

Understanding Alcohol Expectancy Effects: Revisiting the Placebo Condition

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This article summarizes a symposium organized and cochaired by Maria Testa and presented at the 2005 Annual Meeting of the Research Society on Alcoholism, in Santa Barbara, California. The symposium explored issues relevant to understanding the function of placebo conditions and to interpreting placebo effects. Cochair Mark Fillmore began with an overview of the use of placebo conditions in alcohol research, focusing on methodological issues. Jeanette Norris and her colleagues conducted a review of studies examining placebo conditions among women. They conclude that expectancy effects are limited to a few domains. Maria Testa and Antonia Abbey presented papers suggesting that placebo manipulations may result in unanticipated compensatory effects in actual or hypothetical social situations. That is, placebo participants may compensate for anticipated cognitive impairment through vigilant attention to situational cues. John Curtin's research suggests that the compensatory strategies of placebo participants appear to involve a sensitization of evaluative control, resulting in improved performance. Kenneth Leonard provided concluding remarks on the meaning of placebo effects and the value of placebo conditions in research.

Key Words: Alcohol Drinking, Placebo Effect, Methods.

THE PLACEBO EFFECT is intimately tied to the concept of expectancy that arose out of the need to specify an internal (i.e., cognitive) representation of the learning experience (Bolles, 1972; Tolman, 1932). When an association between 2 events is learned, the first event is said to elicit an expectancy of the second event. Moreover, once learned, the expectancy itself can elicit the associated outcome, and thus expectancies are considered to be an important determinant of behavior (Kirsch, 1999).

The placebo has a long history as a control-comparison condition in studies of drug effects on behavior (Kirsch, 1999). Early medical reports of the beneficial effects of placebos led to considerable interest beyond their use as control

conditions. In particular, the placebo effect has received much research attention from those who study the behavioral effects of alcohol. In alcohol research, the placebo is intended to measure behavioral effect of expecting to receive alcohol. Research has shown that individuals report expectations about alcohol effects on a variety of social, affective, cognitive, and motor behaviors (e.g., Goldman et al., 1999). These expectancies have been of particular interest because of their relationship with alcohol use and the possibility that they might predict potential alcohol-related problems, such as risk for alcoholism. In recent decades, interest in placebos in studies of acute alcohol effects on behavior has concerned the following 2 major issues: (1) methodological considerations of the placebo as an effective control-comparison condition and (2) the placebo as an experimental condition to study the effects of expectancy on intoxicated behavior. These issues are reviewed briefly here.

On methodological considerations, problems concerning implementation of placebo controls were revealed by research that used the 4-group, balanced placebo design that crossed the administration of alcohol or placebo with instructions designed to create the expectation of drinking alcohol or placebo (Rohsenow and Marlatt, 1981). Problems primarily concerned threats to the credibility of the placebo as an alcoholic beverage. Compared with placebo capsules used in other drug research, a credible placebo for alcohol poses unique challenges because it is administered as a beverage that is often familiar to subjects who can

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detect the presence or absence of its alcoholic content by taste, olfactory, somatic, and other subjective cues. Such cue-based discrimination of alcoholic content has been especially problematic for the "antiplacebo" condition in which subjects are given alcohol, but instructed that the beverage is nonalcoholic.

Alcohol placebos are also limited in terms of the alcohol dose that subjects can reasonably be led to expect (Martin et al., 1990). Postexperiment manipulation checks often reveal that subjects in a placebo condition report receiving alcohol doses that are considerably less than those doses administered in the active dose conditions. Instructional set has been another long-standing issue. The credibility of the placebo can be affected by the initial information given to subjects on the content of the beverages to be consumed, as typically provided in consent documents. A related issue is the potential influence of demand characteristics on the validity of manipulation checks on the credibility of the placebo. Some evidence shows that participants in placebo conditions may be under considerable experimenter demand to report having consumed alcohol despite their awareness that the beverage was nonalcoholic (Knight et al., 1986).

Despite the methodological problems associated with placebos as control conditions, the placebo has been a highly useful tool for understanding how alcohol-related expectancies can mediate behavioral responses to the drug itself. In particular, placebos have provided important insights into how alcohol expectancies contribute to individual differences in alcohol responses and how expectancies can foster the development of alcohol tolerance.

Individual differences in response to alcohol have been recognized for some time in experimental studies. Even when subjects receive a standardized dose of alcohol and attain the same blood alcohol level, some individuals display a large degree of impairment while others display little or no impairment. Some evidence suggests that this variability may, in part, be due to differences among drinkers in the type of alcohol effect they expect (e.g., Fillmore and Vogel-Sprott, 1995; Vogel-Sprott and Fillmore, 1999). Studies of alcohol effects on motor and cognitive functioning have shown the individual differences in responses to alcohol are related to the specific types of effects that drinkers expect. In general, those who expect the least impairment are least impaired and those who expect the most impairment are most impaired under the drug. Moreover, this same relationship is observed in response to placebo. Taken together, the findings suggest that the drinker's expectancies may represent an important cognitive factor that actually mediates the behavioral responses to alcohol.

