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Tobacco Abstinence, Smoking Cues, and the Reinforcing Value of Smoking

KENNETH A. PERKINS,[1] LEONARD H. EPSTEIN, JAMES GROBE AND CAROLYN FONTE

Western Psychiatric Institute & Clinic, University of Pittsburgh School of Medicine, Pittsburgh, PA 15213

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PERKINS, K. A., L. H. EPSTEIN, J. GROBE AND C. FONTE. *Tobacco abstinence, smoking cues, and the reinforcing value of smoking.* PHARMACOL BIOCHEM BEHAV 47(1) 107–112, 1994.—One definition of the reinforcing value of a drug is the degree to which an organism will work to obtain it. Male and female smokers (n = 8 each) engaged in a task involving concurrent schedules of reinforcement for responding to receive cigarette puffs versus money on four occasions, following overnight abstinence versus no abstinence and in the presence of a lit cigarette (smoking "cue") or with no cigarette (2×2 design). Reinforcement schedule for puffs ranged from variable ratio 4 (VR4) to VR32, with schedule order during the first five trials (VR4 first, VR32 first) counterbalanced and repeated in reverse sequence during the second five trials. Schedule for money remained at VR4 during all trials. Results indicated significantly greater responding for puffs after overnight abstinence and in the presence of the smoking cue, although effect of the cue was specific to the "leaner" VR schedules (VR16, VR32). Unexpectedly, not only was reinforcement schedule for puffs a significant determinant of responding, but the order of these schedules (i.e., VR4 first vs. VR32 first) produced a significant overall difference in responding for puffs, especially in the presence of the cue. There was no difference in responding between males and females. These findings indicate that the reinforcing value of smoking is increased by overnight abstinence, the presence of a lit cigarette under lean reinforcement conditions, and the order in which reinforcement schedules are presented.

Tobacco smoking Reinforcement Abstinence Drug cue Concurrent schedules Smokers

ASSESSING whether or not a drug is reinforcing is the hallmark of determining its abuse liability (9). A definition of the reinforcing value of a drug is the degree to which an organism will work to obtain it (24). However, it has long been apparent that this "value" is not fixed, but varies depending on many conditions surrounding the drug intake: amount of drug per reinforcement, reinforcement schedule, availability of competing reinforcers, specific environmental context of intake, and so on (9,24). The reinforcing value of drugs may also vary depending on characteristics of the organism, such as prior drug history, length of abstinence from the drug, and other individual differences (13).

Nicotine has clearly been shown to be the constituent of tobacco smoke which reinforces smoking behavior (21). Operant procedures have been used in animal research to assess differences in nicotine's reinforcing value as a function of various manipulations of conditions. For example, Goldberg et al. (7) found that responding reinforced by nicotine injection can be reduced by removing a visual stimulus associated with nicotine or by pretreating animals with mecamylamine, a nicotine antagonist. Similar procedures have very recently been employed to examine changes in the reinforcing value of tobacco smoking and other substances in humans following specific manipulations in order to better understand conditions which elicit increased smoking behavior or which might discourage smoking. Bickel et al. (1) showed that increasing the response requirement (i.e., number of responses per reinforcement) for smoking decreased smoking as well as coffee consumption, but increasing the response requirement for coffee decreased coffee consumption without affecting responding for smoking. Epstein et al. (6) found that overnight smoking deprivation increased the reinforcing value of smoking in a group of female smokers, as determined by increases in the behavior reinforced by puffs on a cigarette. Similar effects of food deprivation were found for the reinforcing value of food (6,12), suggesting some generalizability of results across reinforcers.

Aside from brief tobacco abstinence, there are numerous other conditions which may elicit changes in the reinforcing value of smoking, changes which may be quantifiable by similar operant procedures. Just as animals have been shown to alter responding to obtain IV nicotine in the presence of visual stimuli associated with nicotine availability (7), one likely elicitor of smoking behavior in the natural environment is the presence of smoking-related stimuli or "cues," such as a lit cigarette or someone else smoking. Although perhaps important in increasing the reinforcing value of smoking during periods of abstinence (15), these cues may also be powerful

[1] Requests for reprints should be addressed to Kenneth A. Perkins, Western Psychiatric Institute & Clinic, University of Pittsburgh School of Medicine, 3811 O'Hara Street, Pittsburgh, PA 15213.

influences on smoking behavior in nonabstinent smokers (19). Notably, it has been shown that the sight of desirable foods increases eating behavior in subjects who are food-satiated as well as food-deprived (4), again suggesting some commonality across reinforcers in conditions which alter their reinforcing value. It is very important to emphasize, however, that despite the likelihood that visual cues do elicit smoking behavior, most research has examined only self-reported desire to smoke following cue exposure (19), a measure not consistently related to smoking behavior (20,23). Thus, there has been a virtual absence of controlled studies of these influences on actual smoking-reinforced behavior (20,21).

