

Expected effect of caffeine on motor performance predicts the type of response to placebo*

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Abstract. Two experiments ($N=56$) investigated the relationship between subjects' expectancies concerning the effect of caffeine on a motor skill, and the type of placebo response. Male subjects were assigned to four groups. Three groups expected to receive caffeine but received a placebo. Prior to the placebo, two of the groups received information about the effect of caffeine on a motor skill task which led one group $E(+)$ to expect enhanced performance, and the other $E(-)$ to expect impairment. The third placebo group received no information $E(?)$. A control group $E(0)$ received no beverage, so neither caffeine nor any effect on performance was expected. The expected type of effect predicted the type of placebo response displayed. Group $E(+)$ displayed greater improvement under placebo than did group $E(0)$, and group $E(-)$ performed more poorly than those in group $E(0)$. No placebo response was observed in group $E(?)$. Placebo effects on mood were correlated with subjects' predictions about the effect of caffeine on mood. The role of expectancies in response to placebos and psychoactive drugs is discussed.

Key words: Placebo – Expectancy – Learning – Humans

The effort to assess the effects of expecting a drug, distinct from the pharmacological properties of the drug, has led to the use of a two factor balanced placebo design (Ross et al. 1962; Rohsenow and Marlatt 1981). The majority of studies using this design have measured social behaviors, such as aggression (e.g., Lang et al. 1975), affect (e.g., Vuchinich et al. 1979), and sexual arousal (e.g., Briddell et al. 1978). Fewer studies have looked at measures of cognitive and psychomotor performance,

such as memory, coding, reaction time, and fine motor coordination (e.g., Connors and Maisto 1980). Reviews of the results of experiments using balanced placebo designs have concluded that expecting alcohol produces robust placebo effects on social and affective behaviors independent of actual beverage consumption, but minimal or no placebo effects are observed in motor and cognitive behavior (Marlatt and Rohsenow 1980; Hull and Bond 1986).

The puzzling absence of placebo effects in cognitive and motor behavior has led to the speculation (Marlatt and Rohsenow 1980) that individuals may share common, explicit cultural expectations about how alcohol influences social and affective behavior, but people may be uncertain as to how alcohol may affect their motor and cognitive performance. In fact, studies of individuals within a subculture indicate that they report widely different expectancies about the effect of alcohol on cognitive and motor performance (Brown et al. 1980; Goldman et al. 1987). The failure to obtain a placebo response in motor performance when subjects expect caffeine has also been attributed to possible variable expectancies about the effect of caffeine on performance (Kirsch and Weixel 1988). Although this explanation makes intuitive sense, it is typically applied retrospectively to account for the presence or absence, as well as the type of placebo response observed in a given behavior. It appears that no studies have been designed to test the ability of these expectancies to predict the placebo response.

An analysis of placebo responses in terms of learning suggests one experimental approach (Vogel-Sprott and Fillmore 1990). Following other theorists, it can be assumed that learning consists of the acquisition of information concerning a reliable association between events (Bolles 1972; Rescorla 1987). Once learned, the term "expectancy" serves as a shorthand label for the acquired information. Four types of events relevant to expectancies can be identified: the stimuli accompanying the administration of drug (S); the stimulus effect of the drug (S_a); the particular effect of the drug on a response

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(R_d) involved in an activity; and the environmental outcome of this effect (S^*). The successive occurrence of these four events provide an opportunity to acquire three expectancies. The expectancy that alcohol has been received is learned by the reliable association $S-S_d$. Balanced placebo design studies rely on this expectancy, assuming it has been learned through prior use of alcohol and will be evoked by presenting S (i.e., liquor bottles, scent of alcohol, instruction). However, the other two expectancies may also affect the placebo response. One of these, termed "response expectancy", may be learned whenever some activity is performed under alcohol and some environmental consequence S^* is reliably contingent upon the behavioral effect of the drug R_d . The acquisition of an R_d-S^* association is important because the desirability of the expected S^* may determine the display of R_d . Considerable support for this hypothesis has been obtained in studies of alcohol effects on cognitive and motor performance, and this research has been reviewed elsewhere (Vogel-Sprott and Sdao-Jarvie 1989).

