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Effects of acute administration of diazepam and *d*-amphetamine on aggressive and escape responding of normal male subjects

Don R. Cherek [2], Joel L. Steinberg [3], Thomas H. Kelly [4], Dean E. Robinson [1], and Ralph Spiga [1]

[1] Human Behavioral Pharmacology Laboratory Department of Psychiatry and Behavioral Sciences University of Texas Medical School, Houston, Texas, USA
[2] University of Texas Mental Sciences Institute, Houston, Texas, USA
[3] V.A. Medical Center, Dallas, Texas, USA
[4] Johns Hopkins University School of Medicine, Baltimore, Maryland, USA

Abstract. Normal males participated in sessions providing two operant response options and were administered either diazepam (study I and II) or *d*-amphetamine (study II). The acute effects of diazepam on human aggressive responding, which ostensibly subtracted points from another person, were determined in study I. Study II was conducted to determine the extent to which social context and response consequence influenced diazepam (study I) and *d*-amphetamine (previous research) effects on aggressive responding. In study II, the other response option was escape responding which protected the subject's counter from point losses. Aggressive and escape responding were engendered by subtracting points from the subject's counter, and maintained by initiation of intervals free of point loss. Point subtractions were attributed to the other person (study I) or to a machine (study II). Responding to accumulate points exchangeable for money was available in both studies. Acute diazepam administration decreased aggressive responding in most subjects (study I), slightly increased escape responding (study II), and decreased responding to accumulate points. In study II, *d*-amphetamine increased both escape responding and responding to accumulate points. The effects of *d*-amphetamine and diazepam were altered by the instructed source of point loss.

Key words: Aggression – *d*-Amphetamine – Diazepam – Escape – Human – Operant

Study I

Preclinical studies reported that diazepam reduced aggressive-threat behaviors in primates (Randall et al. 1961), spontaneous fighting in mice (Krsiak 1979), isolation-induced aggression in mice (Valzelli et al. 1967; Poshivalov 1981; Skolnick et al. 1985), shock-elicited and septal lesion induced fighting in rats (Christmas and Maxwell 1979), and shock-elicited biting in squirrel monkeys (Emley and Hutchinson 1983).

Many clinical researchers have reported that benzodiazepines are useful in the management of violent patients (Kalina 1964; Goddard and Lokare 1970), particularly in the absence of major psychiatric illness, e.g., depression, mania or schizophrenia (e.g., Eichelman 1977; Cherek and Steinberg 1987). However, diazepam administration has resulted in "paradoxical" increases in aggressive behavior among some patients (Feldman 1962; DiMascio et al. 1970; Lion et al. 1975; Brown 1978; Hall and Zisook 1981).

Laboratory studies with human subjects have also observed increased hostility among individuals residing on a research ward following diazepam administration (Griffiths et al. 1983). Wilkinson (1985), utilizing the Taylor competitive reaction-time task, found that subjects given 10 mg diazepam increased the intensity of their aggressive responses, i.e., set higher shock intensities for their opponents, than subjects given placebo.

The present study was undertaken to determine the effects of acutely administered diazepam on aggressive responding of normal male subjects using our methodology (Cherek 1981).

Method

Subjects. Nine males were recruited by advertisements for behavioral research. Subjects were excluded if during a physical exam or structured psychiatric interview using the Schedule for Affective Disorders and Schizophrenia Lifetime Version (SADS-L) any physical illness or current or historical psychiatric disorder was detected. To avoid problems associated with drug usage by our subjects, urine samples were obtained throughout the study and screened for the presence of drugs. Also, breath alcohol levels were determined using an Intoximeter Model 3000 III, prior to each daily session. Detection of any drug in the subject's urine or alcohol in the subject's breath sample resulted in the removal of the subject from the study.

Instructions. The research project was described as a study of the effects of diazepam on motor performance and physiological responses and that the investigators were interested in how efficiently subjects responded on a monetary reinforced task. In addition, a thermistor was attached to the subject's left hand presumably to monitor body temperature, pulse rate and peripheral blood flow during experimental sessions. These diversions served to emphasize that monetary reinforced responses and physiological measures provided valid experimental data and de-emphasized aggressive responses as the primary dependent variable.

Subjects were shown a response console containing two push buttons and a counter, and were told that pushing button A would result in the accumulation of points ex-

Offprint requests to: D.R. Cherek, University of Texas Mental Sciences Institute, 1300 Moursund, Houston, TX 77030, USA

changeable for money. Subjects were informed that their console would be connected to the consoles of other people participating in the research project. As a result of these connections, subjects could subtract points from the other people, and they in turn could subtract points from the subject.

Response measures. Subjects were able to press either button A or B mounted on a response console (HTC-603, BRS/LVE) during daily experimental sessions. The non-aggressive response option was pressing button A which was maintained by a fixed ratio (FR) 100 schedule of point presentation, i.e., 100 consecutive responses produced one point. Subjects were paid 10 cents for each point on the counter at the end of each session.