It is well established that learning factors can play an important role in alcohol tolerance. Several studies have shown that tolerance to the impairing effects of alcohol is readily acquired in drinking situations in which subjects receive positive reinforcement for displaying unimpaired performance (e.g., Vogel-Sprott, 1992). The placebo has

been a useful tool in this research for understanding the underlying mechanisms of the behavioral tolerance in these situations. The tolerance-enhancing effects of reinforcement have been attributed to the acquisition of a compensatory, adaptive response that counteracts the drug effect. Tests for compensatory responses have been conducted by surreptitiously substituting a placebo for alcohol. These tests generally find a compensatory improvement in performance following placebo in alcohol-tolerant subjects. Moreover, the magnitude of the compensatory response is related to the degree of alcohol tolerance observed, such that individuals who display greater compensatory responses to placebo are generally more tolerant to the impairing effect of alcohol.

This brief overview on the use of placebos in alcohol research highlights methodological problems in their implementation but also describes some of their scientific utility in better understanding the nature of behavioral responses to alcohol itself. The speakers in this symposium continue to address these issues in their own areas of investigation on the effects of alcohol effects on social cognition, sexual behavior, and decision making.

EXPERIMENTAL EXPECTANCY SET EFFECTS IN WOMEN: A REVIEW

Jeanette Norris, Kristin A. Mariano, Margaret C. Thomas, Kim J. Nomensen, and William H. George

Expectancy set effects are widely documented in the alcohol research literature. However, most previous reviews have examined experimental studies in which most research participants were male or have not examined gender effects separately (Bushman and Cooper, 1990; Hull and Bond, 1986; Ito et al., 1996). To date, there has not been a systematic examination of studies that have documented the presence or absence of expectancy set effects in women. Because of different societal expectations for men and women on alcohol consumption (Crowe and George, 1989; Wilsnack and Wilsnack, 1997), men's and women's behaviors can differ after drinking even within the same social context. The purpose of the present study was to conduct a qualitative review of experimental studies that examined alcohol expectancy set effects on social and cognitive behaviors in women.

Several steps were followed to ensure the widest inclusion of appropriate studies. First, a computerized search of PsycInfo was conducted, with no time limit, using the key words "alcohol and placebo." This yielded 1,064 candidate studies. Second, searches of Medline and targeted searches of the work of researchers known to work in the area were also conducted. Third, computerized searches were repeated using more specific keywords such as "alcohol and placebo+stress, social influence, etc." Dissertations and meeting presentations were excluded. There were 2 criteria for studies to be included in the review, first, studies had to have only female subjects or female subjects whose

data were analyzed separately from males' data. Second, studies had to have a placebo condition *and* a no alcohol–told no alcohol control condition. The majority of studies were excluded because they used only alcohol and placebo conditions; therefore, they could test only for the physiological effect of alcohol but not for expectancy set effects.

The final sample included 61 articles published between 1975 and 2005, plus 1 in press (belonging to the first author), which presented a total of 63 experiments. Forty-two had been published since 1990. Thirty-two were published in journals devoted to alcohol and/or drug issues; the rest were in psychology journals. The topics covered in these papers included aggression ($n = 7$), cognitive/motor performance ($n = 10$), creativity ($n = 4$), decision making/risk taking ($n = 11$), mood/emotion ($n = 2$), sexual aggression ($n = 6$), sexuality ($n = 3$), social influence ($n = 3$), and stress/anxiety ($n = 11$). There were also 6 studies that covered a variety of miscellaneous topics, such as helping behavior and heart rate. In 1986, Hull and Bond conducted a meta-analytic review to investigate the relative importance of physiological versus expectancy set effects across multiple topics. Of the 34 studies examined by Hull and Bond, 8 met our inclusion criteria and are also included here. They address the following areas: 1 aggression, 2 sexuality, 3 stress/anxiety, and 2 miscellaneous.

Overall, 38% of the experiments found expectancy effects. All 3 of the social influence studies found that expectancy set increased susceptibility to social influence, whereas none of the aggression studies found effects for expectancy set. Studies on creativity, mood/emotion, sexual aggression, sexuality, and miscellaneous topics yielded mixed findings and there were too few within each topic to consider further. Three topics, cognitive/motor performance, decision making/risk taking, and stress/anxiety, included at least 10 studies and were examined at more depth.

In the area of cognitive/motor performance, only 3 of the 10 studies found expectancy set effects. In their meta-analysis, Hull and Bond (1986) concluded that expectancy set did not influence memory or motor performance; thus, these later studies, which were not included in the earlier review, are largely in agreement with Hull and Bond's conclusion. As is the case with many areas of research, several subtopics and methodologies are represented among these studies, which might account for some studies finding expectancy set effects and others not.