In addition to environmental factors such as smoking cues, individual differences may also determine the reinforcing value of smoking. Aside from the obvious characteristic of smoking history, subject gender may also be influential. There is some evidence suggesting that males and females differ in their smoking patterns, and that females may be more sensitive to nicotine than males (8). However, the observation that females may compensate less in their smoking behavior following nicotine-preloading suggests that females may be less sensitive to nicotine (18). Thus, gender differences in the reinforcing value of nicotine may exist, but it is unclear whether females find it more or less reinforcing than males.

Finally, it is often advantageous to examine changes in the value of one reinforcer within the context of the availability of a second reinforcer [i.e., concurrent reinforcers (22)]. This allows for a determination of specific versus nonspecific changes in responding (i.e., for one versus both reinforcers) due to manipulations and more closely mirrors the natural environment, which usually offers multiple competing reinforcers. Behavioral economic theory has recently been employed to provide a clearer understanding of changes in behavioral choices between two concurrent reinforcers [e.g., (1,6)].

In this study we used a procedure involving concurrent schedules of reinforcement to examine the effects of overnight abstinence from smoking and presence of a lit cigarette (smoking cue) on the reinforcing value of puffs on a cigarette and money in male and female smokers. We hypothesized that subjects would work more for puffs (i.e., reinforcing value would increase) when abstinent and when in the presence of the smoking cue.

METHODS

Subjects

Subjects were eight male and eight female smokers similar in age (mean ± SE = 22.4 ± 1.1 vs. 22.3 ± 1.0 years, respectively), smoking history (21.9 ± 2.0 cigarettes/day for 4.4 ± 1.2 years vs. 18.5 ± 1.4 cigarettes/day for 2.6 ± 0.7 years), and nicotine content of preferred brand (0.79 ± 0.09 vs. 0.87 ± 0.09 mg yield). Potential subjects were those smoking at least 15 cigarettes/day for at least 1 year. Informed consent was obtained from all subjects after the nature and consequences of their participation were explained.

Concurrent Schedules Task

The concurrent schedules of reinforcement for smoke puffs and money were presented via "Applepicker" (16), in which subjects manipulate a computer joystick to work for "apples" on one of two "fields" (monitor screens). Each field represents one of the available reinforcers and contains its own schedule of reinforcement. The reinforcers concurrently available in this study were money ($0.02 per reinforcement) and one puff of their preferred brand of cigarette (via computer instructions to standardize exposure per puff). The schedule of reinforcement for money remained at variable ratio 4 (VR4) for each of the 10 trials, while the schedule for the cigarette puff ranged across VR4, VR8, VR12, VR16, and VR32. The order of the puff schedule (i.e., VR4 first on up to VR32 vs. VR32 first on down to VR4) was counterbalanced between subjects and repeated in reverse sequence after a 5-min rest (example: VR32, VR16, VR12, VR8, VR4, rest, VR4, VR8, VR12, VR16, VR32). The same schedule order was used within subjects across days. Each trial consisted of a 40-s practice period to enable the subject to learn the reinforcement frequency (i.e., schedule) on each field, followed by 2 min of free choice to work on either field to earn reinforcers.

Procedure

Each subject participated by himself or herself in five experimental sessions: task introduction on day 1, followed by four days involving Overnight Smoking Abstinence/No Abstinence × Smoking Cue/No Cue, in a 2 × 2 within-subjects design. Order of the four conditions was counterbalanced between subjects. Each session began at 1200, and subjects were instructed to maintain their same morning pattern of eating and activity across days.

On day 1, subjects were presented with detailed instructions via audiotape on how to perform the Applepicker task and engaged in as many practice games as required to become familiar with it, as demonstrated by identifying which reinforcer was easier to obtain for each game. Then, subjects proceeded to engage in the entire sequence of 10 trials at the various reinforcement schedules for puffs (VR4 to VR32) versus money (VR4 only). The sequence of schedules was presented in the same order as that used on all subsequent days for that subject. During this introductory day, subjects were not required to be abstinent from smoking and were not provided with any reinforcers "earned," since this session was labeled as practice and the data were not used.