The aggressive response option was pressing button B which ostensibly delivered an aversive stimulus, i.e., a point subtraction, to another person following the completion of each fixed ratio (FR) 10 on button B.

These two response options were concurrently available as non-reversible options. The first response on either button A or B illuminated the button pressed and inactivated the other button. When the ratio requirement for the illuminated button was completed (either 10 or 100 responses), the stimulus light on that button was extinguished and both response options became available.

Provocations (subtraction of points). Aggressive responses were initiated by subtracting points from the research subjects. These provoking point subtractions were: (1) attributed to the other person, (2) signalled by an audible click and illumination of a stimulus light, and (3) were scheduled to occur at random times throughout the daily experimental session.

Consequences of the subject's aggressive responses. In addition to ostensibly subtracting a point from the other person, ten aggressive responses on button B initiated a provocation-free interval (PFI) during which point subtractions were not presented. At least one point subtraction was presented to the subject before aggressive responses resulted in the initiation of a PFI. Following the termination of the PFI, at least one point subtraction was presented before aggressive responding initiated another PFI. Therefore, subjects periodically received point subtractions throughout each session.

Subjects were assigned to PFI durations of either 125 or 500 s. Subjects assigned to a PFI duration of 500 s received approximately 6–10 point subtractions per session, while subjects assigned to a PFI duration of 125 s received from 16 to 23 point subtractions per session. These different PFI values varied both the density and frequency of provocation. Subjects were not informed of these contingencies.

As a result of this contingency, the subject's aggressive responding resulted in a temporary reduction in provocation, i.e., a suppression of the other person's aggressive responding directed at the subject. This contingency served to maintain the subject's aggressive responding over sessions and allowed dose-response determinations which required extended periods of time.

Diazepam. All research subjects came into the medical center for daily 50-min sessions, 5 days per week. Thirty minutes before the daily session, subjects were required to swallow two number #00 gelatin capsules containing either placebo or diazepam. The diazepam was administered in doses of 2.5, 5 and 10 mg per 70 kg body weight. Successive drug doses were separated by at least 96 h and were administered when the frequency of aggressive and non-aggressive responses during the placebo sessions were within variability ranges observed prior to drug administration. All placebo and drug doses were administered double-blind. Drug doses were presented initially in an ascending sequence and then randomly over successive sessions, with each drug dose presented three times.

Questionnaires. Subjects completed the Profile of Mood States (POMS) questionnaire at the end of each session (McNair et al. 1971). Subjects also completed the Buss-Durkee Hostility Questionnaire at the end of the study (Buss and Durkee 1957).

Debriefing. Prior to debriefing, subjects completed a series of brief questionnaires to determine if the instructional deception had been successful and subjects thought that they were paired with other subjects during the experiment. Research subjects were not actually paired with other people, and they were debriefed and informed of this at the end of the experiment.

Statistical analysis. An analysis of variance (ANOVA) was performed for each response option with repeated measures on the factors diazepam dose and sessions (Winer 1971). Placebo sessions immediately preceding drug sessions were utilized in the ANOVA analysis. PFI duration was a between-subjects factor in this analysis. If the main effect of diazepam dose was significant, then post-hoc comparisons between each dose were performed using the Tukey Honestly Significant Difference (HSD) Test (Winer 1971). Total hostility scores on the Buss-Durkee Hostility Questionnaire were correlated with changes in aggressive responding following the administration of 10 mg diazepam per 70 kg dose.

Results

The effects of placebo (0) and three doses of diazepam (2.5, 5 and 10 mg per 70 kg) on the number of aggressive responses per session for all subjects are shown in Fig. 1. Seven of the nine subjects decreased aggressive responding following the administration of the highest diazepam dose (10 mg per 70 kg). Subject S-173 increased aggressive responding at the highest diazepam dose when assigned to PFI of 500 s, and this effect was replicated when this subject participated in a second dose-response determination at PFI value of 125 s. A repeated measures ANOVA indicated that the main effect of diazepam dose was significant ($F=3.70$, $df=3, 24$, $P<0.025$). Post-hoc comparisons using Tukey's Honestly Significant Difference (HSD) Test (Winer 1971) indicated that the changes in aggressive responding following the highest diazepam dose (10 mg per 70 kg body weight) differed significantly from placebo ($P<0.05$). The other two diazepam doses did not produce changes in aggressive responding which differed from placebo. Only data from the first dose-response determination for subject S-173 was used in all statistical calculations.