Several subtopics are represented within the area of decision making/risk taking. In studies concerned with risk perception and behavioral skills related to sexual decision making, the findings were mixed; about half found expectancy set effects, and half did not. In other subtopics, there are still too few studies to draw firm conclusions. However, this is currently a very active area of research, and future work should clarify whether expectancies play a significant role in affecting these types of responses.

Studies of stress and anxiety can include self-report or behavioral indicators of stress/anxiety, physiological

assessments, or both. Of the studies that examined self-reported anxiety and/or behavioral indicators, 4 found no effects, 5 found that expectancy set decreased anxiety, and 2 found that expectancy set increased it. Findings were similarly mixed when examining physiological responses, 1 study found no effect for expectancy set, 2 found that expectancy set increased skin conductance, and 1 found a decrease in stress. Hull and Bond's (1986) meta-analysis found that, in general, expectancy set did not consistently affect mood, including anxiety.

The presence of expectancy set effects in women seems to depend on the specific area of research, as well as a number of other qualifying factors. In some areas, too few studies have been conducted to draw firm conclusions. Of the 3 areas of research that included at least 10 studies, cognitive/motor performance studies do not, for the most part, yield expectancy set effects, whereas the areas of decision making/risk perception and stress/anxiety offer mixed findings.

Whether expectancy set effects occur may depend on factors such as the dependent measures used, the interaction between the belief that one has had alcohol and preexisting alcohol expectancies, and the specific experimental procedures. Marlatt and Rohsenow (1980) suggested that expectancy set effects should be strongest when there is a relationship between a particular set of preexisting expectancies and dependent measures that are closely related to them. Unfortunately, few studies that have tested for expectancy set effects have included assessment of preexisting expectancies. In addition, the means by which expectancy set is induced can affect whether the effect occurs. Ideally, the occurrence of an expectancy set effect should not be limited to 1 set of experimental procedures; however, some protocols may be more effective than others in producing the deception needed to convince experimental subjects that they have had alcohol when they have not.

Because this review was limited to consideration of published studies, it is possible that it overestimates the presence of expectancy set effects since negative or null findings may not be published. More studies are needed in several areas before more conclusive statements can be made about the nature of alcohol's influence on a variety of behaviors, that is, the extent to which alcohol's physiological and expectancy effects each contribute, relatively speaking, to behavioral outcomes. In particular, to clarify the role of expectancies, future experimental studies that use an expectancy set design should include measures of preexisting expectancies and should test the interaction between these and the belief that one has consumed alcohol.

COMPENSATORY EFFECTS OF ALCOHOL-SEXUALITY EXPECTANCIES WITHIN A PLACEBO CONDITION

Maria Testa, Carol VanZile-Tamsen, and Jennifer A. Livingston

The current study was designed to examine the role of alcohol consumption in women's responses to a hypothetical

social situation that contains a risk of sexual assault. Prior experimental analog research indicates that intoxicated women are less able to recognize sexual assault risk (Testa et al., 2000) and to respond effectively to unwanted sexual advances (Stoner et al., 2005). Such effects have frequently been viewed as consistent with alcohol myopia theory (Steele and Josephs, 1990), which maintains that the pharmacological effects of alcohol make it more difficult to recognize the less salient risk aspects of the situation and to respond effectively in a situation involving conflicting motives. Dating situations frequently involve conflict, in that the desire for sexual intimacy or establishment of a relationship conflicts with the desire for sexual safety. Although pharmacologically based alcohol myopia theory appears to explain the tendency for women to appear less cautious in these high conflict situations, alcohol expectancy effects may be operating as well. That is, situations involving the potential for sexual intimacy presumably involve sexual arousal, and sexual arousal is one of the domains in which alcohol expectancy effects have been noted. For example, women who believe they have consumed alcohol report higher subjective sexual arousal (George and Stoner, 2000) and perceive greater relationship potential despite partner HIV risk (Murphy et al., 1998). Thus, it is possible that women's interest in pursuing sexual intimacy at the cost of personal safety following alcohol consumption may reflect alcohol expectancy rather than, or in addition to, pharmacological effects.

To examine the effects of women's alcohol consumption on their responses to a dating scenario that involves potential risk of sexual assault, we included an alcohol condition, a placebo condition, and a no alcohol/told no alcohol condition. Female participants were asked to project themselves into a hypothetical scenario that juxtaposed desire for intimacy with an attractive male acquaintance against the risk of sexual assault posed by his escalating sexual advances. We hypothesized that relative to sober women, those who consumed alcohol would perceive less risk in the situation and consequently would express stronger intentions to engage in sexual approach behaviors and weaker intentions to engage in direct resistance behaviors. A pattern of results in which placebo participants respond similarly to those in the alcohol condition provides evidence for an expectancy effect. Conversely, similarity between placebo and no alcohol/told no alcohol participants, coupled with riskier intended behavior by alcohol participants, is consistent with a pharmacological effect.

