



0091-3057(94)E0111-T

BRIEF COMMUNICATION

Effects of Δ^9 -Tetrahydrocannabinol
and Social Context on Marijuana
Self-Administration by HumansTHOMAS H. KELLY,*¹ RICHARD W. FOLTIN,† MATTHEW T. MAYR‡
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Received 8 September 1993

KELLY, T. H., R. W. FOLTIN, M. T. MAYR AND M. W. FISCHMAN. *Effects of Δ^9 -tetrahydrocannabinol and social context on marijuana self-administration by humans*. PHARMACOL BIOCHEM BEHAV 49(3) 763-768, 1994. — The effects of time of day and social context on daily patterns of marijuana self-administration were examined in two groups of three adult male marijuana smokers during a 12-day residential study. Days were divided into 6.5-h work and social-access periods. Order of occurrence (i.e., work before social access or social access before work) was counterbalanced between groups and reversed for both groups on day 8. Up to eight marijuana cigarettes (0.0% or 2.3% Δ^9 -THC) could be smoked each day. Stable patterns of marijuana smoking were observed across days for each subject. Three subjects smoked more marijuana during the social-access period, regardless of when it occurred. The other three smoked more marijuana during the first period, regardless of whether it was a work or social-access period. The number of marijuana cigarettes smoked was unrelated to THC content. In contrast, subjective reports of "High," "Liking," "Potency" and "Drug" on visual-analog scales were increased on active marijuana days. Subjective reports of drug effects were not predictive of drug self-administration.

Marijuana	Self-administration	Δ^9 -Tetrahydrocannabinol	Context	Reinforcement
Subjective effects	Human			

PREVIOUS studies of marijuana self-administration with humans have not convincingly demonstrated that Δ^9 -tetrahydrocannabinol (THC), the principal behaviorally active component in marijuana smoke, is involved in the reinforcing effects of marijuana. Studies have either not examined the effects of varied concentrations of THC on rates of marijuana self-administration (e.g., 7,13,14), or failed to detect any effect of THC concentration on marijuana consumption (e.g., 2,16). However, when patterns of marijuana self-administration across the day were measured (e.g., 7,13,14), variations in rates of self-administration across time were observed, with

increased rates commonly observed in the evening, when social and recreational activities also occurred. Although such patterns suggest that the reinforcing effects of THC may vary as a function of time of day or social context, studies have not determined whether such daily smoking patterns are related to THC content.

The purpose of the current study was threefold. First, patterns of marijuana self-administration across the day were determined as a function of THC concentration in marijuana cigarettes. Second, the relative effects of social context and time of day were examined by manipulating the time of day in

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which access to social activities was available. (In previous studies, the independent effects of time of day and social activity were not examined.) Third, subjective reports of smoked marijuana were also measured to determine the relation between verbal report of drug effect and the number of self-administered cigarettes.

METHOD

Subjects

Two groups of three healthy adult male marijuana smokers, between 27 and 34 years of age (30.5 ± 1.4 years [mean \pm SEM]), selected from a pool of respondents to local newspaper advertisements, gave written consent to participate in 12-day studies after passing medical and psychological examinations. Subjects reported between four and 30 occasions of marijuana use per month (19.7 ± 5.3), with marijuana use validated through urinalysis. Two of six also reported smoking 20 tobacco cigarettes per day. Ad lib access to preferred brands of tobacco cigarettes was available to these two subjects throughout the study (12). Subjects were paid for participation, and the protocol was approved by the Johns Hopkins University Joint Committee on Clinical Investigation.

Laboratory

The study was completed in a residential laboratory (7,10) designed for continuous observation and analysis of human behavior (1). Each subject was assigned to one of three color-coded private rooms. One illuminating button, labeled "MARIJUANA," was mounted on a wall in each private room, and three additional color-coded buttons (matching the room colors) were mounted on a wall of the common area. All communications between subjects and experimenters occurred over a networked computer system (i.e., no direct contact between subjects and experimenters occurred throughout the study). Communications were limited to the reporting of food consumption and protocol compliance. No other communication was permitted, and to limit the potential effects of external events on behavior, telephones, television, newspapers, and mail were not made available.

Standard Day

Subjects were awakened at 0900. The structured portion of the day was divided into 6.5-h work and social-access periods, beginning at 1000 and 1630, with the order of exposure to periods varying across days. The daily schedule of work and social-access periods is presented in Table 1.