The effects of placebo (0) and the three doses of diazepam (2.5, 5 and 10 mg per 70 kg) on the number of non-aggressive responses per session for all subjects are shown in Fig. 2. Diazepam produced small changes in non-aggres-

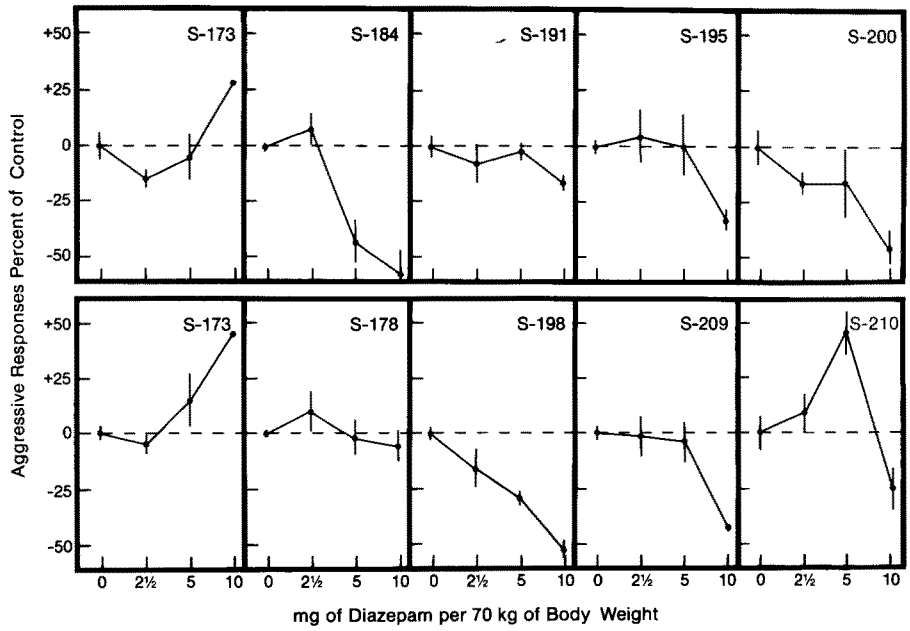

Fig. 1. The effect of placebo (0) and three doses of diazepam (2.5, 5 and 10 mg per 70 kg body weight) on number of aggressive responses per session. Data points are expressed as per cent changes from mean placebo values set at zero. Placebo values represent sessions immediately preceding drug administration. Drug data points represent the mean of three different sessions. Vertical lines at all data points represent ± SEM. Subjects assigned to PFI duration of 500 s (low frequency of provocation) are shown in the top half of the figure, and those assigned to PFI durations of 125 s (high frequency of provocation) are shown in the bottom half of the figure

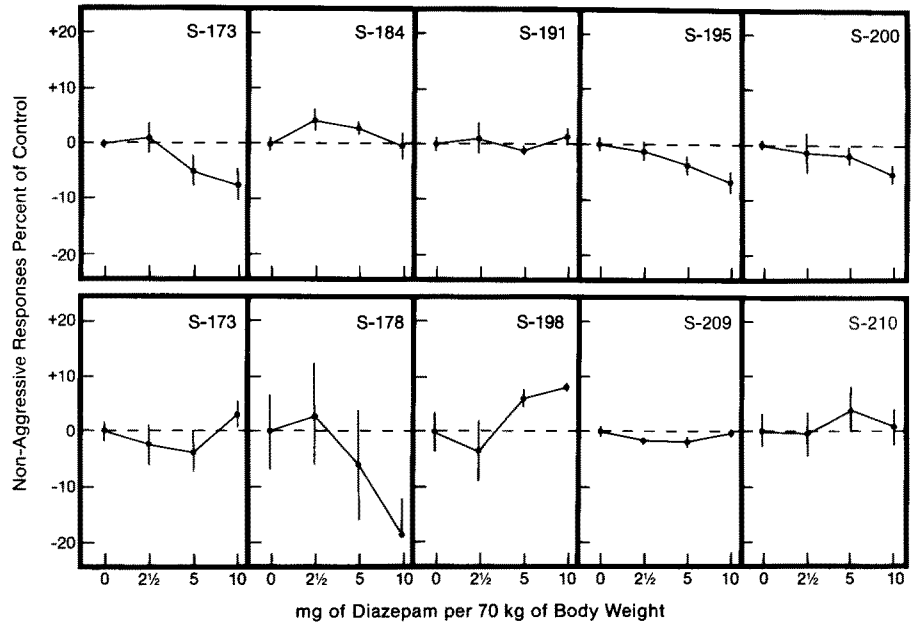

Fig. 2. The effect of placebo (0) and three doses of diazepam (2.5, 5 and 10 mg per 70 kg body weight) on number of non-aggressive monetarily reinforced responses per session. Data points are expressed as per cent changes from mean placebo values set at zero. Placebo values represent sessions immediately preceding drug administration. Drug data points represents the mean of three different sessions. Vertical lines at all data points represent ± SEM. Subjects assigned to PFI durations of 500 s (low frequency of provocation) are shown in the top half of the figure, and those assigned to PFI durations of 125 s (high frequency of provocation) are shown in the bottom half of the figure

sive responding in most subjects. Only subject S-178 had a 20% reduction in non-aggressive responding following the highest diazepam dose. Diazepam had no effect upon aggressive responding in this subject.