Participants ($n = 101$) were recruited from among 937 young women, ages 21 to 32, who had completed a 3-wave longitudinal study of substance use and victimization (e.g., Testa et al., 2003). Women were excluded if they were married, pregnant, or alcohol dependent; did not drink at least 3 drinks per occasion at least monthly; or had medical contraindications to alcohol consumption. They were scheduled for individual laboratory sessions and offered \$50 or \$100, depending on the length of the session. Women were randomly assigned to 1 of 3 beverage conditions—alcohol,

placebo, or no alcohol. Drinks were consumed in a simulated bar setting. In the alcohol condition, a 0.66 mg/kg dose of ethanol was administered using 80-proof vodka mixed with tonic in a 3.5:1 ratio. Women in the no-alcohol condition received a comparable amount of tonic. Standard placebo manipulations (e.g., flat tonic poured from a vodka bottle) were used. After a 15-minute absorption period, breathalyzer readings were taken. Women in the alcohol and placebo conditions were both told that their blood alcohol level (BAL) was 0.04. In actuality, the mean BAL was 0.070% (SD = 0.02%) for the alcohol condition and 00% for the placebo condition. Consistent with other studies involving a placebo manipulation, placebo participants believed themselves to be more intoxicated than no-alcohol-told no alcohol participants, but less intoxicated than women who had received alcohol.

Women were asked to put themselves in the place of the female protagonist in a written scenario that described initial interest and attraction to a man, followed by increasingly aggressive sexual advances made by the man. Following the mild sexual advances (kissing despite her hesitation) and again following the more aggressive advances (he gets on top of her, removes her clothing), women completed measures of Risk Perceptions, Approach Behaviors, and Resistance Behaviors. Risk Perceptions consisted of 10 items assessing the likelihood that positive and negative outcomes would result from the situation (e.g., concern for your safety), scored so that higher scores indicate greater perceived risk. Approach behaviors (10 items) assessed the desire to engage in behaviors likely to facilitate a relationship (e.g., make out). Resistance behaviors included 3 subscales, direct resistance (forcefully push him away), polite resistance (make an excuse), and passivity (just go along with what he is doing even though I don't want to).

Risk perception, approach, and resistance measures were analyzed using MANOVA with 1 between-subjects factor (beverage condition) and 1 within-subjects factor (time). There was a significant multivariate condition \times time effect, $F(10, 190) = 3.54$, $p < 0.001$. There were no differences according to beverage at Time 1; however, there were differences on all 5 measures at Time 2. Tukey post hoc tests probing the simple effects of beverage condition at Time 2 revealed that the alcohol condition differed significantly from placebo on all 5 measures. Women in the placebo condition perceived more risk and anticipated less approach behavior, less indirect resistance, less passivity, and more direct resistance compared with those in the alcohol condition. Means for the no alcohol condition fell in between and did not differ from placebo.

We next explored the correlations between alcohol-related expectancies and the 5 dependent measures. Alcohol-related expectancies were assessed as part of the Wave 3 assessment using the AESASVQ (Abbey et al., 1999). Higher scores on these subscales—sexual affect, sexual drive, and sexual vulnerability—indicate stronger beliefs that alcohol influences one's own sexual behavior. We expected

that among women who consumed or believed they had consumed alcohol, stronger expectancies would be associated with stronger intentions to engage in sexual approach behaviors and polite resistance and weaker intentions toward direct resistance. In the alcohol condition, correlations between expectancies and outcome measures were in the expected direction but of a modest magnitude. For example, sexual affect expectancy correlated -0.19 with direct resistance. In contrast, in the placebo condition correlations were in the opposite direction as expected on all 5 measures. That is, women who believed most strongly that their behavior was influenced by alcohol perceived more risk in the scenario ($r = 0.31$), lower intentions toward sexual approach behaviors ($r = -0.28$) and passivity ($r = -0.36$), and greater intentions toward direct resistance ($r = 0.34$) and polite resistance ($r = 0.34$). Comparison of correlations for the alcohol and placebo conditions using Fisher's Z revealed significant differences on direct resistance ($Z = 2.14$) and passivity ($Z = 2.24$).