Snacks, drinks, and frozen meals were available ad lib throughout the day, when overhead lights were illuminated (e.g., 6,8). Overhead lights could be turned off between 2300 and 2400, after subjects completed drug-rating forms. Subjects were required to sleep or rest in their private rooms between 2400 and 0900. Clocks and watches were not permitted, and subjects were notified via the communication system at transition times (e.g., 0900, 1000).

Work Period

During the work period, subjects remained in their private rooms completing computerized performance tasks: a digit-symbol substitution task, a number recognition task, a differential reinforcement of low-rate schedule of point presentation, a repeated acquisition task, and a second-order repeated acquisition task. Task and performance details have been presented elsewhere (e.g., 10,11). Subjects received a minimum of 2 days of training and practice on the tasks, which was sufficient to establish consistent performance patterns across work periods (i.e., stable baselines), before the start of the study.

Social-Access Period

During the social-access period, subjects could engage in recreational activities in their private room (e.g., reading, listening to music) or in the common area (e.g., watching videotaped movies, playing board games) without restriction. During each social-access period, three movies were available. If requested by any one subject, a movie was played in its entirety without interruption in the common area.

Marijuana Self-Administration

Subjects were told before the study that they could smoke up to eight marijuana cigarettes per day, anytime between 1000 and 1530 and between 1630 and 2200, but that cigarettes could not be smoked "back-to-back." A 20-min inter-cigarette interval was operative during the availability intervals, but subjects were not told this duration. Subjects were also told that different strengths of marijuana would be available from day to day, but that the strength would not change during any given day. Subjects requested marijuana cigarettes for self-administration by responding on the appropriately color-coded "MARIJUANA" buttons located in the private rooms or in the common area. Buttons were illuminated after 10 responses if a marijuana cigarette was available, but remained dark if a cigarette was not available (i.e., before 1000; between

TABLE 1
STUDY DESIGN

Day	1	2	3	4	5	6	7	8	9	10	11	12
Dose (% THC)*	—	0	0	2.3	2.3	2.3	0	0	2.3	2.3	2.3	0
Group 1												
1000-1630	W	W	W	W	W	W	W	R	R	R	R	R
1630-2300	R	R	R	R	R	R	R	W	W	W	W	W
Group 2												
1000-1630	R	R	R	R	R	R	R	W	W	W	W	W
1630-2300	W	W	W	W	W	W	W	R	R	R	R	R

*Marijuana cigarettes could be smoked between 1000 and 1530 or between 1630 and 2200. W, Work period; R, Social-access period.

1530 and 1630; after 2200; or within 20 min. of the previous marijuana cigarette).

Marijuana was smoked in the room in which the button was pressed (i.e., private room or common area), using a paced puffing procedure. Subjects took three puffs from each cigarette, one per minute, as cued by signal lights. Each puff consisted of a 5-s inhalation interval, a 10-s interval in which smoke was held in the lungs, and a 45-s exhalation and rest interval. No restrictions on other behaviors (e.g., task performance, movie watching) were imposed during marijuana cigarette smoking, but smoking topography was always determined by signal cues, regardless of ongoing behavior.

The dose schedule is presented in Table 1. Excluding day 1, which served as an acclimation day, machine-rolled, unfiltered marijuana cigarettes, provided by the National Institute on Drug Abuse, containing 0% (placebo) or 2.3% (active) Δ^9 -THC (wt./wt.), were available. Cigarettes were identical in size and shape, with leaf material hidden to maintain blind dose conditions.

Drug Rating

Excluding day 1, every evening between 2300 and 2400, before turning off their overhead lights, subjects completed four visual-analog drug ratings ("Liking," "Potency," "High," and "Drug") by placing a mark along a 10-cm line anchored with endpoints of "Not at all" on the left and "Extremely" on the right ("Dislike" and "Like" on the "Liking" scale). Ratings were scored by measuring the distance between the left endpoint and the subject's mark.

Statistical Analysis

The order of work and social-access periods was reversed during days 2-7 and 8-12. Within each of these intervals, data were averaged within placebo and active dose conditions. Outcomes were analyzed with repeated-measures analysis of variance, using both dose (placebo or active) and period order (work/social-access or social-access/work) as factors. Differences were considered significant at $p < 0.05$. Data from day 1 were excluded.