The other association is one that links the drug stimuli (S_d) with a particular type of response (R_d). The S_d-R_d relationship is considered to provide information about the specific behavioral effect that alcohol exerts on an activity. Since a drug may produce a number of different types of behavioral effects, the acquisition of specific information in this relationship may be crucial in determining the type of placebo response that is displayed. No research has yet tested this possibility, but the predictions of the learning analysis are clear. The S_d-R_d association provides information about the type of effect a drug exerts on a given activity. The acquisition of this information permits a subject to expect a particular drug effect and this expectation should predict the type of placebo response displayed. The present study was designed to test this hypothesis with respect to motor performance.

Although the question about placebo responses primarily stems from research on alcohol, several considerations suggested that an adequate experimental test of the hypothesis might be difficult to achieve with alcohol. The credibility of an alcohol placebo could be problem (Martin et al. 1990) and there is controversy over whether subjects in an experiment actually do expect alcohol when they receive a placebo (Knight et al. 1986, 1988; Collins and Searles 1988). Caffeine appeared to be a particularly suitable drug because a very credible placebo for the drug exists in the form of decaffeinated coffee, and, as in the case of alcohol, subjects who expect caffeine but receive a placebo also report changes in mood and fail to demonstrate a reliable placebo response in psychomotor performance (Kirsch and Weixel 1988). However, in the case of caffeine, it seemed that the expected type of drug effect could likely be more adequately and effectively manipulated because caffeine is a central stimulant that has no particular consistent effect on motor performance (Weiss and Laties 1962). Thus, the present research tested the placebo response of subjects who expected to receive caffeine in the form of coffee.

Two experiments tested the hypothesis that the type of effect that caffeine is expected to exert on psychomotor

performance predicts the type of placebo response. The second experiment was designed to check the reproducibility of the findings when subjects were tested by an assistant who was blind to the treatment conditions. Both experiments involved four groups. Two groups received explicit information associating the drug (S_d) with a particular type of effect (R_d). A description of the impairing effect of caffeine on psychomotor performance was provided to allow one group of subjects to expect impairment. Another group was given information that led them to expect caffeine would improve their performance. The group who expected impairment $E(-)$ was predicted to show poorer performance after receiving a placebo (decaffeinated coffee) than the group who expected enhancement $E(+)$ of performance. Moreover, the influence of different expectancies should be immediately evident in subjects' performance under the placebo. The remaining two groups received no information about the effect of caffeine. One of these groups, $E(?)$, received the placebo and its treatment thus represented the traditional placebo test procedure which has failed to reveal any reliable placebo effect on motor performance. The fourth group, $E(0)$, received neither information nor the placebo. Because no drug was expected or received, the $E(0)$ group was predicted to display performance intermediate to groups $E(+)$ and $E(-)$ and to be comparable to group $E(?)$.

Materials and methods

Subjects

Two studies involved a total of 56 male university student volunteers between 19 and 29 years of age. In each experiment ($n=28$), subjects were randomly assigned to one of four groups (group $n=7$) and were paid 8 dollars for their participation. Volunteers were asked to take no medication for 3 days prior to the experiment, and to abstain from any source of caffeine (e.g., coffee, cola, chocolate), as well as any fluids, for 2 h prior to the experiment. These restrictions were imposed to encourage the belief that caffeine was to be administered.

At the outset of the study, subjects' daily consumption of coffee was recorded with a questionnaire which has been employed in other research (Kirsch and Weixel 1988). A 4 group \times 2 experiment variance analysis of daily coffee consumption showed no significant group effect [$F(3,48)=0.42$, $P=0.741$], or group \times experiment interaction [$F(3,48)=1.30$, $P=0.285$] or main effect of experiments [$F(1,48)=0.28$, $P=0.601$]. The entire sample ($N=56$) drank a mean of 1.7 cups (SD = 1.9) of coffee per day, and 22 subjects consumed no coffee.

