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THE CONTRIBUTION OF POSTINGESTIVE ASSOCIATIONS TO ALCOHOL SELF-ADMINISTRATION

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Drugs, including alcohol, that are abused function as powerful reinforcers. Effective drug and alcohol addiction treatments decrease the reinforcing efficacy of the abused substance. Reinforcing efficacy arises from a variety of sources, documentation of which may aid in designing treatment and prevention interventions. Understanding the origin of the reinforcing efficacy may also prove useful in understanding both the initiation and maintenance of drug-taking behavior. This article reports results from 2 studies conducted to begin examining the degree to which postingestive consequences alter the reinforcing efficacy of alcohol. Participants consumed identical low-dose alcohol drinks (Experiment 1) or placebo drinks (Experiment 2) and then completed a set of laboratory tasks designed to mimic drug impairment or enhancement of performance. Following this, participants could choose to consume one of the drinks. Participants generally selected the beverage that had previously been associated with earning greater amounts of money. This effect was more pronounced and durable for the placebo beverage than for the low-dose alcohol beverage.

It is well established that certain drugs, including alcohol, function as powerful reinforcers (Thompson & Schuster, 1968). For this reason, successful strategies of substance abuse treatment should involve decreasing the reinforcing efficacy of the abused drug or increasing the reinforcing efficacy of alternative nondrug reinforcers (Skinner, 1938; Volkow, 2006). Although this strategy sounds simple, there is considerable difficulty involved in altering reinforcing efficacy. A major complexity derives from correctly identifying the nature of the reinforcing event. The reinforcement derived from alcohol consumption likely arises from multiple sources. For example, alcohol users may drink alcohol because of the pharmacologic activation of certain neural

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circuits related to the pursuit of survival behavior, such as eating, drinking, and reproduction. They may also drink to alleviate withdrawal symptoms experienced upon the termination of intoxication. Moreover, they may drink to reduce stress or anxiety (anxiolysis). All of these are factors that could modulate drinking, and they are neither exhaustive nor mutually exclusive.

Treatments that constrain the potential factors that occasion drinking to only one of these contributions to reinforcing efficacy will likely be less successful than those that consider all of them. To design such all-encompassing treatments, it is necessary to more fully understand the different contributions to a drug's reinforcing efficacy. The experiments described in this article were designed to further elucidate the degree to which postingestive consequences, events, or experiences alter the likelihood of an individual's consuming alcohol in the future.

Our understanding of conditioned reinforcement is relevant here. Broadly defined, a conditioned reinforcer is a once-neutral stimulus that acquires reinforcing function (Hendry, 1969; Hull, 1943; Kelleher & Gollub, 1962; Keller & Schoenfeld, 1950; Williams, 1994). Although the precise mechanism(s) in which a conditioned reinforcer acquires its reinforcing efficacy is not universally agreed upon Williams, 1994), it is apparent that stimuli associated with other reinforcers acquire reinforcing properties and become conditioned reinforcers (Fantino, 1977; Fantino, Preston, & Dunn, 1993; Kelleher, 1961, 1966; Mazur, 1991, 1995; Mazur & Romano, 1992; Nevin, 1969; Pliskoff & Tolliver, 1960; Weiss, Panlilio, & Schindler, 1993). This effect has been described for a variety of reinforcers, species, and settings (Bersh & Lambert, 1975; Brun, 1970; Salzinger, Freimark, Fairhurst, & Wolkoff, 1968).

The role of conditioned reinforcement in the maintenance of drug and alcohol self-administration is widely appreciated. For example, the cues such as taste that are paired with cigarette smoking can come to acquire the properties of conditioned reinforcers based on their association with the pharmacologically derived reinforcers a cigarette smoker experiences (e.g., Palmatier et al., 2006; Rose, 2005), and these associations likely contribute to the maintenance of smoking. However, this direction of association, in which juxtaposition of a drug with a neutral stimulus confers reinforcing properties to the previously neutral stimulus, is not the focus of this article.