The findings reveal significant differences between placebo and alcohol participants. In response to escalating sexual advances, placebo women were significantly more cautious in their perceptions and their intended behavior relative to women who received alcohol, with means for the no alcohol condition falling in between. Contrary to hypotheses, correlational data indicated that women in the placebo condition behaved in a manner opposite to their beliefs. That is, stronger beliefs that alcohol influences one's sexual desire were associated with lower intentions to engage in sexual approach behaviors and higher intentions to resist sexual advances. In general, women recognize that alcohol increases vulnerability to sexual assault (Norris et al., 1996). We speculate that women who believed that they were drinking, but did not actually experience any cognitive impairment, responded to the scenario with increased vigilance and caution. Thus, the placebo condition may not be functioning as a way of controlling for alcohol expectancies but rather may induce its own demands for behavior. The nature of the expectancy may determine the type of placebo effects that are observed. If the outcome is desired, for example, sexual intimacy with one's partner, then believing that one has consumed alcohol may be sufficient to induce alcohol-like effects (e.g., increased sexual arousal). However, if the potential outcome is negative, such as sexual assault, women who are led to believe they are drinking may recognize the need for caution to avoid alcohol-related vulnerability.

DO PLACEBOS HAVE UNANTICIPATED EFFECTS IN ALCOHOL ADMINISTRATION STUDIES?

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There is a long history of research that documents the myriad of cultural expectations associated with alcohol

consumption (MacAndrew and Edgerton, 1969). Thus, it is important to include "intoxicated" (participants drink alcohol and know it), "sober" (participants do not drink alcohol and know it), and "placebo" (participants do not drink alcohol but believe they did) conditions in alcohol administration studies to distinguish between expectancy and pharmacological effects of alcohol.

Paradoxically, despite the many cultural stereotypes about alcohol's effects, evidence for placebo effects is mixed. Placebo effects are most consistently found in sexual arousal studies (George and Stoner, 2000). Across different domains of social behavior, there is only modest evidence to support expectancy hypotheses, even when individual differences in alcohol expectancies are taken into account (Chermack and Taylor, 1995; Fromme et al., 1999; Maisto et al., 2004).

Researchers use a variety of well-rehearsed strategies to convince placebo participants that they have consumed alcohol, such as placing napkins soaked in alcohol in the room in advance, pouring tonic out of a vodka bottle that appears to be unopened, and floating a small amount of vodka on the placebo beverage. These strategies are usually effective. Although there are some failures, most placebo participants report that they consumed alcohol. However, placebo participants do not typically report feeling as intoxicated as do participants who consumed alcohol (Fromme et al., 1999; Maisto et al., 2002; Marczinski and Fillmore, 2005). This raises the concern that the intoxicated and placebo conditions are not as equivalent as researchers would like to believe. There is evidence that alcohol expectancies differ for various levels of alcohol consumption (Southwick et al., 1981; Wall et al., 2000). Thus, if placebo participants feel mildly intoxicated, whereas drinkers feel moderately intoxicated, different expectancies may be evoked, thereby encouraging different types of behavior.

Another potential unanticipated difference between placebo and intoxicated participants is in the domain of compensatory effects. Several researchers have found that when participants think they are drinking alcohol, they are hypervigilant in an attempt to compensate for their anticipated poorer performance. For example, Marczinski and Fillmore (2005) conducted a within-subject study and found that participants made fewer errors on an inhibition task when they were in the placebo condition compared with when they were in the sober condition. Thus, placebo participants may actually perform better on some tasks than sober participants because hypervigilance enhances their performance.

The goal of this paper was to conduct secondary data analyses of this research team's past alcohol administration studies to determine whether there were any unanticipated placebo effects. We focused on 2 studies and examined variables that were not central to the study's main hypotheses. In Abbey et al. (2005), 153 male college students interacted with a female confederate whom they believed was a fellow

college student. The confederate was trained to act friendly, but not flirtatiously, during their 20-minute interaction. In Abbey et al. (2003), 180 male and female college students read a vignette about a couple in which the male character wanted to have sex but the female character did not. In both of these studies, intoxicated participants drank a quantity of alcohol intended to raise their blood alcohol concentration (BAC) to 0.080%. As found in past research, placebo participants believed they consumed alcohol and reported achieving a BAC comparable to that of intoxicated participants. Also, as found in past research, although placebo participants reported feeling significantly more intoxicated than did sober participants, their subjective intoxication levels were significantly lower than those of intoxicated participants.

In the social interaction study (Abbey et al., 2005), the primary dependent measures focused on perceptions of sexual behavior. As hypothesized, intoxicated participants rated themselves significantly higher on sexual variables than did sober and placebo participants. Thus, there was evidence for pharmacological effects of alcohol, but no evidence for placebo effects. In the new analyses conducted for this paper, differences were also examined in perceptions of how boisterous, bold, and outgoing participants acted during the interaction. For all 3 of these measures, significant differences were found between placebo and intoxicated participants, with sober participants' scores falling in between. Intoxicated participants reported feeling significantly more boisterous, bold, and outgoing than did placebo participants, $F_s = (2, 150) = 12.41, 28.34, 10.77, p_s < 0.05$, respectively. These findings reinforce those that were found for subjective intoxication levels by demonstrating that placebo and intoxicated participants do not have similar affective responses to their beverages. They support the hypothesis that the alcohol expectancies evoked in placebo and intoxicated participants may differ because placebo participants feel only mildly intoxicated.