On subsequent days under the four experimental conditions (i.e., abstinence vs. no abstinence and cue vs. no cue), subjects initially engaged in three nonreinforced trials to refamiliarize themselves with the task before proceeding to the 10 trials involving opportunities to earn reinforcers. Overnight smoking abstinence (on 2 days) was verified by expired-air carbon monoxide (CO) ≤ 13 ppm. On the two "no abstinence" days, subjects were not required to abstain before the session, and they smoked one cigarette ad lib just after the 3 initial, nonreinforced trials and prior to the 10 reinforcement trials. CO was assessed in all subjects prior to the 10 reinforced trials (after the ad lib cigarette on no abstinence days) to determine similarity of exposure between cue and no cue sessions and to verify difference in smoking exposure due to the abstinence/no abstinence manipulation. On two days, the smoking cue was then presented. This cue consisted of keeping a lit cigarette in an ashtray next to the subject while they engaged in the task. The ashtray was monitored continuously to ensure that the cigarette was not moved. Feedback on reinforcers earned was provided at the end of each trial, and reinforcers earned during a trial were presented to subjects immediately following that trial. Earned smoke puffs were consumed according to instructions on a computer monitor to

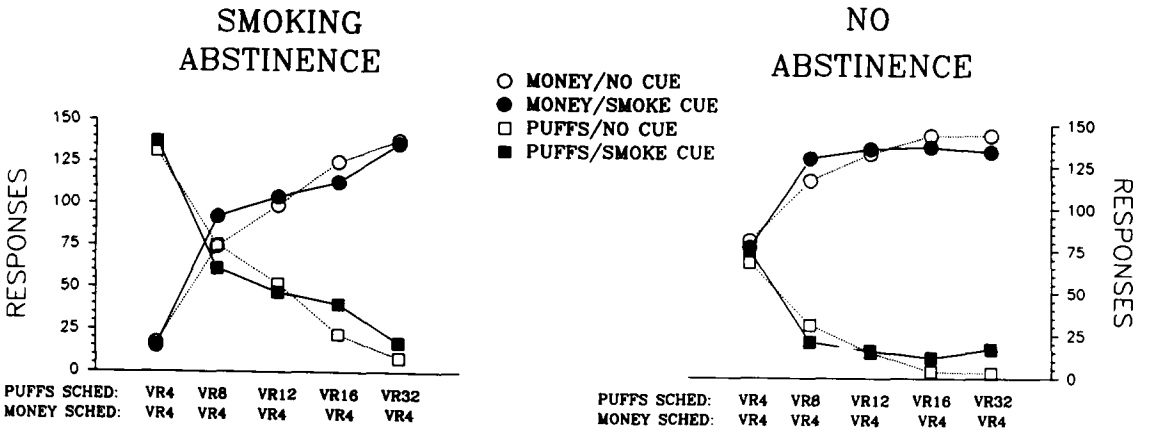

FIG. 1. Number of responses by male and female smokers (n = 16) toward earning cigarette puffs vs. money across reinforcement schedules in the presence or absence of a lit cigarette smoking cue following overnight smoking abstinence (left) or no abstinence (right). Values are number of responses summed across two exposures to each schedule.

standardize the duration of each puff. Subjects lit one of their preferred brands without inhaling and then inhaled, held the puff for 3 s, and then exhaled on visual command every 20 s for as many puffs as were earned during the immediately preceding trial. This procedure has been employed in several previous studies of controlled smoke exposure (17). "Desire to smoke" (100-mm visual analog scale) was obtained before the three initial nonreinforced trials (baseline), immediately prior to the first trial but following presentation of cue or no cue ("pre"), after the brief rest period following the fifth trial ("mid"), and after trial 10 ("post"). CO was also obtained at the same time points.

Responses for smoke puffs and total responses were analyzed by analysis of variance (ANOVA), with gender and reinforcement schedule order (two levels; VR4 first vs. VR32 first) as the between-subjects factors and abstinence (two levels), smoking cue (two levels), phase (two levels; first five vs. second five trials), and VR schedule (five levels) as within-subjects factors. Desire to smoke was analyzed by a similar ANOVA involving gender, abstinence, cue, and session period (four levels; baseline, pre, mid, post trials) as factors. Follow-up comparisons were performed by Fisher's LSD t-test (11).