Instead, we examine the related idea that alcohol itself can *acquire* reinforcing efficacy based on events that follow its ingestion. This idea necessitates a broader perspective for understanding alcohol consumption by combining in one stimulus (i.e., alcohol) both pharmacologically derived reinforcement and additional reinforcement resulting from the association of alcohol consumption with other sources of reinforcement. Additionally, this analysis suggests that treatment strategies that do not attempt to decrease all sources of reinforcement associated with the alcohol will be less successful. For instance, treatment with a pharmaceutical agent in the absence of some supportive behavioral intervention would only reduce the pharmacologically derived reinforcement, not the reinforcement derived from previous experience with the postingestive conditioning processes.

Some nonhuman work suggests that the reinforcing efficacy of alcohol can be modified by postingestive consequences. In several studies, investigators have demonstrated that arranging reinforcers contingent on alcohol consumption, can alter the reinforcing properties of the alcohol (Grant & Johanson, 1989; Grant & Sampson, 1985; Samson, Tolliver, Lumeng,

& Li, 1989). In Grant and Sampson took rats that did not consume alcohol and then made sucrose availability contingent on alcohol consumption. This had the effect of increasing alcohol consumption. More importantly, when the sucrose outcome was eliminated, lever pressing was maintained solely by alcohol delivery. In other words, alcohol by virtue of being associated with another reinforcer acquired reinforcing function. Grant and Johanson extended this finding with primates,

We are unaware of any laboratory studies exploring this phenomenon with alcohol in humans; however, Johanson, Mattox, and Schuster (1995) did explore it using placebo capsules. In that study, participants were given experience with two placebo capsules, each colored differently. Next, participants took part in several difficult performance tasks, during which they were led to believe that the amount of money they earned depended on their performance. The participants did earn money during the tasks, but the amount earned depended on the color of the capsule ingested and was independent of their performance. The participants were then asked to choose and consume their preferred capsule. The results showed that participants were more likely to choose the capsule that was associated with the higher monetary payoff, suggesting that the preferred capsule had acquired greater reinforcing properties than the capsule associated with lower payoff. This study established the methodology for assessing whether alcohol and other drugs might also acquire reinforcing function if they were associated with differential postingestive monetary outcomes.

Using a similar procedure Alessi, Roll, Reilly, and Johanson (2002) demonstrated that preference for placebo relative to 5 mg of diazepam could be reversed. The majority of participants who initially avoided diazepam self-administered it following the conditioning procedure in which diazepam was associated with presumed enhanced performance and higher monetary payoff, relative to placebo. In addition, verbal behavior associated with the drug-induced state was also altered such that participants reported that diazepam made then feel more alert than placebo following the conditioning of a preference for diazepam.

In a related line of inquiry, Griffiths and colleagues have demonstrated that the reinforcing efficacy of stimulants (i.e., caffeine and cocaine) is enhanced when participants know they are going to engage in an attention-demanding vigilance task relative to situations in which relaxation tasks are to be subsequently engaged in (e.g., Jones, Garrett, & Griffiths, 2001; Silverman, Kirby, & Griffiths, 1994; Silverman, Mumford, & Griffiths, 1994).

Further evidence suggesting that the reinforcing properties of drugs might be influenced by a postingestive conditioning process can be inferred from naturalistic observations of drug use. Individuals frequently take drugs or drink alcohol immediately prior to, or while engaging in, behavior that results in the delivery of powerful sources of reinforcement. For example, ecstasy (MDMA) is frequently consumed before individuals attend raves (all-night dance parties; Ramirez, Gallion, Espinoza, McAlister, & Chalela, 1997). Social interaction, which can be a powerful source of reinforcement (Ayllon & Haughton, 1962; Wikler, 1973), is available in abundance at raves. Thus, the temporal relationship between the social reinforcers available at the rave and the ingestion of ecstasy could potentially increase the reinforcing efficacy of ecstasy. Similarly, individuals frequently use alcohol prior to sexual activity (Battjes, Leukefeld, & Amsel, 1990). Sexual activity is a powerful source of

reinforcement (Crawford, Holloway, & Domjan, 1993); thus, it is likely that it confers additional reinforcing efficacy to the alcohol with which it is associated. (See Troisi & Akins, 2004, for a related study demonstrating the ability of sexual access to enhance cocaine's reinforcing efficacy in male Japanese quail.)