A repeated measures ANOVA indicated that the main effect of diazepam dose was not significant ($F=1.31$, $df=3$, 24, NS). A planned comparison indicated that non-aggressive responding following the highest diazepam dose was not significantly different from placebo responding ($F=0.98$, $df=1.8$, NS).

There was no correlation ($r=-0.09$) between the changes in aggressive and non-aggressive responding following the administration of the highest diazepam dose.

Seven of the subjects had total Buss-Durkee Hostility scores between 17 and 25. Subject S-210 had a slightly higher total hostility score of 31, and subject S-173 had much higher total hostility score of 46. Both of these subjects increased aggressive responding following diazepam administration. Statistical analysis indicated a significant correlation ($r=0.78$, $P<0.01$) between the total hostility score on the Buss-Durkee Hostility Questionnaire and the change in aggressive responding following the highest diazepam dose. To determine the contribution of S-173 to this correlation, the data was analyzed again without this subject's data. The correlation was slightly higher ($r=0.86$), excluding S-173.

An ANOVA analysis indicated that the various category scores of the POMS were not affected by diazepam administration.

Following the administration of the highest diazepam dose subjects reported that they were aware of a drug effect and some subjects evidenced signs of intoxication at the end of these sessions (nystagmus, difficulty walking a line, light headedness).

Subjects also completed a series of questionnaires to determine if the deception had been successful, i.e., subjects actually believed that they were paired with other subjects during their participation. The subjects reported in their written answers that: (1) the other people subtracted more points (8/9) or the same number of points (1/9), (2) they were paired with three (6/9) or more (3/9) people during the study, and (3) they thought they were paired with other people (8/9) or occasionally questioned whether someone was paired with them, but on the whole thought they were paired with someone (1/9). Possible answers included reporting that they were paired with zero subjects, and that they doubted that they were paired with anyone.

Discussion of study 1

The acute administration of diazepam resulted in decreases in aggressive responding in the majority of subjects. The decrease in aggressive responding observed in most subjects following the administration of diazepam is consistent with previous reports of anti-aggressive activity of benzodiazepines reported historically in the animal and clinical literature (e.g., Avis 1974; Azcarate 1975; Essman 1978; Itil and Seaman 1978). However, our results do differ from the Wilkinson (1985) report of increased intensity of aggressive responses among subjects administered 10 mg diazepam utilizing the Taylor competitive reaction time paradiagm. With this methodology (Taylor 1967), the measure of aggression is the intensity of shock the subject sets for his opponent prior to competing in a visual reaction time task. Two obvious differences may account for the conflicting results obtained in the Wilkinson (1985) study and the present experiment: (1) different methodologies were employed which measured different aspects of aggressive responding, and (2) the Wilkinson study involved increasing intensity of provocation by the opponent throughout the experimental session, while in our study the frequency of provocation was relatively constant for each subject.

Many researchers (Cook and Kelleher 1963; Thompson and Boren 1977; Miczek and Krsiak 1979) have emphasized the critical importance of determining the specificity of drug action when evaluating the effects of any drug on aggressive behavior. Several researchers have argued that the only valid method of assessing the behavioral specificity of drug effects on aggression is to determine the effect on a range of behaviors within the same test environment (e.g., Avis 1974; Rodgers and Waters 1985). The decreases in aggressive responding observed in most subjects in the present experiment cannot be attributed to a non-selective depressant action of diazepam, since non-aggressive monetarily reinforced responding was not affected. Emley and Hutchinson (1983) reported similar selectivity for diazepam which decreased post-shock biting at doses which increased pre-shock lever pressing in squirrel monkeys.

In summary, acute administration of diazepam to normal male subjects in a laboratory setting resulted in a selective decrease in aggressive responding in the majority of subjects, while non-aggressive responding was not altered. The decreased aggressive responding following diazepam administration was the result of a reduction in the probability that presentation of an aversive stimulus (point subtractions) would set the occasion for retaliatory aggressive responding.

Study II

Since aggressive responding in study I and in a previous *d*-amphetamine study (Cherek et al. 1987) was maintained by escape from point loss, the question remains whether such responding represents escape rather than aggressive responding, and subjects were simply responding to environmental stimuli independent of any actual or presumed relationship to another person. As Lindsley (1966) concluded, "stimuli cannot be functionally defined as social unless the subject responds to them differently from the way he would respond if they were mechanical". Rather than attributing subtractions to another person, subjects could be instructed that points losses were programmed by a machine and that they could respond to escape from such point losses. These instructions would remove such responding from the previous social context. The present experiment was undertaken to determine the effects of *d*-amphetamine and diazepam on responding maintained by escape from point loss which was attributed to a machine.

Method

Subjects. Ten males participated after giving their informed consent. Volunteers were recruited, screened and monitored for alcohol and drug use as described in study I.

Instructions. Subjects were informed that point subtractions could occur during daily sessions. Pushing button B after a point loss would protect their counter from subsequent point losses for a brief period of time. However, responding on button B would not avoid point losses.