In the potential date rape study (Abbey et al., 2003), alcohol consumption had an indirect effect on perceptions of the likelihood that the male character in the vignette would force sex on the female character through its impact on perceptions of the female character's sexual arousal and the appropriateness of the male character's actions. As found in the study by Abbey et al. (2005), there were no placebo effects associated with the primary dependent measures. In the new analyses conducted for this paper, differences were also examined in perceptions of the man's behavior early in the interaction. Placebo participants were least likely to believe that the man cared about the woman or would stop if she said "no," $F_s = 2, 177 = 3.01, 3.45, p_s < .05$, respectively. These findings support the hypervigilance hypothesis. Placebo participants, believing that they would be less alert than usual because they were drinking, may have paid particularly close attention to the details of the story. Thus, placebo participants noticed details that

both sober and intoxicated participants missed, which foreshadowed the man's later willingness to force sex.

These findings need to be replicated in studies designed to disentangle these different hypotheses about placebo effects. They suggest that it is extremely important to include a sober (told no alcohol and given no alcohol) control group in alcohol administration studies. It cannot be assumed that placebo participants' mental state, expectancies, and motivations are identical to those of intoxicated participants except for the effects of alcohol.

ALCOHOL CHALLENGE AND EXPECTANCY EFFECTS ON ERP CORRELATES OF COGNITIVE CONTROL

John J. Curtin

Converging lines of evidence suggest that alcohol's effect on behavioral responding occurs most reliably in experimental paradigms or real-world environments that elicit response conflict (Steele and Josephs, 1990; Steele and Southwick, 1985). For example, laboratory alcohol challenge studies consistently document deficits in paradigms requiring response inhibition (e.g., Go/No-Go, Finn et al., 1999; Go/Stop, Fillmore and Vogel-Sprott, 1999; N-back, Casbon et al., 2003). Similarly, theorists have observed that many of the real-world behaviors that are associated with alcohol intoxication, such as impulsivity, aggression, and sexual risk taking, also involve response conflict between competing response options (Curtin and Fairchild, 2003; Steele and Southwick, 1985). These consistent observations of altered responding during response conflict can guide research to determine the neurocognitive attention mechanisms through which alcohol produces these effects and the mechanisms that may be used to overcome these intoxicated deficits.

The pattern of behavioral findings highlighted above suggests that cognitive control processes may be particularly sensitive to impairment by alcohol challenge. Cognitive control has been defined as effortful activation and allocation of cognitive resources in the selection and processing of task-relevant information for purposes of maximizing performance on tasks involving high difficulty, complexity, response conflict, or novelty (Botvinick et al., 2001; Miller and Cohen, 2001). Cognitive control is important to volitionally guide behavior in a flexible fashion. It biases processing of information in favor of task-relevant stimuli and adaptive responses, particularly when response conflict exists, and it establishes the appropriate stimulus-response mapping given current goals.

Theory on cognitive control draws important distinctions between 2 components of control, referred to as evaluative and regulative control (MacDonald et al., 2000). Evaluative control is responsible for monitoring the need for control and signaling when adjustments in control are necessary. Recent evidence suggests that evaluative control processes monitor both task errors and response conflict and that this monitoring is accomplished in the anterior cingulate cortex

(ACC; Botvinick et al., 2001). Regulative control includes the processes related to the actual implementation of control, that is, establishing the appropriate stimulus response mappings and biasing of response toward task-relevant or goal-directed behaviors. Various sectors of the prefrontal cortex (PFC) are thought to be particularly important for regulative control.

To evaluate the effects of alcohol challenge and the expectancy of alcohol intoxication, we conducted 2 laboratory studies that involved variants of the Stroop task. In both studies, task performance was examined by observing error rates across trials. Both studies also involved the measurement of event-related brain potentials (ERPs) to index activation of cognitive control processes during Stroop task performance. Specifically, 2 frontal components of the ERP waveform have been observed to be influenced by anterior attention system cognitive control processes responsible for adaptive performance of the Stroop task. The N2 is a phasic negative deflection of the ERP waveform with a frontocentral distribution that peaks between 400 and 500 milliseconds after stimulus onset in the Stroop task (Liotti et al., 2000; Rebai et al., 1997; West and Alain, 1999). Available evidence suggests that N2 covaries with evaluative control processes that are important for the detection of response conflict. The NSW is a frontocentral slow wave that can be most readily observed during the latter part of a trial epoch after the initial, more phasic, ERP components have resolved (West and Alain, 1999, 2000). Available evidence suggests that NSW covaries with activation of regulative control processes.

