compensatory performance. No environmental consequence was reliably associated with the performance of subjects in the C group of both experiments.

Criterion measures. The effect of alcohol was measured in each session by subtracting a subject's drug-free criterion score from each of his trial scores under alcohol during the session. Thus, a zero difference indicated performance equal to the drug-free level of achievement, a positive score indicated slower (i.e., impaired) performance, and a negative score indicated faster (i.e., improved) performance after drinking. The profile of impairment under a dose was examined by the measures of change in trial scores during each dose.

Preliminary analyses tested and confirmed the consistency of the evidence from the two experiments. Performance displayed by the two E groups of both experiments was assessed by a two (experiment) × two (E treatment) × three (session) analysis of variance (ANOVA). No main effects or interactions with experiment approached significance. Therefore, the E groups of both experiments were combined to make a single E group $n = 24$). Similarly, a two (experiment) × three (session) ANOVA assessed the comparability of the C groups from both experiments. The session × experiment interaction did not approach significance. However, a main effect of experiment, $F(1, 10) = 7.42$, $p = 0.021$, indicated that the C group of one study tended to display greater mean impairment on all sessions. This could not be attributed to differences in the BACs between the two C groups because an analysis of their BACs at intervals over sessions did not differ, $F(1, 10) = 0.10$, $p = 0.760$. Further, an analysis of BACs including all groups of both experiments obtained no significant effect of experiment, $F(1, 34) = 2.64$, $p = 0.114$. These results justified a combination of the data from the two experiments to obtain one E group $n = 24$) and one C group $n = 12$).

RESULTS

Table 1 shows the mean (±SEM) BAC during each trial after drinking commenced, averaged over groups and sessions. A mean peak BAC of 78 mg/100 ml (SEM = 1.5) was

TABLE 1

MEAN (SEM) BAC (mg/100 ml) AT NINE TRIAL INTERVALS DURING THREE ALCOHOL SESSIONS (N = 36)

	Test trials								
	1	2	3	4	5	6	7	8	9
Minutes after drinking began	20	40	60	70	80	90	100	110	130
Mean BAC	26	50	78	76	73	70	67	64	60
(SEM)	1.1	1.5	1.5	1.3	1.1	1.1	1.0	1.0	1.1

obtained during the third trial of a session, 60 min after drinking commenced.

The mean change in performance on the nine trials of each session is shown for the E and C groups separately in Figs. 1A and 1B. The abscissa plots the time of the nine trials as BACs rose and fell during every session. The mean change in performance is shown along the ordinate, where zero represents the drug-free baseline prior to drinking in each session. A positive change indicates impairment with respect to the drug-free baseline. The figures show impairment increasing in the trials as the peak BAC (60 min) is reached under each dose. Figure 1A (group E) suggests that the overall degree of impairment decreases from sessions 1-3. Figure 1B (group C) suggests an overall increase in impairment from sessions 1-3.

Profile of Impairment

A three (session) × nine (trial) variance analysis of change in performance by the E group revealed a main effect of trials, $F(8, 184) = 25.96$, $p < 0.001$, a main effect of session, $F(2, 46) = 11.24$, $p < 0.001$, and no session × trial interaction, $F(16, 368) = 1.14$, $p = 0.321$. The trial effect reflects the influence of rising and declining BACs during each dose. The session effect reveals an overall reduction in impairment on