Apparatus

Psychomotor performance was measured using a computerized pursuit rotor task (PR). A computer operated the program that displayed a white rectangular track with a black background on a computer monitor. The computer terminal and monitor were placed on a desk and subjects performed the task while seated in front of the terminal and monitor. Tracking was performed by moving a "mouse" on a flat surface which in turn controlled a sight displaying cross hairs on the screen. Subjects controlled the sight (diameter = 1.3 cm) to track a moving target (diameter = 1.3 cm) rotating clockwise at 20 rpm around the track. The computer program

automatically presented three blocks of four 50 s trials, separated by a 30-s inter-trial interval. At the end of each block, a message displayed on the computer screen instructed the subject to "take a break". The duration of rest between blocks was two minutes and was also automatically timed by the computer. This computerized version of pursuit tracking controlled the entire testing of performance allowing each subject to perform alone in the room thereby eliminating any influence on performance of the presence of the experimenter.

Measures

Performance on each PR trial was measured by the percentage of time the subject's sight was on target (%TOT). The scores were automatically recorded and stored in the computer, so neither the subject nor the experimenter had access to this information during the experiment.

Kirsch and Weixel (1988) found that subjects report changes in alertness and tension after receiving a placebo which they believe is caffeine. The possibility that subjects' expectations about the effect of caffeine on these states would also predict their reported change in mood under placebo was explored in the present research. Subjective mood was measured by asking subjects to rate each of 15 adjectives on 10-point Likert-type scales used by Kirsch and Weixel (1988). Two subscales were derived from these ratings: alertness (score range = zero to 63) and tension (score range = zero to 45). Subjects completed the questionnaire three times to rate their (a) mood prior to placebo, (b) mood expected under strong coffee, and (c) mood experienced under placebo.

The experiment also measured subjects' a priori expectancies about the effect of caffeine on their performance. Before the treatment was administered, all subjects were asked to predict how coffee would affect their performance on the PR, using a nine-point Likert-type scale ranging from 1 "largely impair", to 9 "largely enhance", and 5 indicating no effect.

Procedure

After explaining the general purpose of the experiment and answering any questions, informed consent was obtained and the coffee consumption questionnaire was completed. Subjects in three groups were told that they would receive a dose of caffeine in the form of coffee. The experimenter weighed all subjects in those groups while explaining that this was necessary in order to calculate a standardized dose of caffeine based on body weight. Although subjects had already been randomly assigned to groups, subjects in the fourth group witnessed a bogus coin toss which, they were told, placed them by chance in the no-drug control group.

Baseline training. Baseline training on the PR task consisted of twelve 50-s trials presented in three blocks of four trials each, with a 2-min rest period between blocks. Previous pilot work indicated that this amount of training was likely to yield 50% tracking efficiency, and would allow ample opportunity for the subsequent display of improved or impaired performance.

Each subject was escorted to a small room containing the PR and performed one 50-s familiarization trial before baseline training began. During the first block of trials the experimenter remained in the room to ensure that the task requirements had been understood, and then left the subject alone to complete the baseline training trials. The subject was asked to complete the subjective mood scale during the rest period between the second and third block of trials.

Treatment. When baseline training concluded, all subjects returned to the waiting room. Three groups of subjects watched the experimenter brew the beverage. Decaffeinated coffee was taken from a jar bearing the label of a common brand of caffeinated coffee that was clearly visible to the subject. As the experimenter placed five

heaping tablespoons onto a coffee filter which rested over a mug, he commented that a "fairly strong" dose was needed to produce effects in a brief period of time. A previous study indicated that subjects were most likely to believe that this apparent dose actually contained caffeine (Kirsch and Weixel 1988). The experimenter explained that the coffee would be brewed in 150 ml (one half-cup) of boiling water. While the water set to boil, the subjects completed a questionnaire asking them to predict the degree and type of effect which this amount of coffee would have on their PR performance. Using the subjective mood scale, these subjects also predicted how this dose of coffee would make them feel. After the water had boiled, the experimenter measured out 150 ml in a clear measuring cup and poured it through the coffee filter, allowing it to brew in the subject's presence. The beverage was served and subjects were given 5 min to finish the drink.