In the first study, participants completed 432 trials of a standard Stroop task with both color-naming and word-reading task blocks and congruent, neutral, and incongruent trials (see Curtin and Fairchild, 2003, for further details). The task, which involves color naming versus word reading, was blocked and the 3 trial types were equiprobable. Analyses of behavioral and ERP indices focused on the color-naming blocks because alcohol had no effect on task performance when participants were required to execute the more strongly established word-reading response. In these color-naming blocks, participants in both beverage groups displayed the typical Stroop interference effect, with increased error rates on incongruent color-naming trials. However, the alcohol challenge produced a relative increase in error rate only when color-naming of incongruent stimuli was required. Thus, intoxicated participants displayed selective impairment on the trials for which cognitive control was most critical, suggesting that deficient cognitive control processes may underlie this behavioral impairment. Consistent with this assertion, alcohol challenge dramatically reduced the magnitude of the 2 electrophysiological indices of cognitive control, N2 and NSW. Specifically, the typical increases in N2 and NSW on incongruent trials were absent in the intoxicated participants.

The second study used a variant of the Stroop task that was designed to selectively manipulate the contribution of evaluative control to task performance (Carter et al., 2000). This Stroop task variant involved the typical trial-type manipulation (e.g., congruent, neutral, and incongruent trials). However, in this variant, trial-type frequencies were manipulated to form a *Mostly Congruent (MC)* condition where 80% of trials are congruent and a *Mostly Incongruent (MI)* condition where 80% of the trials are incongruent. Carter and colleagues have demonstrated that this manipulation of trial-type frequency powerfully alters ACC evaluative control activation and overall trial-level dynamic recruitment of cognitive control processes. In the MI condition, participants adopt a strategy in which cognitive control is tonically active across trials because of the high frequency of incongruent trials. Individuals quickly recognize how difficult these trials are and focus attentional resources across all trials on suppressing word information. Thus, evaluative control becomes less important because trial-level adjustments in cognitive control are not necessary. In contrast, participants in the MC condition tend to use word information because it aids performance on the majority of trials. However, on the infrequent but critical incongruent trials in this MC condition, participants experience a high degree of response conflict and neuroimaging evidence confirms strong phasic ACC activation and large changes in the level of regulative control across the incongruent trial. Therefore, this Stroop variant provides an attractive test for disentangling evaluative and regulative control processes. In the MI condition, ACC is not strongly activated and regulative control is high but statically active with little trial-level adjustment. In the MC condition, cognitive control processing is highly dynamic, with strong ACC activation and subsequent large changes in regulative control on incongruent trials. Therefore, task-related deficits across both conditions would suggest problems with regulative control, whereas selective deficits only in the MC condition would suggest a more specific problem with evaluative control.

To test for pharmacological and expectancy effects of alcohol, separate alcohol versus placebo and placebo versus no alcohol contrasts were conducted. No significant beverage group effects were observed in the MI condition, which encouraged static recruitment of regulative control and little involvement of evaluative control. However, the pattern of beverage group effects was quite different in the more dynamic MC condition. First, the alcohol versus placebo contrast revealed that alcohol selectively increased the error rate on incongruent color-naming trials, but only in the dynamic MC condition. Moreover, contrasting the placebo and no alcohol groups revealed that alcohol expectancy selectively reduced the error rate on incongruent color-naming trials in the MC condition. Specifically, a strong compensatory effect was observed. Participants who believed they were intoxicated outperformed the

participants in the no-alcohol control group in the critical condition that required dynamic detection of response conflict and trial-level adjustment in the implementation of cognitive control.

Examination of the NSW component of the ERP provided a test for predicted alcohol challenge and compensatory alcohol expectancy effects on cognitive control processes. First, NSW results from the alcohol challenge contrast replicated findings from the first Stroop study. Specifically, intoxicated participants did not display the same magnitude of dynamic, adaptive, trial-specific adjustments in cognitive control indexed by the NSW that was observed in placebo participants. Second, NSW results from the alcohol expectancy contrast suggested that the attentional signature of the compensatory processes used by placebo participants involved cognitive control processes. Specifically, placebo participants displayed much stronger, dynamic trial-specific adjustments in cognitive control than did no-alcohol control participants. After exposure to an infrequent, incongruent trial, placebo participants compensated by robustly increasing the level of top-down cognitive control to improve task performance and compensate for the alcohol-induced deficits that they expected to experience.

Synthesis of results across this pair of laboratory tasks suggests that alcohol challenge interferes with adaptive behavior during response conflict, as modeled in these studies by incongruent color-naming trials. It appears that impaired cognitive control processes may contribute to these behavioral problems. In addition, results for the second Stroop study suggest that impairment in the evaluative component of cognitive control, which is most important for dynamic adaptive adjustments in the level of cognitive control, may be particularly important for understanding alcohol challenge effects. Finally, the second study suggests that participants who expect to receive alcohol can and do engage in compensatory strategies that can improve task performance in conditions that involve response conflict. These compensatory strategies appear to involve a sensitization of evaluative control that leads to improved, fine-grained adaptive adjustments in cognitive control across trials as needed. Unfortunately, the alcohol challenge data suggest that these attentional processes that are required to compensate for expected intoxication are the same processes that are impaired when the individual actually consumes alcohol.

