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Human Avoidance Responding With Added Point Loss: Effects of Tobacco and Abstinence

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BENNETT, R. H. AND D. R. CHEREK. *Human avoidance responding with added point loss: Effects of tobacco and abstinence.* PHARMACOL BIOCHEM BEHAV **41**(1) 139–144, 1992.—Male smokers responded on a free-operant avoidance schedule with a response − point loss interval of 20 seconds and a point loss − point loss interval of 5 seconds. Unavoidable point losses were presented at variable times during the sessions. In Experiment 1 subjects were exposed to three tobacco abstinence conditions and an ad lib smoking condition. The conditions were nicotine gum, placebo gum, and no gum or cigarettes. In Experiment 2 subjects were administered tobacco smoke which delivered varying doses of nicotine. The smoke was administered by the spirometric method. Responding in each experiment was assessed during the session and also for 10 seconds following each of the unavoidable point losses. Results for Experiment 1 showed that the effect of smoke/nicotine abstinence on overall responding and for the interval following point losses differed across subjects. Results for Experiment 2 showed very little effect of acute nicotine dosing on the overall responding and varying effects on the responding during the interval following unavoidable point losses. These results are contrasted with previous research which has investigated tobacco smoke/nicotine abstinence and acute tobacco smoke dosing in experimental situations which were established as social via instructions.

Avoidance schedule Nicotine Nicotine abstinence Tobacco abstinence Tobacco administration
Added point loss Human

SEVERAL laboratory studies have observed that tobacco self-administration increases in stressful or anxiety-producing situations. In one study, the number of cigarettes smoked and the number of puffs per cigarette increased with increases in the amount of stress, which was operationally defined as the manipulation of shock intensity and instructions (15). Blasts of white noise were also employed to manipulate the aversiveness of an experimental situation. This manipulation increased the frequency and duration of cigarette puffs (12). In subjects performing an operant task cigarette puffing increased as the intensity of background industrial noise presentation increased (4). In a study of irritability subjects who smoked high nicotine yield cigarettes reported less irritation in contrast to those who smoked low nicotine yield cigarettes when exposed to periodic episodes of simulated aircraft overflights (14).

The positive relationship between cigarette smoke and nicotine self-administration and stressful and/or anxiety producing environmental situations observed in these studies suggest that a function of smoking and nicotine self-administration may be to attenuate the characteristic response (i.e., anger, anxiety, aggression) elicited by these situations. Researchers have observed that smoking reduced muscle tension and a reflexive response (8) and attenuated a startle response to loud acoustic stimuli (9). Aggressive operant responding occasioned by point loss presentation was also reduced by administration of nicotine (3).

A recent laboratory study investigated the effects of nicotine gum and tobacco smoking on free-operant avoidance responding in humans. In this study the avoidance of an aversive stimulus (loss of points exchangeable for money) was employed as a means to manipulate stress and anxiety in the experimental situation. The results showed an increase in responding following smoking however there were no increases following chewing of nicotine gum. The blood levels of nicotine produced by each method of administration were similar. The results indicated that behavioral effects of nicotine were related to dose amount and the method of administration (6).

The research reported here investigated the acute effects of tobacco smoke and nicotine abstinence on avoidance responding. The free-operant avoidance situation was also manipulated so that a varying number of unavoidable point losses occurred at varying time points during the sessions. Previous research has presented unavoidable shocks within an avoidance paradigm with primates. These studies indicated that presentation of an unavoidable aversive stimulus (electric shock) both maintained the avoidance behavior and increased the responding above the baseline rate (11,16). In another study noncontingent shocks were presented following avoidance schedule training. The results showed that the majority of increased responding occurred immediately following the added unavoidable shocks (13). The question of interest which is investigated in these studies is what effect would nicotine administration or tobacco abstinence have upon the increased avoidance responding engendered by the pre-

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sentation of unavoidable point losses.