RESULTS

Baseline CO values indicated similar smoking exposure between the cue and no cue conditions on no abstinence days (29.3 ± 3.8 vs. 25.4 ± 2.8 ppm, respectively) and on abstinence days (8.9 ± 0.5 vs. 8.3 ± 0.7 ppm). Thus, smoking exposure prior to the task trials was not different between cue and no cue days but was different between abstinence and no abstinence days, as planned. ANOVA results indicated that there were no main or interaction effects of gender on responding for cigarette puffs, suggesting that the reinforcing

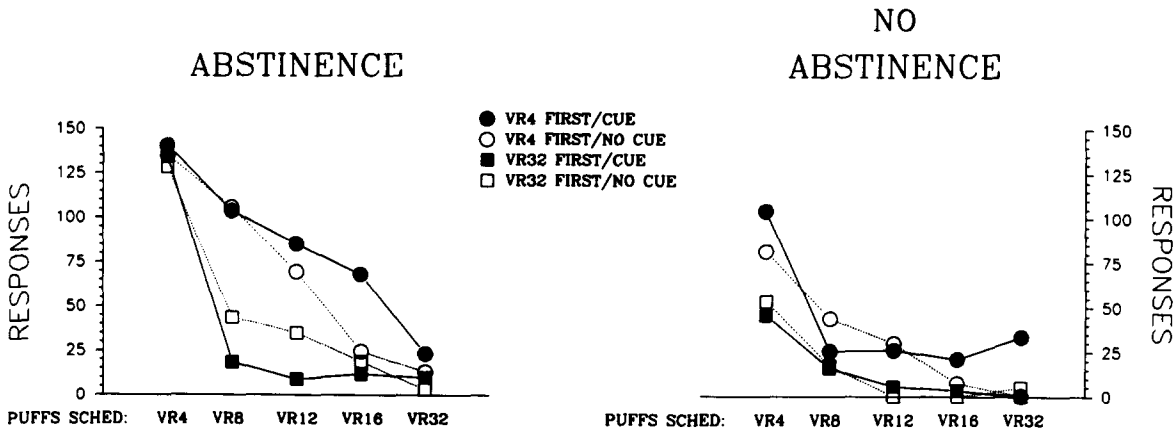

FIG. 2. Number of responses toward earning cigarette puffs across VR4–VR32 reinforcement schedules for puffs in the presence or absence of a lit cigarette smoking cue following overnight smoking abstinence (left) or no abstinence (right). Data are presented separately for subjects exposed to the VR4 schedule for puffs first (n = 8) and for those exposed to the VR32 schedule for puffs first (n = 8).

TABLE 1

MEAN ± SE NUMBER OF RESPONSES PER SESSION REINFORCED BY CIGARETTE PUFFS OR MONEY AND TOTAL RESPONSES AFTER OVERNIGHT SMOKING ABSTINENCE/NO ABSTINENCE AND IN THE PRESENCE OF A SMOKING "CUE"/NO CUE

Condition	VR4 First (n = 8)	VR32 First (n = 8)	All Subjects (n = 16)
Puffs			
No Abst/No Cue	162.9 ± 26.8	75.9 ± 23.3	119.4 ± 20.5
No Abst/Cue	210.1 ± 26.6	70.8 ± 22.0	140.4 ± 24.5
Abstin/No Cue	346.9 ± 35.3	228.6 ± 24.3	287.8 ± 25.7
Abstin/Cue	419.9 ± 52.4	182.8 ± 16.5	301.3 ± 40.5
Money			
No Abst/No Cue	567.4 ± 20.7	672.1 ± 17.3	619.8 ± 18.8
No Abst/Cue	538.3 ± 37.3	688.9 ± 17.0	613.6 ± 27.7
Abstin/No Cue	399.3 ± 28.3	505.4 ± 26.9	452.3 ± 23.3
Abstin/Cue	335.9 ± 51.3	584.0 ± 14.0	459.9 ± 41.0
Total			
No Abst/No Cue	730.3 ± 15.5	748.0 ± 12.3	739.1 ± 9.8
No Abst/Cue	748.4 ± 16.9	759.6 ± 7.4	754.0 ± 11.6
Abstin/No Cue	746.1 ± 15.5	734.0 ± 11.6	740.1 ± 9.5
Abstin/Cue	755.8 ± 11.7	766.8 ± 9.3	761.3 ± 7.4

Data are presented separately for subjects exposed to VR4 schedule for puffs first and for those exposed to VR32 schedule for puffs first.

value of smoking did not differ between males and females in this study. Because of this null finding, results will be presented collapsed across males and females.