Response measures. The escape response option was pressing button B which protected the subject's counter for some period of time from further point losses initiated by a machine. The completion of a fixed ratio (FR) 10 on button B initiated a 125-s interval during which point subtractions were not presented. Subjects were not studied under conditions of a 500-s interval (as in study I) since we wanted to engender more escape responding to allow comparisons with aggressive responding.

In summary the antecedent stimulus, i.e., a point subtraction, and the consequence of button B presses, i.e., initiation of an interval free of point subtractions, were identical to the antecedents and consequences of the previous experiments. These previous studies differed from the present experiment in that button B responses were defined as aggressive and subjects were instructed that the source of point losses was another person.

d-Amphetamine and diazepam. All research subjects ($N=10$) came into the medical center for daily 50-min sessions, 5 days per week. Five subjects were assigned to the diazepam treatment as in study I. Five subjects assigned to the *d*-amphetamine treatment were required to drink 16 oz tonic water containing *d*-amphetamine elixir or placebo 30 min prior to sessions. Food coloring was added to the tonic water to obtain the same orange color as the *d*-amphetamine elixir. *d*-Amphetamine was administered in doses of 5, 10 and 20 mg per 70 kg body weight. Successive drug doses were separated by least 48 h.

Questionnaire. Subjects completed the Profile of Mood States (POMS) questionnaire at the end of each session.

Statistical analysis. Both escape and point-maintained response data were analyzed by analysis of variance (ANOVA) using a three-factor mixed design with repeated measures on two factors (Winer 1971; Bruning and Kintz 1977). The between-subjects group factor was drug (diazepam versus *d*-amphetamine), and the within-subjects factors were dose and session. A similar statistical analysis was utilized to contrast the effects of *d*-amphetamine on escape responding in the present experiment and aggressive responding maintained by the same contingency in an earlier study (Cherek et al. 1987). The between-subjects group factor was instructions regarding the source of point loss, i.e., machine versus another person. The within-subjects factors were dose and session. A similar comparison was made regarding diazepam effects upon escape responding in the present experiment and aggressive responding in study I.

Results

The effects of placebo (0) and three doses of *d*-amphetamine (5, 10 and 20 mg per 70 kg) on the number of escape and point-maintained (monetary reinforced) responses for all five subjects are shown in Fig. 3. Escape responses are shown in the top half of the figure and point-maintained (monetary reinforced) responses are shown in the bottom half. Escape responses were slightly increased relative to placebo following *d*-amphetamine administration. Maximal increases were not observed at the highest *d*-amphetamine dose, however, with four of the five subjects evidencing the largest increases in escape responding at 5 or 10 mg per 70 kg. Point-maintained, monetary reinforced responses were increased following *d*-amphetamine administration in a dose-dependent manner with the highest increases ob-

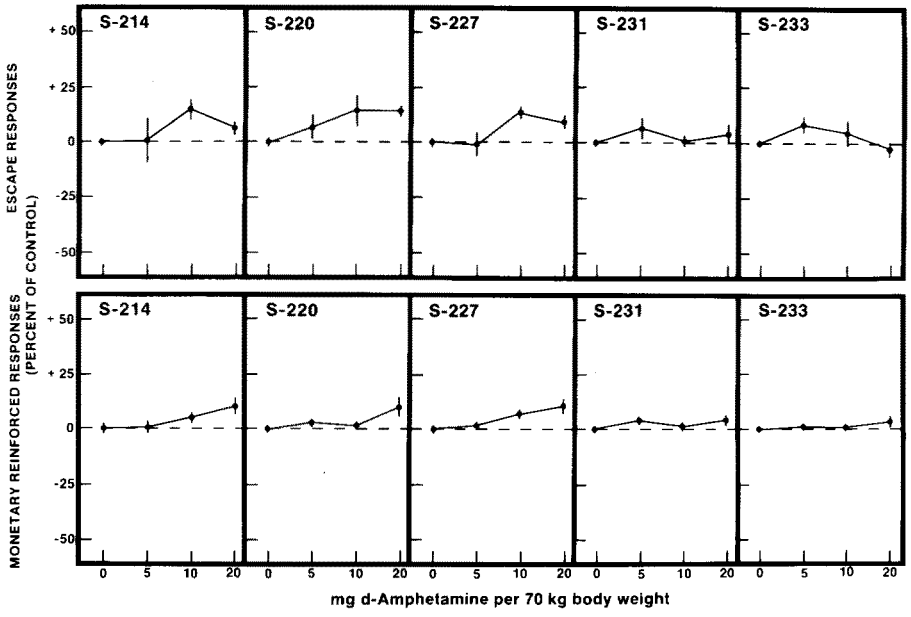

Fig. 3. The effects of placebo (0) and three doses of *d*-amphetamine (5, 10 and 20 mg per 70 kg body weight) on escape responding (*top half*) and point maintained responding (*bottom half*). Data points are expressed as per cent changes from mean placebo values set at zero. Placebo values represent sessions immediately preceding drug administration. Drug data points represent the mean of three different sessions. Vertical lines at all data points represent ± SEM