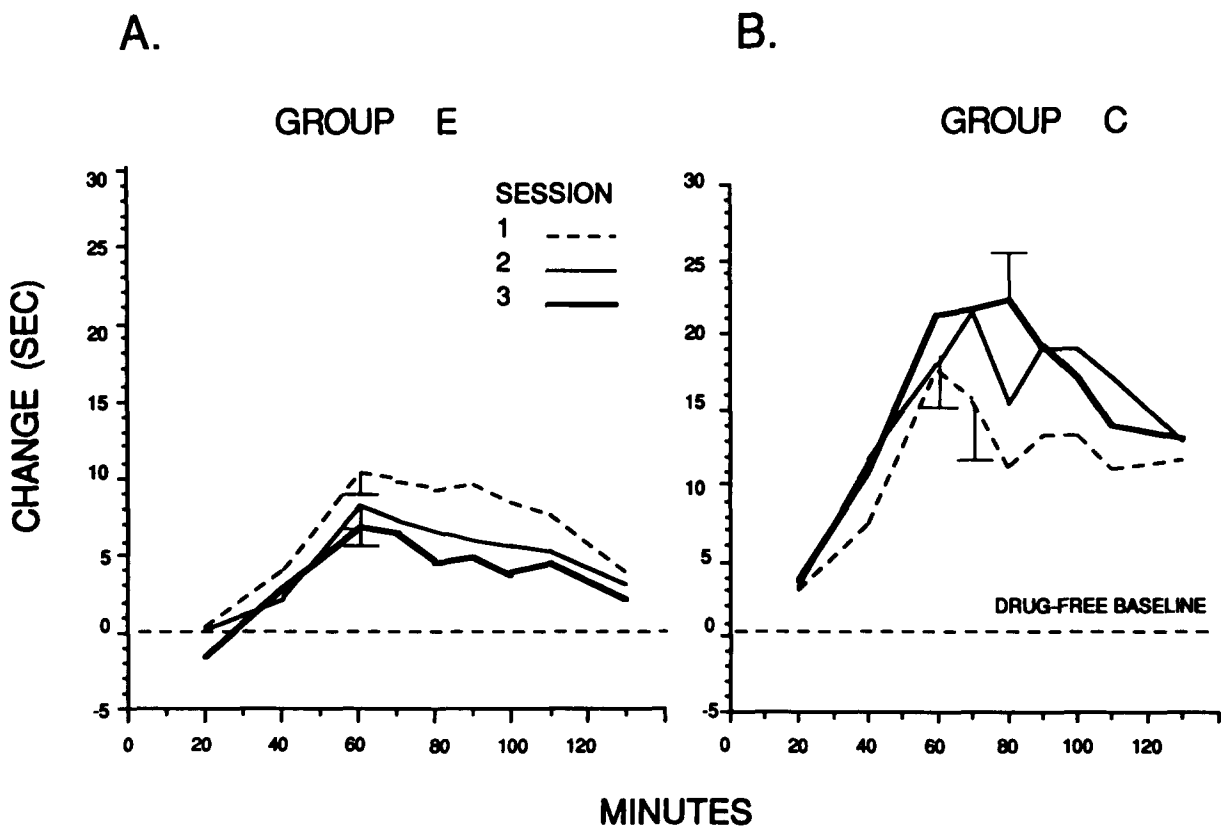

FIG. 1. (A) Mean change in performance on nine trials at intervals on each session for group E. Vertical bars show the largest SEM on a trial in a session. (B) Mean change in performance on nine trials at intervals on each session for group C. Vertical bars show the largest SEM in a trial in a session.

successive sessions. The absence of an interaction indicates the reduction of impairment across sessions was displayed on all trials under each dose (see Fig. 1A).

If the E treatment diminished impairment because of learning the response-outcome association, then learning during the first dose should be retained and carry over to reduce impairment on the initial trials during rising BACs on each subsequent dose. This prediction was tested by analyzing the change in performance on the first two trials (i.e., during the first 40 min under the dose) of the three training sessions. This three (session) × two (trial) analysis confirmed that impairment diminished progressively during the second and third sessions, $F(2, 46) = 3.50, p = 0.039$.

A three (session) × nine (trial) variance analysis of change in performance in the C group revealed a main effect of trials, $F(8, 88) = 18.54, p < 0.001$, a marginally significant main effect of sessions, $F(2, 22) = 3.42, p = 0.051$, and no session × trial interaction, $F(16, 176) = 1.23, p = 0.252$. The session effect suggests impairment intensified on successive sessions (Fig. 1B). The absence of an interaction indicates that the increased impairment across sessions was displayed on all trials under each dose. Although these findings imply a carryover effect of C treatment, the effect is marginal because the impairment in initial trials during successive doses was not affected. A three (session) × two (trial) analysis of the impairment displayed by the C group in the first two trials showed no increase over sessions, $F(2, 22) = 0.77, p = 0.475$.

Although the analyses of both groups showed a constant change in impairment in all trials during successive sessions, additional analyses checked the possibility that performance on rising vs. falling limbs of the BAC curve might be affected differently across sessions. However, these analyses also confirmed that the amount of change on the two limbs of the alcohol curve did not differ significantly in either group.

Rate of Recovery

Figure 1A shows that the E group tended to recover from impairment during every session while BACs declined (trials 4–9, 70–130 min postdrinking). The rate of recovery during these trials in each session was tested by a three (session) × six (trials) variance analysis. A significant linear effect of trials was obtained, $F(1, 23) = 19.32, p < 0.001$. Because this linear effect did not interact with sessions, it indicates a constant rate of recovery on each session.

Figure 1B shows that the C group also tended to recover from impairment during every session while BACs declined. Using the measures from trials 4–9, a three (session) × six (trials) variance analysis revealed a significant linear effect of trials, $F(1, 11) = 9.00, p = 0.012$, that did not interact with sessions. Thus, group C also displayed a constant rate of recovery on each session.

The effect of the E and C treatments on the rate of recovery was tested using the groups' linear rates of recovery, based upon the average over all three sessions. The recovery rates of the two groups did not differ significantly, $F(1, 34) = 1.03$, $p = 0.318$, indicating that these treatments did not produce different rates of recovery. The rate of recovery, expressed as the mean reduction in impairment for the entire sample, was -0.084 s/min (SEM = 0.012).

Additional regression analyses compared the rates of decline in impairment and in BAC during the 70- to 130-min period of the sessions (i.e., trials 4–9). For this purpose, the mean BAC and impairment in trial 4 were each set at a 100% maximum value and subsequent trials were transformed to a percent of trial 4. The impairment reduced at an average of -0.720%/min (SEM = 0.093), while the BAC declined at a mean rate of -0.357%/min (SEM = 0.016). These analyses indicate that impairment was declining twice as fast as the BAC.