Another manner in which a drug could acquire reinforcing efficacy is via an association with "escape" from an aversive environment. Many individuals report consuming alcohol to cope with, or gain a respite from, undesirable circumstances, such as economic or social despair (Kleber, 1994). Basic research has shown that humans and animals will work to escape from aversive situations (Dinsmoor & Clayton, 1966; Evans, 1962) and that stimuli associated with escape become conditioned reinforcers (Miller, 1968). To the extent that an intoxicated state provides an escape from an aversive circumstance, it would be expected that the intoxicant would acquire additional reinforcing efficacy. In support of this, Henson (2006) observed that alcohol abuse did not decrease the quality of life of individuals with an anxiety disorder as it did for those without an anxiety disorder, suggesting that the anxiolytic properties of alcohol provide a pharmacological respite from anxiety. Such an arrangement would be expected to increase alcohol's reinforcing efficacy.

In this article we present results from two human laboratory studies designed to demonstrate that reinforcing efficacy can be enhanced for one beverage over another, identical beverage based on postingestive consequences. We have elected to use preference as a measure of relative reinforcing efficacy in these studies, as was done in Johanson, Mattox, and Schuster (1995) and Alessi et al. (2002). Preference is easily assessed. Furthermore, there is a rich history of using preferenceto infer reinforcing efficacy (e.g., Higgins, Bickel, & Hughes, 1993; Higgins, Roll, & Bickel, 1996; Johanson & de Wit, 1989; Johanson et al., 1995; Woolverton & Johanson, 1984).

General Method

These studies were approved by appropriate institutional review boards. Participants with no evidence of psychiatric disorder, including substance abuse, or physical impairment, between the ages of 21 and 45, were recruited. All participants were recreational/social drinkers, which was defined as having consumed an alcoholic beverage on more than two occasions but less than 12 occasions during the past month. Participants were recruited through local area newspaper advertisements, notices posted on various community bulletin boards, and word of mouth. Participants were paid $50 for the initial screening and $40 for each of the laboratory sessions in which they participated. In addition, they received a $100 bonus for completion. Participants were also able to earn additional money (approximately $30) during some sessions (described later). This is equivalent to approximately $9 per hour ($580 total possible earnings) and is commensurate with what other participants in similar studies are paid.

Experiment 1

Seven participants completed the study. Six of the individuals were male. The age ranged from 23 to 30 years, with a mean of 26 years.

Experimental Protocol. The procedure consisted of ten 5-hr experimental sessions. A minimum of 2 days and a maximum of 7 days separated the sessions. Testing took place in a room that permitted relatively unobtrusive monitoring of participants. As in past research of this type, several participants were occasionally participating at the same time. This room had a variety of recreational activities available. When participants arrived, breath and urine samples were collected and screened (on a random basis) for the presence of illicit drugs. Vital signs were collected, and a field sobriety test was conducted. Any individual with aberrant vital signs or who showed impairment on the field sobriety test would not have been allowed to participate in the scheduled session, although this did not happen. Similarly, the presence of illicit drugs (metabolites) in the urine specimen was grounds for exclusion; however, this did not happen. Participants were not allowed to smoke during experimental sessions.