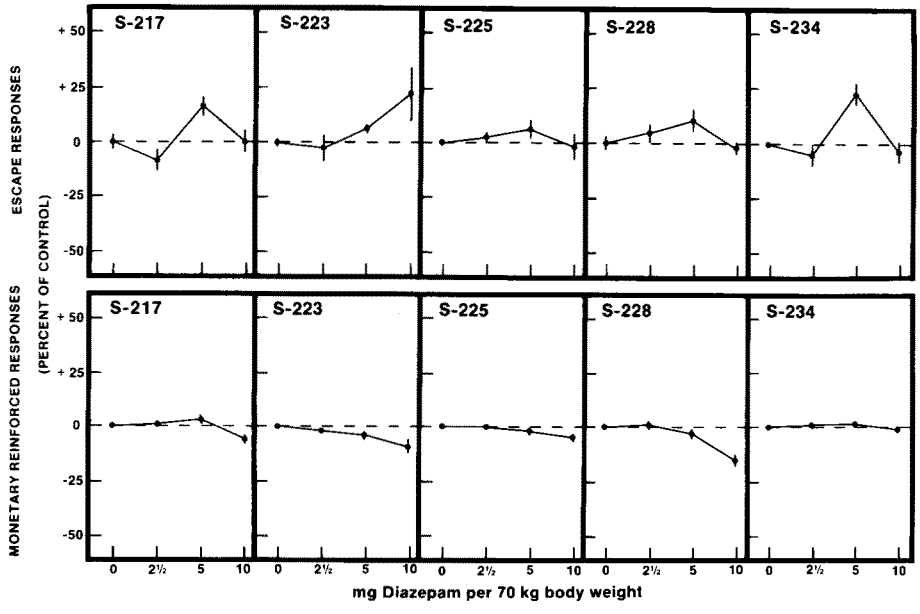

Fig. 4. The effects of placebo (0) and three doses of diazepam (2.5, 5 and 10 mg per 70 kg of body weight) on escape responding (*top half*) and point maintained responding (*bottom half*). Data points are expressed as per cent changes from mean placebo values set at zero. Placebo values represent sessions immediately preceding drug administration. Drug data points represent the mean of three different sessions. Vertical lines at all data points represent ± SEM

served following administration of the 20 mg per 70 kg dose.

The effects of placebo (0) and three doses of diazepam (2.5, 5 and 10 mg per 70 kg) on the number of escape and point-maintained (monetary reinforced) responses for all five subjects are shown in Fig. 4. Escape responses (top half of figure) generally increased following diazepam administration, with four of the five subjects showing the largest increase at 5 mg per 70 kg dose. One subject (S-223) had a dose-dependent increase in escape responding. Point maintained (monetary reinforced) responses were decreased following diazepam administration, with the largest decreases occurring following administration of the highest diazepam dose.

The effects of diazepam and *d*-amphetamine on escape responses were analyzed using a three-factor mixed design with repeated measures on two factors, dose and session. The main effect of the between-subjects group factor drug treatment (diazepam versus *d*-amphetamine) was not significant ($F=0.06$, $df=1,8$ NS) for escape responses. Likewise, the main effect of dose ($F=0.34$, $df=3,24$ NS) and session ($F=3.14$, $df=2,16$ NS) were not significant. One interaction was significant, the session × drug ($F=5.25$, $df=2,16$, $P<0.02$). An inspection of data suggest that somewhat larger increases in escape responding were observed during the initial exposure to a given *d*-amphetamine dose than during the two subsequent exposures to those same doses.

The effects of diazepam and *d*-amphetamine on point maintained (monetary reinforced) responses were analyzed as described above. Again, the main effect of the between-subjects group factor drug treatment was not significant ($F=0.97$, $df=1,8$ NS). The main effect of dose was significant ($F=7.81$, $df=3,24$, $P<0.001$), as well as the dose × drug interaction ($F=7.62$, $df=3,24$, $P<0.001$). The main effect of session was not significant ($F=0.06$, $df=2,16$ NS), and no other interactions were significant.

The statistical analysis suggests that escape responses were not affected by diazepam or *d*-amphetamine administration, although there was change in the effect of drug administration on escape responses over successive repetitions that varied in the two groups of subjects. This effect was attributed to *d*-amphetamine. In contrast, point maintained responding was affected by doses of the two drugs, and this change in responding differed with the two drugs. Post-hoc comparisons using the HSD Test (Kirk 1968; Winer 1971), indicated that the 20 mg per 70 kg *d*-amphetamine dose differed significantly ($P<0.05$) from placebo values, and the 10 mg per 70 kg diazepam dose differed significantly ($P<0.05$) from the lower diazepam doses and all *d*-amphetamine doses.

An ANOVA analysis indicated that the various category scores of the POMS were not affected by either diazepam or *d*-amphetamine administration.