EXPERIMENT 1

Experiment 1 investigated the effects of three tobacco abstinence conditions (nicotine gum, placebo gum, and no gum) on free-operant avoidance responding with added unavoidable point losses.

METHOD

Subjects

Six male tobacco smokers were recruited via newspaper advertisements soliciting participation in behavioral research projects. Subjects (24 to 41 years) self-reported smoking 20 to 50 cigarettes per day for at least 6 years (6 to 24 years). Subjects with histories of psychiatric disorders, including substance abuse, or medical illness were excluded. Extraneous drug use by subjects was monitored throughout the study by collecting urine samples and expired air samples on arrival each day. Complete drug screen analyses were performed on the urine samples and alcohol content of expired air was assessed by an Alco-Sensor III (Intoximeters, Inc.). Drug-free urine samples and alcohol-free expired air samples were required for subjects to maintain participation. All subjects reported no previous experience in research projects or prior experience with nicotine gum.

Apparatus

Subjects responded on a Lindsley manipulandum (BRS/LVE) mounted on a response console (BRS/LVE HT 603) housed in a sound attenuating chamber ($1.32 \times 1.62 \times 2.23$ m). A digital counter was located at eye level adjacent to the manipulandum, a green light was located directly above the counter and a red light was located directly below the counter at a distance of 2 cm. Three stimulus lights (blue, red, white) were located 12 cm to the left of the counter. All experimental conditions and data collected were controlled by a Micro Computer Systems II Rockwell computer located outside the chamber.

Schedule of Reinforcement

During the twenty-minute experimental sessions the subjects responded under a free-operant avoidance schedule in which point subtractions were every five seconds (point loss − point loss interval) and each response postponed the next subtraction by twenty seconds (response − points loss interval). A tandem schedule of point loss was superimposed on this schedule. Each twenty-min session was divided into four 5-min components, unavoidable point losses were presented during components II and IV (5–10 minutes into the session and 15–20 minutes into the session). Either 0, 1, 2, 3, or 4 point losses were presented each session and each of the possible number of point losses was presented in random order over the five sessions each day. Fifty points were displayed on the counter at the beginning of each session and each point loss was accompanied by an audible auditory click and a one-second illumination of the red light immediately below the counter. Session time was indicated by an illumination of the white light located to the left of the counter.

Total responses within the session and responses which occurred during the 10-s period following each of the unavoidable point losses were collected.

Instructions

Prior to the initial session the subject was read the following instructions:

"Pulling the lever during the twenty-minute experimental sessions will prevent the loss of points on the counter mounted adjacent to the lever. This counter will be set at fifty (50) at the beginning of each session. This represents a potential payment of $5.00 (one point represents 10 cents). You will be paid ten cents for each point remaining on the counter at the end of each session." Do you have any questions?

Questions were addressed by reading appropriate parts of the instructions.

Daily Procedure

Subjects participated in five sessions daily (M-F). Sessions began at 0850, 0950, 1150, 1350, and 1550 hours. A lunch was served at 1220. Expired air carbon monoxide (CO) level was assessed prior to each session by a Minico analyzer (Catalyst Research Corp.) to validate compliance with no smoking restrictions during no smoking conditions and to measure CO increases during smoking conditions. The subject's initial CO level was measured at 0830 daily. If the initial CO level was <21 ppm he received $5.00, if the CO level was <11 he received $10.00. Subjects stayed alone in a waiting area when they were not in the experimental chamber. A television, magazines and drinking water were available in the waiting area. An electronic air purifier was also located in the room and was always functioning throughout the day.

Experimental Conditions

Over successive days (M-F) subjects were exposed to four experimental conditions which defined what was permitted during the experimental day (0830 to 1630) when they were not in the experimental chamber.

During baseline conditions (ad lib smoking) subjects were provided with two packs of their preferred brand of cigarettes and instructed that they could smoke whenever they wanted. Subjects inserted butts into an opaque container (the number of cigarettes smoked each day could then be counted). Baseline conditions continued until operant responding was stable over successive sessions. Once responding was stable, subjects were exposed to one of the gum/no smoking conditions; no gum, placebo gum, or nicotine gum for a single day. Following one day of exposure baseline conditions were reinstituted until responding stabilized (typically 1–2 days) and subjects were exposed to another gum/no smoking condition for a day.