During the drinking period, subjects in one group E(-) were told that research has shown that caffeine impairs fine motor coordination, and the purpose of this study was to understand how a large dose of caffeine causes this impairment. Subjects in another group E(+) were told that caffeine enhances fine motor coordination and the purpose of the study was to determine how caffeine produces this enhancement. Subjects in the third group, E(?), received no information concerning the type of effect associated with caffeine. The coffee brewing and drinking required about 10 min. A fourth group, E(0), received no drink and spent this time in the waiting room where they completed a questionnaire asking them to predict the degree and type of effect which coffee (in general) would have on their PR performance. Using the subjective mood scale, they also rated how coffee (in general) would make them feel. No reference to a specific dose was made. During the remainder of the time, these subjects remained at leisure in the waiting room, read magazines, or chatted with the experimenter.

Post-treatment test. All subjects subsequently entered the test room alone and performed 12 trials on the PR, comparable to those administered during baseline training (i.e., three blocks of four trials). During the rest period between the second and third block of trials, subjects also completed the subjective mood scale.

The experimental procedure of the two experiments differed in two respects. The first study had been conducted by one experimenter who administered the expectancy treatments and also explained the PR task to the subjects. In the second experiment subjects received their introduction and instruction about the PR task from a technician who was unaware of the purpose of the experiment, and had no information about a subject's group assignment. In the first experiment subjects in group E(0) were told that they were control subjects before they performed their baseline training trials. In the second experiment this information was withheld until after the baseline training.

A post-experimental inquiry revealed that all subjects who received the placebo in both experiments ($n=42$) reported that they thought the beverage contained caffeine.

Results

PR performance

Because performance on the PR task improved gradually with successive trials, the mean of the last three pre-treatment trials was used to measure subjects' performance at the conclusion of baseline training. A 4 group \times 2 experiment variance analysis of these pre-treatment measures obtained no significant group \times experiment interaction [$F(3,48)=1.16$, $P=0.336$] or main effect of experiments [$F(1,48)=0.24$, $P=0.627$], or groups [$F(3,48)=2.62$, $P=0.061$]. The overall sample mean ($N=56$) pre-treatment % TOT scores of the final three trials was 54.256 (SD = 13.185).

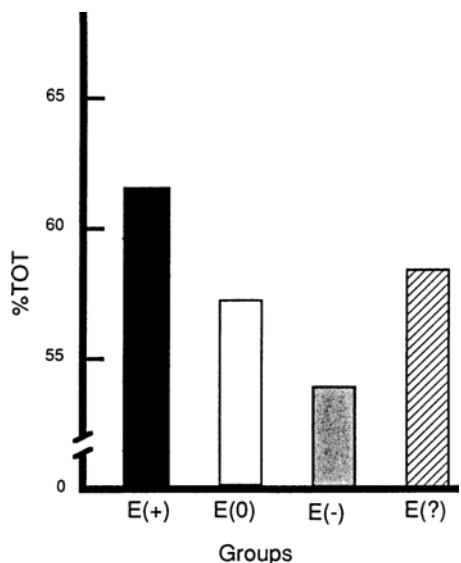


Fig. 1. Mean adjusted post-treatment performance (%TOT) of four groups (group $n=14$)

The post-treatment performance was measured by the mean of the first three trials' scores obtained immediately after treatment. A significant regression of the post-treatment scores on pre-treatment scores [$F(1,54)=271.58$, $P<0.001$] indicated that individual differences in pre-treatment performance accounted for 83.4% of the variability in subjects' post-treatment performance. To control pre-treatment differences, the analyses of post-treatment performance used subjects' pre-treatment performance scores as a covariate.

The pre-treatment scores showed no significant interaction with groups [$F(3,48)=0.40$, $P=0.754$], indicating that the assumption of homogeneity of slopes was tenable and a 4 group \times 2 experiment covariance analysis was valid. The analysis revealed a significant group effect [$F(3,47)=4.38$, $P=0.008$], with no significant group \times experiment interaction [$F(3,47)=0.62$, $P=0.608$], or main effect of experiments [$F(1,47)=2.60$, $P=0.113$]. Given the absence of any significant effects of experiments, a covariance analysis of post-treatment performance was performed ignoring the experiment factor. This analysis also yielded a significant group effect [$F(3,51)=4.69$, $P=0.006$]. The adjusted group means are depicted in Fig. 1. As predicted, group E(+) showed the largest increase in %TOT following the placebo administration. Group E(-) showed the smallest increase in %TOT following the placebo, while the magnitude of change for group E(0) fell between group E(+) and E(-). The same conclusion would be derived from the unadjusted group means: E(+)=67.5 (SD=10.27); E(0)=57.62 (SD=9.98); E(-)=49.17 (SD=14.20); E(?)=57.10 (SD=11.78).