Responding for smoke puffs across VR schedules was highly significant, $F(4, 56) = 69.04$, $p < .001$, as expected. As shown in Fig. 1, there was also a significant main effect of smoking abstinence on responding for cigarette puffs, $F(1, 14) = 43.88$, $p < .001$. There was no significant main effect of the smoking cue (lit cigarette) on responding for puffs, $F(1, 12) < 1$). However, the interaction of smoking cue by VR schedule was significant, $F(4, 56) = 2.67$, $p < .05$, as presence of the cue increased responding for smoke puffs more at the "leaner" schedules (VR16 and VR32) than the other schedules, (VR4, VR8, VR12) $t(31) = 4.46$, $p < .001$, as also shown in Fig. 1. As would be expected, number of puffs actually earned was also greater on the smoking abstinence versus no abstinence days (11.5 vs. 5.3 puffs), as was boost in expired-air CO (+5.2 vs. −2.3 ppm), and money earned was less ($0.56 vs. $0.74). (CO declined on no abstinence days because of the high baseline value following the initial ad lib cigarette and the continued clearance of CO from the lungs over the course of the session.) There was no difference in total puffs earned due to the presence versus the absence of the cue (8.5 vs. 8.3), probably because the increased responding due to the cue occurred at the leaner schedules, when reinforcement was less available. There was also no difference in CO boost (+2.0 vs. +1.0 ppm).

Unexpectedly, there was also a significant interaction be-

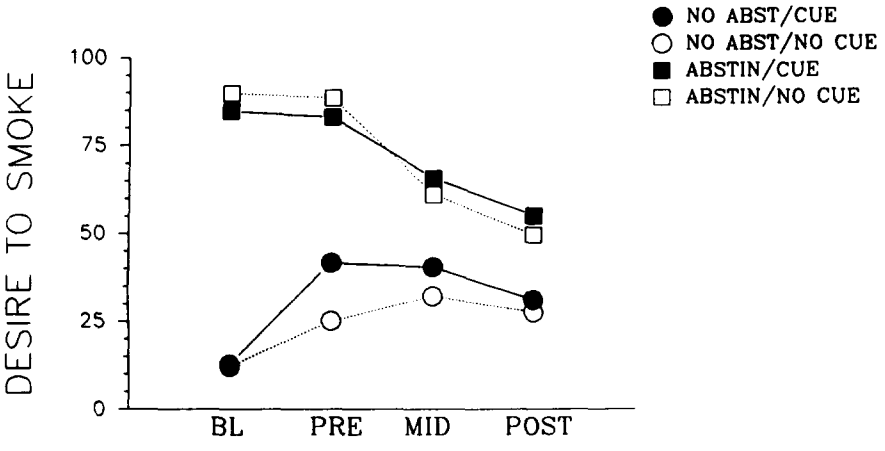

FIG. 3. Desire to smoke (0–100) at baseline (BL) and across subsequent task trial periods in the presence or absence of a lit cigarette smoking cue following overnight smoking abstinence or no abstinence.

tween cue presence and schedule order, (i.e., VR4 or VR32 first) $F(1, 14) = 7.40, p < .02$. Subjects exposed to VR4 first responded for puffs significantly more in the presence versus the absence of the cue, $t(15) = 4.26, p < .001$, while subjects exposed to VR32 first responded for puffs somewhat less in the presence of the cue, $t(15) = 1.78, p < .10$, as shown in Fig. 2. Again, because this difference in responding due to the cue was primarily at the "lean" schedules, there was no significant difference in the number of puffs earned in the presence versus the absence of the cue (10.9 with cue vs. 10.2 without cue for VR4 first group, 6.0 with cue vs. 6.4 without cue for VR32 first). The main effect of schedule order was also highly significant, $F(1, 14) = 31.42, p < .001$, as subjects exposed to VR4 first responded for puffs approximately twice as much as subjects exposed to VR32 first (see Table 1). Furthermore, subjects exposed to VR4 first responded for puffs less over the first five (123.2 responses) versus last five (159.5 responses) trials, while subjects exposed to VR32 first responded for puffs more over the first five (97.3) versus the last five (40.3) trials, (Order × Half interaction) $F(1, 12) = 15.22, p < .005$. There was no significant main effect of first- versus second-half trials and no other interactions involving first- versus second-half trials, schedule order, or abstinence. There were also no significant differences in total responding across any conditions or schedule orders (Table 1), except presence of the smoking cue, which was associated with a 2–3% increase in total responding, $F(1, 14) = 30.03, p < .001$.