DISCUSSION

Kenneth E. Leonard

The papers presented in this symposium document several aspects of the effects of placebo controls in alcohol research. Overall, they suggest that the effects of placebos are often weak and quite variable. Moreover, the placebo effects that are observed often appear to be due to the individual attempting to compensate for the expected

effects of the alcohol, rather than the individual behaving according to some alcohol expectancy. Consequently, the papers raise the issue of meaning of placebo effects and, ultimately, the value of the placebo in alcohol research.

The premise that underlies the use of a placebo is that it reflects the effects of the expectancy of receiving a specific substance. In the context of medical research, this expectancy may simply be that the substance will ameliorate some targeted symptoms. Because the participant has little, if any, experience with the active substance, there is little to conflict with the expectancy of benefit that may be supplied by the experimenter. In alcohol research, the context in which a placebo is administered is quite different. Participants in alcohol research are required to have some experience with alcohol at the dose administered. As a result, the participant already has a rich history of expectancies, and alcohol is not assumed to provide expectancies, but rather to activate existing ones. It is this aspect that probably accounts for the variability in the placebo response. To the extent that individuals differ from each other in their alcohol expectancies, we would expect variability in behavior. Moreover, because an individual may maintain a variety of expectancies on alcohol, his or her behavior may be very different depending on the specific expectancy that is activated. We often presume that the expectancy that is activated is one that is congruent with the behavior of interest, but this presumption is not necessarily well founded. In many of the paradigms described in the present series of papers, multiple expectancies could be activated. For example, in the studies described by Abbey and Testa, expectations about alcohol and sociability, sexual arousal, and aggression may all be relevant.

It is worth noting that in certain contexts, robust placebo effects are observed. Studies of expectancy challenges utilize nonalcoholic beverages in group party contexts. There are many aspects of these contexts that do not correspond with the usual laboratory experiments focused on the effects of alcohol. Because these challenges are not described to participants as a study of the effects of alcohol, it seems unlikely that they would focus their attention on the alcoholic beverage or monitor its effects. Participants consume at their own rate, in contrast to lab experiments in which participants are given a significant amount of alcohol and asked to consume it quickly. Given the social setting, there can be a significant degree of contagion, which may guide behavior, and many aspects that might distract participants from their physiological experience. In some studies, procedures adapted from this context may be useful.

In addition to the variability in behavior that might arise from different expectancies both within and across participants, the extent to which these expectancies are viewed with desire or trepidation may impact the observed behavior. For example, while there is a strong expectation that alcohol increases sexual arousal, many individuals may not desire such an outcome in an unfamiliar lab setting

with strangers of the opposite gender. Under such circumstances, the belief that one has consumed alcohol may activate an expectation of sexual arousal, but this expectation might enhance anxiety and vigilance and lead to restrained behavior. In contrast, the expectation might have a completely different effect with an intimate partner in a more private setting. In short, success in activating a specific expectancy will not necessarily result in behavior congruent with that expectancy, but it may activate behaviors with the motivation of avoiding or compensating for the expected outcome. The research described in Curtin's paper demonstrates this in a very sophisticated way. This compensatory effect appears to occur through increased evaluative control and action monitoring processes, the very effects that are impaired by alcohol.

The possibility of a compensatory placebo response raises the issue of whether it would ever be advisable to utilize a 2-group design involving placebo and alcohol. Such a design has been used with increasing frequency for obvious reasons; it requires only 2/3 of the subjects required for a standard 3-group design and it appears to test the effect of alcohol over and above the effect of the alcohol expectancies. However, in contexts in which a compensatory effect might occur, one cannot discern whether a difference between a placebo and alcohol reflects an effect of alcohol, a compensatory effect, or some combination.

The papers in this symposium raise concerns about the use of alcohol placebos in research. If placebos largely have no effect on behavior, or if there are many instances of compensatory responses, we must ask under what conditions are placebos necessary control procedures, and under what circumstances can placebo conditions be omitted. It is clear that research on alcohol-related behaviors that have not been well studied would benefit from the inclusion of placebo conditions. For well-studied behaviors, it is incumbent on the investigator to examine the literature carefully, and to choose control conditions accordingly. In some instances, the absence of any systematic placebo effect would be an argument for omitting the placebo condition. Clearly, however, there is a need for systematic meta-analyses of the alcohol-placebo literature to help guide these decisions, and for more basic research to understand the processes underlying placebo effects.

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