Subjects experienced each gum/no smoking condition twice with baseline conditions reinstituted to stabilize responding between each exposure. During the initial series, placebo gum always preceded the nicotine gum condition to ensure one measure of the effects of placebo gum prior to exposure to active gum. The second series of exposure to the experimental conditions was balanced across subjects. Gum pieces were administered double-blind and subjects were instructed regarding chewing the gum and possible side effects.

During the days of a gum condition subjects were given two pieces of gum to chew 30 minutes prior to each experimental session. Immediately prior to the session subjects were required to expectorate the gum. The Nicorette gum 2 mg and the placebo gum were manufactured by Merrill-Dow-Lakeside Pharmaceuticals. Subjects were not allowed to smoke cigarettes while in the laboratory during gum/no smoking conditions. During no gum days subjects did not receive gum nor could they smoke throughout the day.

Following experimental participation a 10 ml blood sample was drawn and immediately centrifuged and plasma drawn off. The plasma was stored at −70°C until analyzed for cotinine

level by gas chromatography method (10). Subjects also completed a smoking history questionnaire and Fagerstrom Tolerance Questionnaire.

RESULTS

The subjects smoked an average of 19 cigarettes (range, 11–25) during the 5.5 hours they were allowed to smoke in the baseline conditions. Plasma cotinine levels ranged from 575 ng/ml to 148 ng/ml. Five of the six subjects had Fagerstrom scores of ≥7, while the other subject had a score of six. A score of 7 or greater indicates a high dependence on nicotine. A score of 6 or less indicates a low to moderate level of nicotine dependence.

Initial CO levels (0830 hours) were maintained at levels which ensured daily payment for having a CO level of less than 21 ppm. During ad lib smoking conditions (baseline) CO generally steadily increased across the day for all subjects. Carbon monoxide level steadily decreased across the day in the gum and no gum conditions which required abstinence from smoking for the day.

During baseline conditions, four subjects responded at less than 1 response per second while two subjects responded at greater than 3 responses per second. Five of the six subjects increased their response rate during the 10-second period following an unavoidable point loss (range, 17% to 53% increase). The other subject did not increase his responding.

Figure 1 shows the avoidance responding during the session under ad lib smoking conditions and the three gum/no smoking conditions. Data are expressed as percent change from ad lib smoking conditions. Subjects S469 and S423 increased responding in the placebo gum and no gum conditions. Subjects S478 and S491 showed decreases in responding during these conditions. The other two subjects, S513 and S528, exhibited little change in responding across the conditions. These two subjects were also the subjects who responded at a much higher baseline rate than the other four subjects. Figure 2 displays the avoidance responding during the ten-second period immediately following the presentation of the unavoidable point losses. Data are presented as percent change from ad lib smoking conditions for the three gum/no smoking conditions. The same subjects who showed increases in overall avoidance responding at the placebo and no gum conditions also showed increases during the ten s periods in these same conditions. Two subjects (S491 and S528) exhibited decreases in responding during the gum/no smoking conditions. The remaining subjects exhibited little change in responding as a function of condition.

Analysis of variance indicated that there was no significant change in responding from baseline rate across the three abstinence conditions for both the overall rate and the rate during the 10 s period following unavoidable point loss. This would be expected based on the variance across the subjects.