Once it was determined that participants were eligible to participate in a given experimental session, they completed a set of mood questionnaires, the data from which are not presented in this article. Following the assessment of mood, participants were given a drink for immediate ingestion. During sessions 1 and 3, the drink was labeled Drink A, and on sessions 2 and 4 the drink was labeled Drink B. Both drinks were orange juice with 0.05 g/kg of the participant's initial body weight of alcohol added. Drinks were administered in the room where testing was conducted. Volume was equivalent across drinks, and the drinks were consumed within several minutes. Participants were instructed to note the letter associated with each drink and to attempt to associate the letter of the drink with the subjective and physiological effects produced by the drink. During sessions 1 through 4, participants performed two computer tasks at specified times (predrink, 30 min postdrink, 60 min postdrink, 90 min postdrink, and 120 min postdrink).

The computer tasks were similar to the ones used in previous research of this type (Allesietal., 2002; Johanson et al., 1995). The first task was a delayed *match-to-sample* procedure in which participants were instructed to report whether two complex stimuli presented sequentially on the computer screen were similar or different. The stimuli consisted of 8-by-8 grids of 64 small red and green filled boxes, with the pattern determined by the distribution of those 64 boxes. After the first pattern was presented for 1 s, there was a 2-s delay, after which another pattern was presented. The participants were instructed to press "s" on the keyboard if the patterns were the same and "d" if they were different. Three seconds separated each trial. The first task lasted a total of 2 min. The second computer task was a dual-component *stimulus-tracking task* in which participants had to keep a cursor inside a horizontally moving box on the lower portion of the computer screen, using the comma and period keys to move the cursor left and right, respectively. Participants also had to simultaneously maintain a small circle inside a big circle using the eight directional keys on the numerical keypad. The second task lasted a total of 2 min.

Participants were informed that they could earn money based on the accuracy of their performance on the two computer tasks. In reality, the monetary payoff schedule was predetermined and independent of their performance. Participants needed to respond in order to earn money, but their accuracy was irrelevant. The ambiguity and difficulty of these tasks effectively mask the independent (i.e., noncontingent) nature of money

earned (Johanson et al., 1995). In the present study, participants reported being unaware of this manipulation during a debriefing session following participation. The actual payoff schedule differed depending on the drink (e.g., A or B) ingested in a given session. For one drink, the payoff was low, with participants earning approximately $9.60 (approximate values: predrink, $3.00; + 30 min., $1.20; +60 min., $1.20; +90 min., $1.20; +120 min., $3.00). For the other drink, the payoff was high, with participants earning approximately $20.40 (approximate values: predrink, $3.00; + 30 min., $4.80; +60 min., $4.80; +90 min., $4.80; +120 min., $3.00). Patterns of payment were designed to convey the impressions of degraded performance (low payoff) or enhanced performance (high payoff). At the conclusion of each trial, the amount of money earned was displayed on the computer screen. Money earned in sessions from the computer task was paid in cash at the conclusion of each of the daily sessions. The determination of which drink was paired with high and low monetary payoff was balanced so that for approximately half of the participants, Drink A was associated with high payoff, and for the other half, Drink B was associated with high payoff.

Following ingestion of the drink and while not performing the computer tasks, participants were free to engage in any of the available recreational activities (e.g., reading, watching videotapes). Mood and vital signs were assessed hourly throughout the study. A lunch was provided 4 hours post–drink ingestion. Participants were allowed to consume noncaffeinated beverages throughout the session. Participants were not released from the laboratory until they had a blood-alcohol level, or BAL, of 0 and passed a field sobriety test.

During the next six sessions, the procedure was identical except that participants were given a choice between Drinks A and B and the computer tasks were omitted. Participants told the research staff which drink they wished to consume (A, B, or neither) at the beginning of each of the six sessions, and then they consumed that drink. This allowed us to collect a preference measure between the two drinks. Participants spent the same amount of time in the research laboratory as in initial sessions to allow us to collect comparable data. Participants were informed that they would not be conducting the computer tasks during this phase of the study.