DISCUSSION

Other research with social drinkers who perform a task under repeated doses of alcohol has led to the proposal that tolerance is enhanced by the acquisition of a response-outcome expectancy based upon a reliable association between drug-compensatory performance and a positive outcome. Control conditions that provide no reliable outcome for performance under alcohol show no such development of tolerance. The present study extended the investigation of these experimental and control treatments to an examination of their influence during rising and declining BACs under repeated doses.

The experimental treatment progressively reduced the amount of impairment during the rising and declining BACs of each dose, and there was a consistent carryover of resistance to impairment from one dose to another. Under control conditions, the amount of impairment during rising and declining BACs during a dose appeared to intensify somewhat over sessions. While this treatment provided no opportunity to associate compensatory performance with a positive outcome, it may have permitted subjects to learn that the effect of alcohol on their performance had no outcome of any importance. If such learning reduced interest in performing well on the task under alcohol, it could account for the tendency of impairment to intensify during rising and declining BACs on successive doses.

Together, the evidence is consistent with the theory that response-outcome relationships are learned and retained as expectancies that affect subsequent performance (4). From this perspective, the results of the present research imply that the expected consequences of performance under alcohol may play an important role in determining whether social drinkers display behavioral tolerance or sensitization to a dose of alcohol.

Although the treatments altered the amount of impairment during each dose, the rates of recovery during declining BACs did not differ or change with repeated doses. A constant rate of adaptation during declining BACs that is unaffected by different practice conditions is a new finding. However, this result is consistent with studies demonstrating that adaptation can be independent of task practice. Studies of humans and animals that have tested subjects once at different times under a dose of alcohol show that impairment at a given BAC reduces with time under a dose (7,10).

In sum, the experimental and control treatments influenced the amount of impairment displayed under repeated doses but did not affect the rate of recovery during declining BACs. These findings imply the influence of two independent processes: response-outcome associations that determine the threshold and hence the amount of impairment displayed under a dose and some adaptive process that determines the rate of recovery with time during exposure to a dose.

In the 1970s, Kalant et al. (8) proposed a theoretical model to account for both acute and chronic alcohol tolerance in terms of changes in threshold and in the rate of adaptation during a dose. The authors pointed out that their assumptions could be tested by measures of the drug effect at short inter-

vals during each dose, but such data were not yet available because studies customarily measured the response to alcohol at one fixed time after a dose. In the model, acute tolerance was attributed to adaptation that resulted in a progressive rise in threshold with time during a single dose. Two alternative hypotheses were offered to account for chronic tolerance: a) The adaptive process operating during one dose may endure over time and progressively increase the threshold for the effect of the next dose. As a result, a constant reduction in the intensity of the effect should be observed at BACs around the curve. b) The rate of adaptation during a dose may become swifter with repeated exposures to alcohol. In this case, the threshold BAC for the onset of impairment would remain constant but recovery would occur at progressively higher BAC thresholds on repeated doses.

The theoretical model of Kalant et al. (8) was offered to explain alcohol tolerance at the cellular level. Yet, their hypothesis a) is entirely consistent with the behavioral effect of moderate doses in social drinkers who received the tolerance-inducing E treatment. Their threshold for the drug effect increased with repeated doses, and a constant reduction in impairment was observed all around the blood alcohol curve. This evidence supports the assumption of an adaptation that endures and accumulates with repeated doses. But, this adaptive process is attributable to learning because it was displayed only by subjects who had an opportunity to learn that a positive outcome was associated with drug-compensatory performance.

There appears to be no other human research reporting behavioral effects during rising and declining BACs under repeated doses of alcohol. However, one experiment examined behavioral impairment in rats that repeatedly performed a task under daily doses of 2.2 g/kg alcohol (9). In that article, Fig. 2 (upper panel) showed that rats displayed a rising threshold and diminishing impairment similar to that observed under the experimental treatment in the present study. The task in the Kalant et al. experiment required the animal to remain on a metal belt that moved continuously over a shock grid. Thus drug-compensatory performance by the animal was reliably associated with a positive outcome (shock avoidance). In this respect, the task was analogous to that used in the present study, and the particular response-outcome association common to the performance of both tasks may account for the similarity of the results.

The present study found no evidence to support hypothesis b) of Kalant et al. (8), which predicted that adaptation during a dose becomes swifter. Perhaps comparatively high doses of alcohol are required to accelerate the rate of adaptation. However, if this is the case it seems unlikely that a progressively accelerating recovery process contributes to the tolerance of social drinkers.

A review of behavioral effects of drugs has noted that tolerance and sensitization to a dose may be affected by prior behavioral history (1). The present research extends these findings by indicating that a crucial component in behavioral history responsible for these effects may be the learned association between the response to alcohol and its outcome. Other research has shown that prior E or C treatment carries over to affect subsequent impairment even when performance under alcohol yields the same outcome (14). The long-term retention of these behavioral history effects suggests that the results of experiments testing individual differences among humans in the response to a single dose of alcohol will be difficult to interpret. The accumulating evidence points to the conclusion that the degree of impairment displayed by a drinker to a dose of alcohol may reflect learned response-outcome associations, physiological characteristics, or their joint influence.

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