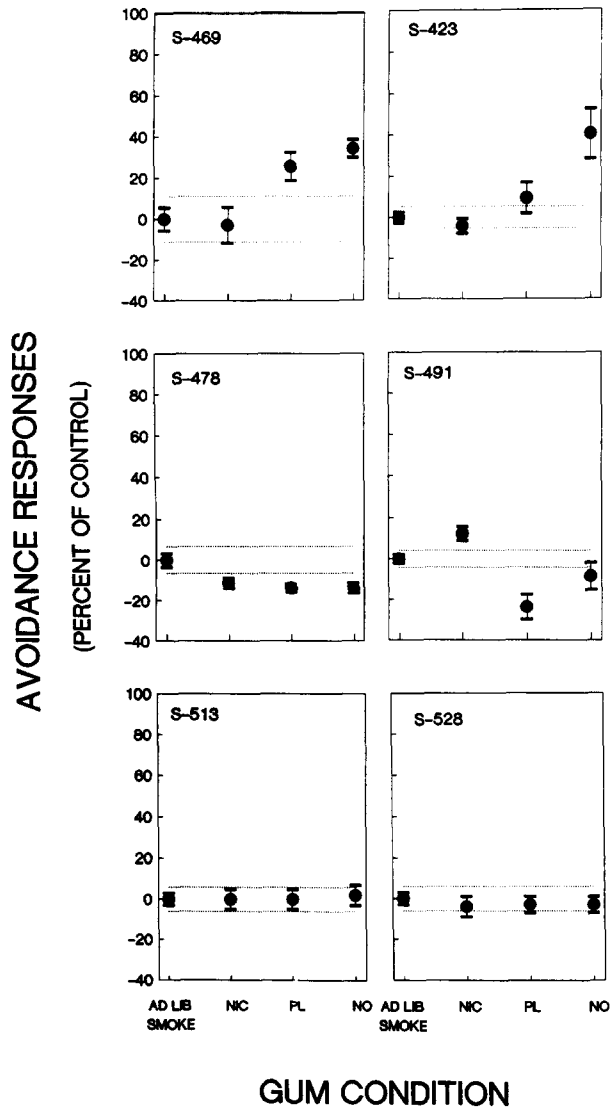

FIG. 1. Overall avoidance responding during each condition for each subject. Data points represent the mean percent difference from the baseline ad lib smoking condition. Vertical lines are standard errors of the mean.

EXPERIMENT 2

Experiment 2 investigated the effects of varying doses of acute nicotine administration on free-operant avoidance responding when unavoidable point losses were presented. The nicotine and cigarette smoke were administered by the spirometric method and the doses were 0.3, 1.2, and 2.7 mg per cigarette, and an air condition in which warm air was delivered to the subject.

METHOD

Subjects

Six male smokers participated. All subjects reported smoking an average of 20 to 30 high nicotine delivery cigarettes daily for at least 4 years. They were recruited by the same means as in Experiment 1. The subjects were required to meet the same requirements for participation and to maintain participation as subjects in Experiment 1.

Apparatus

The same apparatus used in Experiment 1 was employed in Experiment 2.

Smoke Delivery System and Procedure

The spirometric smoke delivery system was used to deliver measured volumes of tobacco smoke and air to the subjects. First, a one-liter air bag was filled with air using a vacuum pump. The air was maintained in the bag, while 60 cc of to-