Results and Discussion. Individual choices for the six choice sessions are presented in Table 1. Participant 4 did not consume any drink during two of the six choice sessions. Using the operational definition of preference established by Johanson et al. (1995) (making a choice twice out of three sessions), it can be seen that five of seven, or 71%, of the individuals evidenced a preference for the drink previously associated with the high monetary payoff (chi-square with Yate's correction = 8.37, one-sided, $p < .05$). If we remove the participant who abstained on two occasions, preference for the high-payoff-associated drink increased to 83% (5/6) (chi-square with Yate's correction = 13.54, one-sided, $p < .05$). This level of preference is similar to that previously reported for placebo by Johanson et al. (1995) and for diazepam by Alessi et al. (2002). Moreover, the preference appeared to be relatively stable over all six sessions, again using the Johanson et al. (1995) criterion for the last three sessions, 66% (4/6) (excluding Participant 4, who elected not to consume on two occasions) evidenced a preference for the drink associated with the high payoff. Participant 6 appeared to show an extinction-like effect, in that preference was not maintained into the last three sessions. Inspection of

Table 1 also shows that choice for the drink associated with the high payoff, while relatively stable over the six choice sessions, was not exclusive. Not one of the participants selected the drink associated with high payoff on every occasion. This is in contrast to the Alessi et al. (2002) and Johanson et al. (1995) studies, in which choice was often exclusive. It is worth mentioning that Participant 1 elected to consume the drink associated with the low payoff on all six choices, perhaps suggesting that the participant was seeking an intoxicated, performance-degrading experience.

Table 1
Individual Participant Choice Data From Experiment 1

	Choice 1	Choice 2	Choice 3	Choice 4	Choice 5	Choice 6
P1	Low	Low	Low	Low	Low	Low
P2	Low	High	High	High	Low	High
P3	High	Low	High	High	High	High
P4	None	Low	None	Low	Low	High
P5	High	High	Low	Low	High	High
P6	High	High	High	Low	Low	Low
P7	High	Low	High	High	Low	High

These results suggest that for the majority of participants, a preference was conditioned to a low-dose alcoholic drink previously paired with high monetary payoff. This is clinically relevant, as it suggests that individuals' consumption of alcohol can be modulated by postingestive consequences of alcohol consumption. As discussed earlier, this has important treatment ramifications. The results obtained from this study, though supportive of the idea that postingestive factors can influence preference for alcohol, were not as robust as have been reported in other studies using a similar paradigm (Alessi et al., 2002; Johanson et al., 1995), in that preference was not exclusive. One potentially important difference between this study and previous studies was the use of a drug (alcohol) with which participants were familiar. The identical drinks, although containing low doses of alcohol, most likely were discriminated as being alcoholic in nature on the basis of the gustatory and olfactory sensations accompanying consumption. Given that, for ethical reasons, participants were selected based on a history of social drinking, it is conceivable that the participants' history with alcohol use interfered with the conditioning process. Experiment 2 was conducted to control for participants' past history with alcohol by utilizing placebo drinks.

Experiment 2

Participants. Fourteen participants were enrolled in the study (11 male). The age range was 22 to 33 years, with a mean of 27 years. As in Experiment 1, none were excluded once they initiated the protocol.

Experimental Protocol. Experiment 2 largely followed the same procedures outlined in Experiment 1, except that sessions lasted 3 hours. In Experiment 2, participants did not actually receive any alcoholic beverages. Therefore, no medical screening or laboratory tests were conducted prior to their participation in the study.

Results and Discussion. Individual choices for the six choice sessions are

presented in Table 2. Due to a technical error, one individual, Participant 13, did not receive exposure to low and high payoff on alternating days but instead received exposure to low payoff on Sessions 1 and 2 and high payoff on Sessions 3 and 4. However, the choice data from this participant were retained. As shown in Table 2, 11 out of 14 participants, or 79%, evidenced a preference for the drink previously associated with the high monetary payoff (using the Johanson et al. [1995] criteria to operationalize preference—chi-square with Yate's correction = 17.120, one-sided, $p < .05$), and this preference was maintained for 50% of the participants during the last three choice sessions. Additionally, 36% of participants exclusively selected the drink associated with the high payoff, compared to none in Experiment 1.