It was predicted that no placebo response would be displayed by group E(?) and thus their post-treatment performance should not differ from that of group E(0). Using the mean square error from the covariance analysis, a comparison of the adjusted mean post-treatment

group means confirmed this prediction ($t=0.687$, $df=51$, $P=0.495$).

The mean %TOT based on all 12 post-treatment trials provided an overview of the performance under placebo of the groups with conflicting expectations, E(+) and E(-), or no expectancy, E(0). A supplementary 3 group \times 2 experiment analysis of covariance, performed on these scores, obtained no significant group \times experiment interaction [$F(2,35)=0.34$, $P=0.716$]. However, significant main effects for groups [$F(2,35)=6.20$, $P=0.005$] and experiments were revealed [$F(1,35)=7.86$, $P=0.008$]. The experiment effect here was attributable to an overall lower level of achievement by the subjects of experiment 2. The unadjusted overall %TOT in experiment 2 was only 57.06 (SD=13.68) whereas the overall %TOT in experiment 1 was 61.24 (SD=12.57). An adjusted overall mean %TOT for each group was obtained by a 3 group covariance analysis and indicated a significant group effect [$F(2,38)=5.33$, $P=0.009$]. Group E(+) continued to show the highest mean %TOT (61.84) on the entire set of post-treatment trials, but groups E(-) and E(0) displayed a similar level of overall performance, with adjusted group means of 57.624, and 57.992, respectively.

Predicted and actual change in performance under placebo

Prior to receiving any information about caffeine effects on performance, subjects in groups E(+), E(-), and E(?) predicted how caffeine would affect their task performance. The range of ratings was very narrow and close to five (i.e., no effect) but no subject used a rating of five. Subjects' ratings were used to classify individuals in terms of their prediction of impairment (score below five) or enhancement (score above five) of performance. Subjects' predictions were independent of group assignment in each experiment, and when the experiment dimension was ignored (Chi-Square=1.36, $df=2$, $P=0.510$).

Because group E(?) received no information about the effect of caffeine, their performance might be thought to relate to their own predictions concerning the effect of caffeine on their performance. This possibility was explored, measuring the change in a subject's performance under placebo by subtracting his pre-treatment score from his post-treatment score so that improved PR performance was indicated by a positive change score. No significant relationship between a subject's actual and predicted change in performance was observed ($r=0.003$, $n=14$, $P=0.992$).

Predicted and actual change in mood under placebo

The expected change in alertness and tension under coffee were obtained for each subject by subtracting his baseline ratings of each mood from his predicted ratings of these states. Thirty-one of the 42 subjects in groups E(+), E(-), and E(?) predicted greater alertness (pos-

itive change score) under caffeine, while 11 subjects predicted a decrease in alertness. The group of 31 subjects who predicted increased alertness displayed a significant mean increase (+11.06) in alertness ratings under the placebo as compared to their baseline ratings ($t=6.24$, $df=30$, $P<0.001$). In contrast, the 11 subjects who predicted they would become less alert reported significantly less alertness (mean change = -9.64) following the placebo ($t=2.35$, $df=10$, $P=0.020$). Subjects in group E(0), who received no beverage, displayed no significant change in alertness (mean = -2.45) during their post-treatment trials ($t=-1.02$, $df=13$, $P=0.326$).

Somewhat similar effects were observed for tension. Thirty-six subjects predicted caffeine would make them more tense, and they did report increased tension (mean change = +5.78) under placebo as compared to their baseline ratings ($t=4.19$, $df=36$, $P<0.001$). Of the remaining five placebo subjects, four predicted caffeine would reduce tension and one predicted no change. The four subjects who expected to become less tense displayed no significant change in tension ratings under placebo, and the subject who predicted no change in tension reported less tension under placebo (change = -5.00). There was no significant change in the tension ratings of group E(0). Their mean change = 2.43, ($t=1.48$, $df=13$, $P=0.163$).