Desire to smoke was significantly greater on abstinence versus no abstinence days, $F(1, 14) = 140.39, p < .001$, as expected, and was marginally increased across periods by the presence of the smoking cue, (Cue × Period) $F(3, 42) = 2.38, p < .10$, as shown in Fig. 3. This effect of the cue was confined to the no abstinence sessions, as the increase in desire from baseline to just prior to the beginning of trial 1 (pre) was greater in the presence versus the absence of the cue on no abstinence days, (+29.0 vs. +13.1) $t(31) = 4.38, p < .001$, but not on smoking abstinence days, (−1.6 vs. −1.3) $t(31) < 1$, perhaps due in part to a ceiling effect (see Fig. 3). Finally, the rating of desire to smoke at the pre and mid points was significantly correlated with the subsequent number of responses for smoke puffs during the five games following each rating ($r = 0.60, p < .001$), suggesting that this rating was somewhat predictive of smoking-reinforced behavior.

DISCUSSION

In this study, the reinforcing value of smoke puffs (i.e., amount of responding reinforced by the opportunity to smoke one puff) was shown to be increased by overnight abstinence from smoking. A putative "cue" for smoking, a lit cigarette in an ashtray, also increased the reinforcing value of smoking, but only under limited conditions. Responding for smoke puffs in the presence of the cue was significantly increased at "leaner" schedules and for subjects who were exposed to the VR4 schedule first. Such responding in the presence of the cue tended to be less for subjects exposed to the VR32 schedule first. There were no differences in the reinforcing value of smoking between males and females.

The results of this study indicate that the reinforcing value of smoking in humans is significantly influenced by the length of abstinence from smoking and the reinforcement schedule, findings consistent with previous research (6). However, the current study also found that the reinforcing value of smoking was increased by the presence of a smoking cue during periods of lean reinforcement, suggesting that stimuli associated with smoking may increase tobacco-seeking behavior when there are constraints (high "cost") on smoking but not when smoking is readily available. On the other hand, self-reported desire to smoke was increased by the cue only during ad lib smoking days and not on the days when smokers had abstained overnight prior to the session. Given the nearly maximal ratings of desire on the abstinent days, it is likely that lack of increased rating of desire due to the cue resulted from a ceiling effect (i.e., ratings were already so high that there was little upward room for increase due to other influences).

Moreover, the importance of the precise conditions of reinforcement on behavior was greatly—and somewhat unexpectedly—supported by the finding that not only was reinforcement schedule per se a determinant of behavior, but also the order of these schedules produced a roughly twofold difference in overall responding for smoking. This effect of schedule order was even more pronounced in the presence of the smoking cue. A simple explanation for the effect of schedule order is not immediately apparent. It is unlikely that changes in smoking satiation across trials due to consumption of earned puffs could explain this effect, since subjects exposed to either schedule order experienced the same abstinence and cue conditions and had exactly the same amount of opportunity to earn puffs at each reinforcement schedule. Furthermore, the schedule order was repeated in reverse sequence in the second half of the 10 trials (i.e., same sequence as the first half of the trials for the other order). Thus, during each session, subjects were either exposed to VR4 first during the first five trials followed by VR32 first for the second five trials, or the other way around, making it even more surprising that a significant overall difference in responding for smoking due to schedule order was found. Whatever the explanation, these results clearly confirm the observation, long recognized in animal studies (24), that the parameters of the reinforcing contingencies are very important in determining responding. One implication of this finding is that altering these parameters, such as by varying reinforcer magnitude and schedule, could produce results different from those observed in this study. Rather than providing methodological difficulties to be overcome, these influences on behavior are worthy of study in their own right.

The concurrent schedules task employed in this study to assess the reinforcing value of smoking was demonstrated to be sensitive to several manipulations (i.e., abstinence and cue), although to differing degrees. One clear advantage of this method is that it may allow for closer comparisons of animal versus human studies of factors influencing the reinforcing value of drugs. Thus, just as similar methods have found that housing conditions [e.g., (2)], genetic differences (13), and prior drug history (10) may affect drug-seeking in animals, so may this operant method objectively quantify possible differences in the reinforcing value of drugs in humans due to environmental experiences (5), family history of substance abuse (14), or typical history of drug exposure (3). Additional research clarifying the parameters of reinforced responding of humans with this method should facilitate its wider application to research of human drug-seeking behavior.

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