Figure 5 shows the effects of *d*-amphetamine (top half) and diazepam (bottom half) on button B responding maintained by escape from point loss obtained in the present experiment and in our previous research. *d*-Amphetamine produced slight increases in escape responding, while resulting in slight decreases in aggressive responding. Diazepam had little or no effect upon escape responding, but produced substantial decreases in aggressive responding at the highest diazepam dose.

A statistical analysis comparing the effects of diazepam or *d*-amphetamine on aggressive and escape responding was

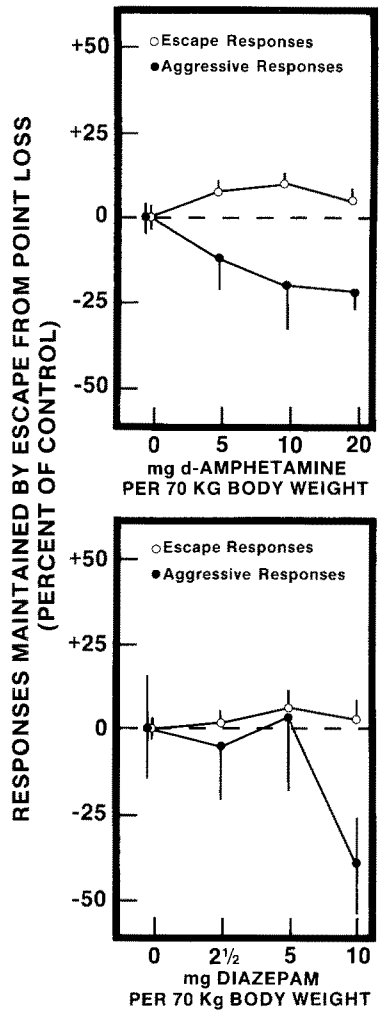

Fig. 5. The effects of placebo and either three doses of *d*-amphetamine (*top half*) or three doses of diazepam (*bottom half*) on escape responses (*open circles*) and aggressive responses (*closed circles*). Data points are expressed as per cent changes from mean placebo session values set at zero. Escape responses represent responding to escape from point loss attributed to a machine. Data points for escape responses represent the means of five subjects from the present experiment. Aggressive responses represent responding defined as aggressive and maintained by escape from point loss attributed to another person. Data points for aggressive responses represent the mean of four subjects obtained in earlier experiments. The *d*-amphetamine data has been previously published (Cherek et al. 1987) and the diazepam data was obtained in study I

performed using a three-factor mixed model with repeated measures on two factors. The between-subjects group factor was instructions regarding the source of point loss (other person versus machine). The within-subjects factors were dose and session. The main effect of instructions (group factor) was significant for *d*-amphetamine subjects ($F=5.74$, $df=1,7$, $P<0.04$) and was close to significant for diazepam subjects ($F=5.12$, $df=1,7$, $P<0.06$). The main effect of dose was significant for diazepam subjects ($F=4.94$, $df=3,24$, $P<0.01$), but not significant for *d*-amphetamine subjects ($F=0.42$, $df=3,24$ NS). The main effect of session was not significant for diazepam subjects ($F=0.01$, $df=2,16$ NS) or *d*-amphetamine subjects ($F=1.18$, $df=2,16$ NS).

The group × dose interaction was highly significant for both diazepam subjects ($F=6.32$, $df=3,24$, $P<0.005$)

and *d*-amphetamine subjects ($F=13.76$, $df=3,24$, $P<0.001$), indicating that the effects of drug dose on responding varied depending upon instructions. The only other significant interaction was group × sessions for *d*-amphetamine subjects ($F=8.56$, $df=2,16$, $P<0.005$), due in part to tendency for the largest increases in escape responding to occur during the initial exposure to a given dose of *d*-amphetamine.

Discussion of study II

In the present experiment, subjects responding to accumulate points exchangeable for money were exposed to unavoidable point losses attributed to a machine rather than another person. However, as in the earlier studies, responding on a second button was maintained by response contingent initiation of 125-s intervals during which no point subtractions were presented. Such responding was defined as escape responding because the subject's responding resulted in a temporary cessation of subsequent point losses only after losing at least one point. In addition, responding during the 125-s interval had no effect upon further point losses after this interval had elapsed (Hineline 1977).

In this study, subjects were assigned to either diazepam or *d*-amphetamine administration, and the effects of these two drugs upon responding maintained by point presentation and escape from point loss were determined. Our results indicate that neither diazepam or *d*-amphetamine administration produced any significant changes in escape responding. In contrast, point-maintained (monetary reinforced) responding was sensitive to the effects of diazepam and *d*-amphetamine. In this study, *d*-amphetamine increased point-maintained responding, while the administration of the highest diazepam dose (10 mg per 70 kg) resulted in decreased responding. The change in point-maintained responding indicated that these drug doses altered fixed-ratio responding, and the failure to observe changes in escape responding does not represent administration of low doses devoid of any behavioral effects.