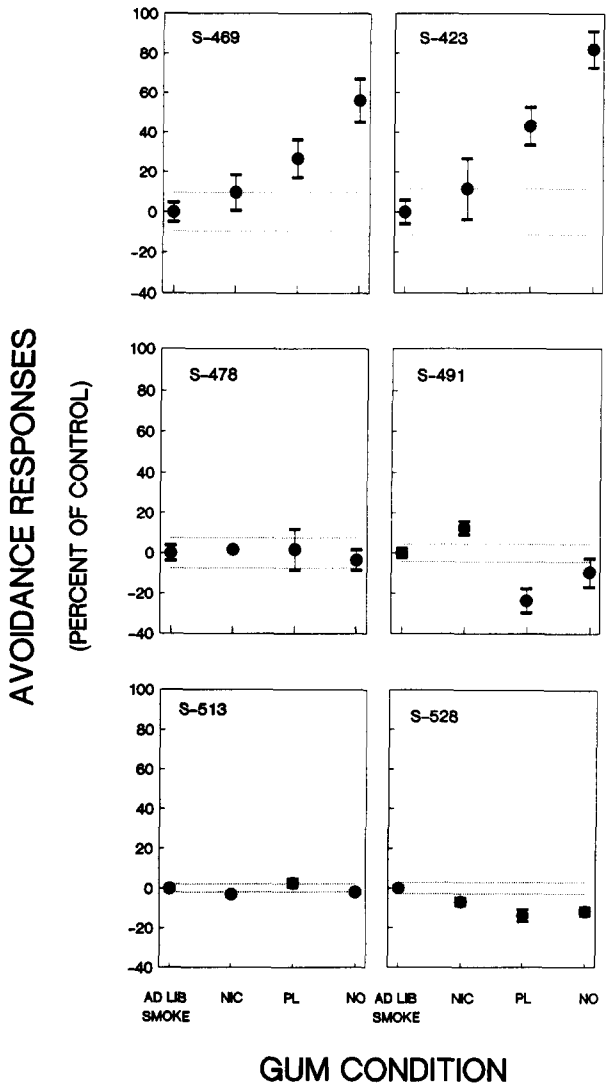

FIG. 2. Avoidance responding during the ten-second period following each of the unavoidable point losses for each subject. Data points represent the mean percent difference from the baseline ad lib smoking condition. Vertical lines are standard errors of the mean.

bacco smoke was extracted using a plastic syringe and then injected into the system. The air in the bag kept the smoke in a large section of tubing. The subject was then instructed to inhale on a tube and a clamp was opened releasing the smoke and air. The one-liter bolus of air forced the smoke deep into the lungs within two to three seconds. During each period of smoke delivery a total of twenty 60 cc puffs were delivered at a rate of one every thirty seconds. The smoke delivery system and its operation have been described in greater detail in a previous publication (7).

Schedule of Reinforcement

The same schedule used in Experiment 1 was used in Experiment 2.

Instructions

The same instructions given to subjects in Experiment 1 were given to subjects in Experiment 2 with two modifications—the counter was set at thirty (30) points at the beginning of the session which represented a potential payment of $3.00.

Daily Procedure

Subjects participated in one twenty-minute session prior to and immediately following each of the four tobacco smoke administration periods throughout the day. Each postinhalation session was separated from the next preinhalation session by a waiting period during which the subjects were required to remain in another room containing a television and reading material. The four smoke administration periods commenced at 0900, 1100, 1300, and 1500. They received lunch at 1200. On arrival subjects provided a urine sample and expired air samples for breath alcohol measurement and carbon monoxide (CO) level assessment. Subjects received $5.00 if their CO was less than 21 ppm at 0830. Subjects were not allowed to smoke additional cigarettes from their time of arrival until they left the laboratory (approximately 8 hours).

Experimental Conditions

Each day subjects received either smoke from a 0.3 mg, 1.2 mg, 2.7 mg nicotine yield cigarette or warm air (sham condition) at the four administration periods. Subjects were administered smoke drawn from a 0.3 mg nicotine yield cigarette until responding stabilized (baseline condition). Once responding was stable, subjects received smoke drawn from 1.2 or 2.7 mg nicotine yield cigarettes or warm air for the day. Baseline conditions (0.3 mg nicotine yield cigarettes) were reinstituted and responding was returned to previously established baseline levels before air or smoke from the other nicotine yield cigarettes was administered. Each subject received air and smoke from 1.2 and 2.7 mg nicotine yield cigarettes for one day. The order of presentation of air and smoke from the 1.2 and 2.7 nicotine yield cigarettes was balanced across subjects.

Research cigarettes were obtained from the University of Kentucky, Tobacco and Health Research Institute (ref. No. 3A1, 1A3, and 1A4). These cigarettes were reported to deliver 0.3, 1.2, and 2.7 mg of nicotine, while reported tar and CO delivery were very comparable.