Table 2
Individual Participant Choice Data From Experiment 2

	Choice 1	Choice 2	Choice 3	Choice 4	Choice 5	Choice 6
P1	High	Low	High	High	High	low
P2	High	High	High	High	High	High
P3	High	High	High	High	High	High
P4	High	High	Low	Low	High	Low
P5	High	High	High	Low	Low	Low
P6	High	High	Low	Low	Low	Low
P7	High	Low	Low	Low	Low	Low
P8	High	High	High	High	High	High
P9	High	High	High	High	High	High
P10	Low	Low	Low	High	High	Low
P11	Low	Low	High	High	Low	Low
P12	High	High	High	High	High	High
P13	High	Low	High	Low	Low	High
P14	Low	High	High	Low	High	High

The data from this study thus replicate Experiment 1, Johanson et al. (1999), and Alessi et al. (2002) by showing that postingestive consequences can alter the likelihood of self-administering a substance. The magnitude of this effect is approximately equal to that previously observed. Thirty-six percent of participants in Experiment 2 demonstrated an exclusive preference over all six choice sessions for the drug associated with high payoff. In Experiment 1, no participant exhibited this exclusive preference. Thus, it appears that for some participants the conditioning effects were more durable for placebo as compared to the alcohol-containing drink used in Experiment 1. This observation provides some support for the suggestion that an individual's history with alcohol interferes with ongoing conditioning to alcohol.

General Discussion

The results of the present experiments demonstrate that postingestive factors, not related to pharmacology, can influence a person's proclivity to imbibe a drink. These results were obtained using a procedure that differentially paid out money according to the drink imbibed. This observation

is strengthened because of the weak, contrived conditioning procedure that we employed. It is our opinion that if such effects can be demonstrated in a laboratory setting, then for naturalistic situations in which much more powerful sources of reinforcement often follow alcohol consumption, the effects could be much stronger.

The results could also have important clinical ramifications for the treatment of alcohol-use disorders, and other types of substance-use disorders. The results confirm and extend earlier research suggesting that alcohol and drugs do not obtain the sum total of their reinforcing efficacy exclusively from pharmacology. Instead, reinforcing efficacy is a compilation of pharmacological and nonpharmacological factors. Other nonpharmacological factors are undoubtedly important, such as socially mediated consequences of drug taking, and future research should explore these factors.

Treatments such as pharmacotherapy and immunotherapy, which only deal with a drug's pharmacology, are not likely to confer a maximal treatment benefit on the individual (e.g., Bogenschutz, DeMarzo, & Roll, 2008). Instead, we believe that treatments incorporating procedures designed to directly alter alcohol's or an abused drug's reinforcing efficacy, like contingency management, regardless of the source of the reinforcing efficacy, are to be preferred. We are not suggesting that the obvious pharmacologic aspects of substance abuse are unimportant, only that treatments focusing on those aspects may not be maximally effective.

Finally, these data, along with those from Johanson et al. (1995) and Alessi et al. (2002), suggest a mechanism for the genesis of drug and alcohol self-administration. Although many people report having negative initial reactions to drugs and alcohol, many go on to become lifelong users of these substances. Perhaps this is a function of individuals' postingestive experiences. For example, an adolescent may not be accepted by a group of peers unless he or she smokes cigarettes or drinks alcohol. To gain access to the powerful social reinforcers controlled by the peer group, the adolescent may begin to regularly consume alcohol or smoke. With the passage of time, the aversion to substances wanes and the adolescent becomes a regular user. In this case, the postingestive consequences would have mitigated the initial aversive response.

These two studies demonstrate that, in some cases, a preference for a specific beverage can be conditioned such that a drink paired with higher monetary reward will be preferred to one associated with lower monetary reward. Future work should examine the procedure with higher doses of alcohol and perhaps with postingestive punishment as well as reinforcement. Additional work investigating the role of instructional control and demand characteristics in this and similar paradigms will also be of interest. Translational efforts are needed to turn these and other laboratory results into effective, pragmatic, and acceptable treatment strategies.

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