In the present experiment we altered the instructions that established button B responding as aggressive, by attributing the point losses to a machine rather than another person. This change in instructions regarding the source of point losses or subtractions (machine versus other person) significantly altered the effects of diazepam and *d*-amphetamine on button B responding. The effect of these two sets of instructions on the dose-response effects of diazepam and *d*-amphetamine was also highly significant. These comparisons lead us to conclude that the effects of *d*-amphetamine and diazepam differ depending upon the instructed source of point losses, even when such responding was occasioned by the same antecedent stimulus (point loss) and maintained by the same consequence (a brief interval of time free of subsequent point losses).

General discussion

In study I, diazepam decreased aggressive responding occasioned by point loss attributed to a fictitious subject but had little or no effect on monetarily reinforced responding. The failure to observe increases in non-aggressive responding following diazepam administration cannot be attributed to a ceiling effect, i.e., non-aggressive responding occurring at such a high rate that further drug-induced increases were not possible. Similar high rates of non-aggressive responding observed in previous studies during placebo sessions, have been increased further by the administration of caffeine (Cherek et al. 1983), *d*-amphetamine (Cherek et al. 1987) and nicotine (Cherek 1981).

The results of study I also indicate that increases in aggressive responding can be observed in normal male subjects in a laboratory setting. The fact that this effect was observed in only a small proportion of subjects is consistent with the clinical literature which reports such reactions in only a small proportion of patients (e.g., Hall and Zisook 1981; Cherek and Steinberg 1987). This increase in aggressive responding cannot be attributed to an idiosyncratic stimulant effect, since non-aggressive responding in these subjects was not affected. The changes in aggressive responding produced by diazepam were correlated with total hostility scores on the Buss-Durkee Hostility questionnaire. In so far as this score reflects relative probabilities of aggressive behavior, the correlation may indicate an effect of diazepam related to past history effects which result in differing probabilities of aggressive responding among subjects. The fact that increased aggressive responding was observed only in subjects with relatively high hostility scores may indicate that such effects will only be observed in subjects with high probabilities of aggressive behavior. Clinical researchers have indicated that increases in aggressive behavior in patients are usually observed in patients with histories of violent behavior and problems with impulse control (DiMascio et al. 1970; Lion et al. 1975; Hall and Zisook 1981; Johnson 1980). Similarly, animal studies have indicated that benzodiazepines have resulted in increased aggression among subjects with high probabilities of aggressive behavior (DiMascio 1973).

The differential effects of diazepam on aggressive and non-aggressive responding cannot be attributed to differences in pattern or rate of responding for these two response options. The rate of responding, i.e., the running rate of button pressing between the initial choice response (which illuminates the button pressed) and the completion of the ratio requirement for that button, is stable and relatively high (4–5 responses per second) and similar rates are observed on both buttons A and B. Subjects typically maintain a fairly uniform rate of button pressing throughout the experimental session and occasionally switch from one button to the other. Post-reinforcement pausing following either point presentations or ostensible point subtractions from the other person are absent. Subjects frequently complete several successive FR 10 ratios on button B, making the pattern of aggressive responding essentially indistinguishable from non-aggressive FR 100 responding maintained by point presentation. In addition, possible rate-dependent effects of benzodiazepines are not apparent in animal studies (Sanger and Blackman 1981) and have not been observed in studies of the effects of diazepam on schedule controlled responding in human subjects (Tewes and Fischman 1982).

Subjects that respond aggressively in the presence of a escape contingency are certainly reducing the frequency of point loss and thus increasing the total number of points accumulated per session. However, subjects that accept the fact that they are paired with another person typically complete several fixed-ratio (FR) 10 on button B, thus ostensibly deducting multiple points from the other person, before returning to the non-aggressive option. Such behavior: (1)

does not maximize earnings which would occur if subjects completed only a single FR 10 on button B, and (2) is not logical if subjects do not believe they are paired with another subject.

The effects of *d*-amphetamine on fixed-ratio (FR) point-maintained responding are similar to effects observed in our previous study (Cherek et al. 1987) and another study reporting effects on FR 30 responding (Tewes and Fischman 1982). Likewise, the effects of diazepam on point-maintained responding observed in this study are similar to those reported in the preceding experiment and in a study assessing effects of diazepam on FR 30 responding (Tewes and Fischman 1982).

In conclusion, results of study II demonstrate that the instructional context of button B responding modulates the effects of drugs on such responding. Attributing point loss to another person and providing a response option which ostensibly subtracts points from that person (retaliation) alters the functional properties of point loss (aversive stimulus) and alters the responding engendered by such point losses. Instructions attributing point loss to another person and emphasizing that button B presses take points away from the other person, establishes button B presses as a social behavior. The results of the present study suggest that aggressive responding occurred in a social context arising out of instructions relating to antecedent stimulus events and subsequent responding. And altering or changing this to non-social context by attributing point losses to a machine changed the functional properties of this same antecedent stimulus. These proposed changes in functional properties are supported by the differing patterns of drug effects on social (aggressive) and non-social (escape) button B responding.

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