RESULTS

Subjects' baseline response rate during the presmoke administration sessions varied across subjects. Subject S434 responded at a mean of 4.21 responses per second, while S481 and S487 responded at 2.12 and 2.85 responses per second respectively. The other three subjects made fewer than 1 response per second. Though response rates varied across subjects few point losses occurred other than those which were unavoidable.

Figure 3 shows subjects' data for overall rate and responding following unavoidable point losses. Data points represent mean percent change between presmoke administration responding and postsmoke administration responding. Subjects who responded >2 responses per second are represented by the open symbols and the subjects who responded at <1 response per second are represented by the filled symbols. With the exception of one subject the overall rate of response changed by less than 10 percent following administration of tobacco smoke at all three nicotine yields or air. Subject S440 increased his overall response rate by a mean 28% following smoking the 2.7 mg nicotine yield cigarettes. The percent changes in response rates following unavoidable point losses between pre- and postsmoke administration sessions was more variable. Two subjects (S453 and S440) emitted a greater number of responses following the point losses

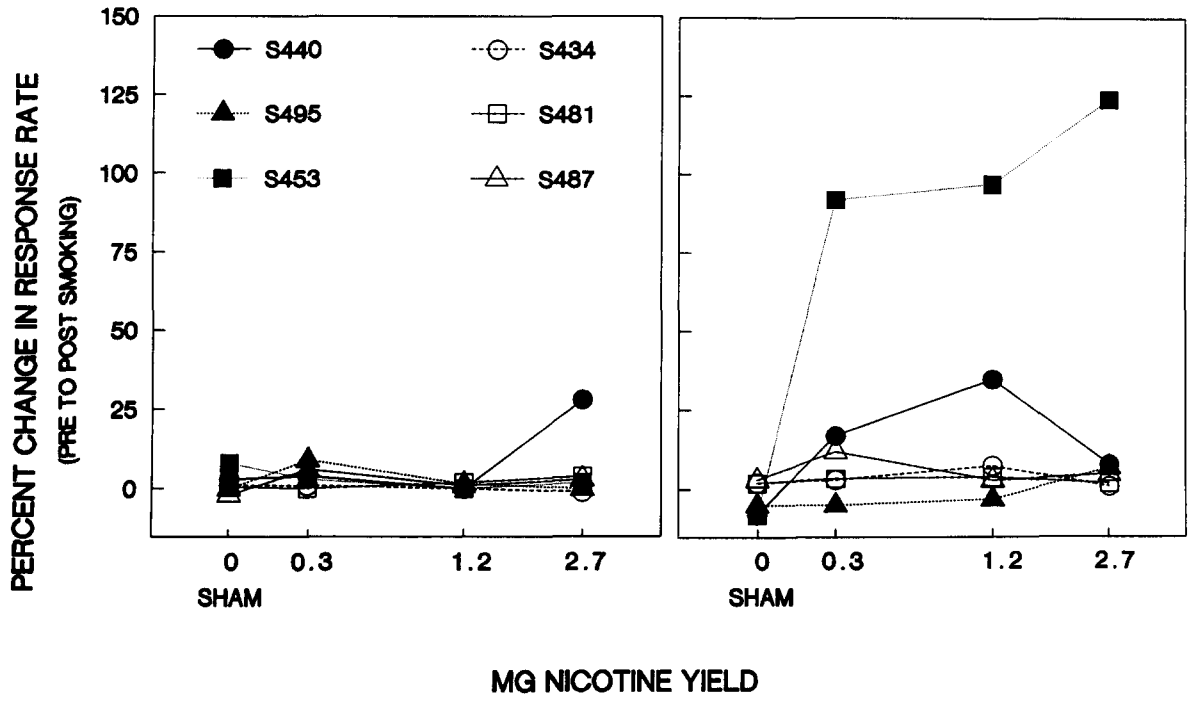

FIG. 3. Left panel shows overall avoidance responding for each of the nicotine yield conditions. Right panel shows avoidance responding during the ten-second period following each of the unavoidable point losses. Data points represent mean percent difference between presmoke administration responding and postsmoke administration responding for each subject. Filled points represent data subjects who responded less than 1 response per second, open points represent data for subjects who responded more than 2 responses per second.

after smoking than following administration of air. The other subjects' changes in responding were relatively minimal.