Discussion

This research demonstrates that a placebo response to caffeine can be obtained in psychomotor performance, and the type of effect caffeine was expected to have on performance predicted the type of placebo response displayed. In accord with the hypotheses, subjects in group E(+), who expected caffeine to enhance performance, displayed a higher %TOT under placebo than control subjects in group E(0), who neither expected nor received any beverage. Subjects in group E(-), expecting impairment, performed more poorly than subjects in group E(0). Group E(?) received no information about the possible effect of caffeine on the motor skill task, and their performance did not differ significantly from the group, E(0), who received no placebo. The failure of group E(?) to display any placebo response is consistent with other studies that provide no information about the type of drug effect, and observe no change in psychomotor performance when subjects expect a drug but receive a placebo.

Although the response to the placebo by subjects in group E(?) was not related to their predictions concerning caffeine's effects, these subjects, and all others in the study, predicted very weak effects of caffeine on performance. It appears that expected effects were too slight to have a detectable effect. Since the groups did not differ in these predictions, or in their familiarity or use of coffee, the evidence implies that the information provided to groups E(+) and E(-) was responsible for producing a placebo response, and the type of reaction displayed was determined by information associating caffeine with a particular type of effect.

The immediacy of group differences in post-treatment performance adds further support to an expectancy interpretation. Different expectancies had been provided just prior to the post-treatment trials and consequently their effects on performance should be immediately evident. This was observed on the initial trials when there was least opportunity for subjects to obtain any information by performing the task under placebo that would conflict with the experimental expectancy. A learned expectancy interpretation could also explain why the group that expected caffeine to enhance performance continued to demonstrate the highest level of performance during all post-treatment trials, while the overall performance of the group expecting impairment became similar to the control group. Because pre-treatment trials did not train performance to stable asymptote, all subjects continued to improve during the post-treatment session. Any perception of this improvement would provide information consistent with the expectation of enhanced performance under caffeine, but it would challenge and discredit the expectation of impairment. Inherent feedback obtained by performing the task may have operated to diminish the expectation of impairment and strengthen the expectation of enhancement of performance.

The exploratory measures of expected and actual change in mood under caffeine also indicated the importance of expectancies. Subjects reported changes in alertness and tension under placebo that correlated with their initial predictions about the effect of caffeine on these moods. In contrast to the apparent hesitancy in predicting any caffeine effects on task performance, most subjects readily predicted strong effects of caffeine on alertness and tension, and subsequently reported sizable changes in these moods under placebo. These observations are consistent with the widely held notion that caffeine enhances alertness, and high doses cause tension.

The evidence on placebo responses to caffeine has important implications for balanced placebo design research using other drugs, including alcohol. It seems likely that attempts to manipulate expectancies about the effect of a drug will be most successful in experimental situations that minimize subjects' prior expectations about the effect of the drug on the behavior under study. In the present research, subjects entered the experiment with very weak expectancies about caffeine effects on performance. However, expectancies concerning the effect of alcohol on performance may be well learned and difficult to alter by instruction alone. Some research suggests this is the case (e.g., Gustafson 1987). Some more salient information consistent with the instruction may be needed (e.g., false performance feedback, vicarious observation of the performance of others).

Efforts to manipulate expectancies concerning alcohol effects have seldom considered the setting or the desirability of displaying the expected behavior. Any perceived adverse consequence for displaying the expected behavior under placebo may reduce the likelihood of its occurrence. The present research ensured that the consequences of performance under placebo caffeine were neutral, thus eliminating any incentive to display or suppress the expected type of effect.

The analysis of expectancies in terms of learned associations between events is consistent with many speculations and assumptions about expectancies which have been used retrospectively to explain results of placebo studies (Maisto et al. 1981; Marlatt and Rohsenow 1980). However, the view of expectancies adopted in the present paper differs in that it analyzes and identifies particular associations between specific events that represent a set of expectancies which may govern a response to a placebo. The approach has led to what appears to be the first test of the assumption that the expected type of drug effect can predict the response to a placebo. This strategy offers a promising experimental approach to testing the determinants of drug – related expectancies, and their role in governing the behavioral response to a placebo or to a drug itself.

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