Comparing the data for the three subjects responding at less than 1 response per second with the data of the high response rate subjects showed different effects of the nicotine administration on the responding following the unavoidable point losses. All three subjects who responded at a low rate increased responding by at least 12% from the sham air condition to the 2.7 mg nicotine yield condition. The high rate of response exhibited by the other three subjects may have resulted in a ceiling effect on the percent change which could be observed.

Analyses of variance were performed on the results for all subjects and also using the two groupings of baseline response rate as a between groups factor. There was no significant effect of nicotine yield.

GENERAL DISCUSSION

The results of Experiment 1 showed that smoke and nicotine abstinence produced different behavioral effects in regular smokers. Two subjects increased overall avoidance responding in the conditions in which no nicotine was available, while two decreased responding and two exhibited no effect. The prevailing smoke/nicotine conditions also had varying effects when unavoidable point losses occurred. During ad lib baseline smoking conditions five of the six subjects increased responding during the ten seconds following the added point losses. Looking at the effects of the abstinence conditions on the post unavoidable point loss responding in terms of percent of control found that two subjects increased responding across conditions, two subjects decreased responding and two subjects' responding altered little.

Experiment 2 also found variability in the response of subjects to the effects of varying acute doses of nicotine. The only effect on overall response rate by administration of the different doses of nicotine was an increase of 28% in the 2.7 mg nicotine yield condition by S440. More variability was observed in the responding following the unavoidable point losses. Two subjects showed substantial increases across the conditions while the remainder of the subjects showed small and variable influences on responding of the nicotine yield conditions.

Early work with humans employed a brief electric shock as the aversive event in avoidance schedules and found that some subjects did not acquire the response and those that did emit avoidance responding did so at different rates (1,2). Subsequent research employed point loss periods as the aversive event and obtained avoidance in all subjects and again their rates varied across subjects and were partially determined by experimental history (17,18). The studies reported here employed point loss as the aversive event and also obtained different rates of avoidance responding. Previous research with humans has not presented unavoidable aversive events (point loss) within an avoidance schedule. Work with animals, however, observed increased avoidance responding following presentation of unavoidable aversive events (13). This study found similar results, the majority of the subjects increased responding immediately following the unavoidable point losses during baseline conditions.

Previous research has suggested that tobacco and nicotine administration may decrease the characteristic subjective and behavioral response to stressful or anxiety producing situations (3,9). In addition, tobacco smoke self administration increases with increases in stress or anxiety (4, 12, 15). These data suggest that in this situation nicotine and tobacco abstinence and

administration had inconsistent effects on the avoidance responding following unavoidable point loss. Some subjects increased responding while other subjects decreased or showed little effect.

Previous research investigated the effects of the tobacco abstinence conditions used in Experiment 1 on aggressive responding in a controlled laboratory situation (5). This research found consistent significant increases in aggressive responding in the no gum condition above the nicotine and placebo gum conditions. In another study, tobacco smoking was observed to decrease aggressive responding (3). A difference between these studies investigating aggressive responding and these present studies is that in the aggressive responding paradigm the situation is presented as a social context in that point losses incurred by the subject were attributed to the behavior of another person. In the avoidance paradigm the context is nonsocial, the point losses are not attributed to the behavior of another person. This difference in social and nonsocial context may contribute to the behavioral effects observed of tobacco and nicotine abstinence and acute administration of nicotine via tobacco smoke. The failure to see a consistent effect on the avoidance responding following the unavoidable point losses may suggest that behavioral effects of tobacco/nicotine abstinence and acute administration may differ in social/nonsocial situations or the effects of nicotine may be more predictable in a social context.

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