RESULTS

Marijuana Self-Administration

The left column of Fig. 1 presents the total number of marijuana cigarettes smoked per day for each subject. Individual differences in the number of marijuana cigarettes smoked per day were apparent, with subjects averaging between 1.9 (S1) and 6.8 (S5) cigarettes per day. In general, the number of marijuana cigarettes smoked per day remained consistent during the study, regardless of dose. Subjects smoked 3.8 ± 0.4 cigarettes on placebo days and 4.0 ± 0.3 cigarettes on active days.

The environmental context under which marijuana cigarettes were smoked was also evaluated. No significant differences were observed as a function of period or time of day. However, the two groups of subjects exhibited differences in the conditions under which marijuana cigarettes were smoked. Subjects in group 1 smoked more placebo and active marijuana cigarettes during the social-access period, regardless of the time of day in which it occurred. During social-access periods between days 2-7 and 8-12, subjects in group 1 smoked 2.6 ± 0.2 and 2.1 ± 0.3 marijuana cigarettes, respectively. During work periods within the same intervals, subjects smoked 0.9 ± 0.3 and 1.1 ± 0.2 marijuana ciga-

rettes. In contrast, subjects in group 2 smoked more placebo and active marijuana cigarettes during the first period of the day, regardless of the whether it was a work period or a social-access period. During morning periods between days 2-7 and 8-12, subjects in group 2 smoked 2.7 ± 0.2 and 2.6 ± 0.3 marijuana cigarettes, respectively. During evening periods within the same intervals, subjects smoked 2.0 ± 0.3 and 1.6 ± 0.4 marijuana cigarettes. All three subjects in each group exhibited the same pattern of marijuana cigarette smoking.

Differences in the conditions under which marijuana cigarettes were smoked during the social-access period were also apparent across these two groups. Subjects in group 1 smoked the majority of their social-access period cigarettes under social conditions in the common area (100, 84, and 78%, respectively for S1, S2, and S3); fewer social-access period cigarettes were smoked under social conditions by subjects in group 2 (38, 16, and 71%, respectively, for S4, S5, and S6).

During the social-access period, subjects smoked the majority of placebo and active marijuana cigarettes during the first 10 min of the period, during the first 30 min of a movie, during a 20-min interval after a movie ended, or during the last 10 min of the cigarette availability interval. The proportion of the total number of social-access period marijuana cigarettes smoked within these intervals was determined separately for each subject, as was the proportion of the total social-access period falling within these intervals (typically between 0.3 and 0.35). A greater proportion of cigarettes was smoked in these intervals than would be predicted based on the amount of available time [$t(5) = 14.7$, $p < 0.05$], suggesting that during the social-access period, marijuana cigarette smoking was temporally related to the beginning or end of the drug-availability interval or of a movie. In contrast, no identifiable environmental event was associated with marijuana smoking during the work period.

Drug Rating

Significant increases in ratings of dose "Liking" [$F(1, 5) = 42.61$, $p < 0.005$], "Potency" [$F(1, 5) = 36.00$, $p < 0.005$], "High" [$F(1, 5) = 24.01$, $p < 0.005$] and "Drug" [$F(1, 5) = 28.70$, $p < 0.005$] were observed on active drug days. An interaction between dose and period order was also observed on ratings of dose "Potency" [$F(1, 5) = 7.50$, $p < 0.05$], due to a decrease in ratings of placebo "Potency" under the social-access before work period conditions. No differences in ratings of active dose "Potency" were observed as a function of period order.

Figure 1 presents individual subject ratings of dose "Liking" (middle column) and "Potency" (right column) across active and placebo dose conditions. In contrast to the number of marijuana cigarettes smoked per day, consistent differences in dose ratings were observed as a function of THC content for every subject. No consistent differences in dose ratings were observed as a function of the order of work and social-access periods during the day.

DISCUSSION

In this study, stable rates of marijuana self-administration were observed across days for each subject. Within each day, stable patterns of marijuana smoking were also observed, with smoking rates varying as a function of either period (group 1) or time of day (group 2). Marijuana consumption in group 1 was clearly related to environmental context, as higher rates of marijuana smoking occurred during the social-access period, regardless of whether that period began at 1000 or 1630. In

Marijuana Cigarettes

"Liking"

"Potency"

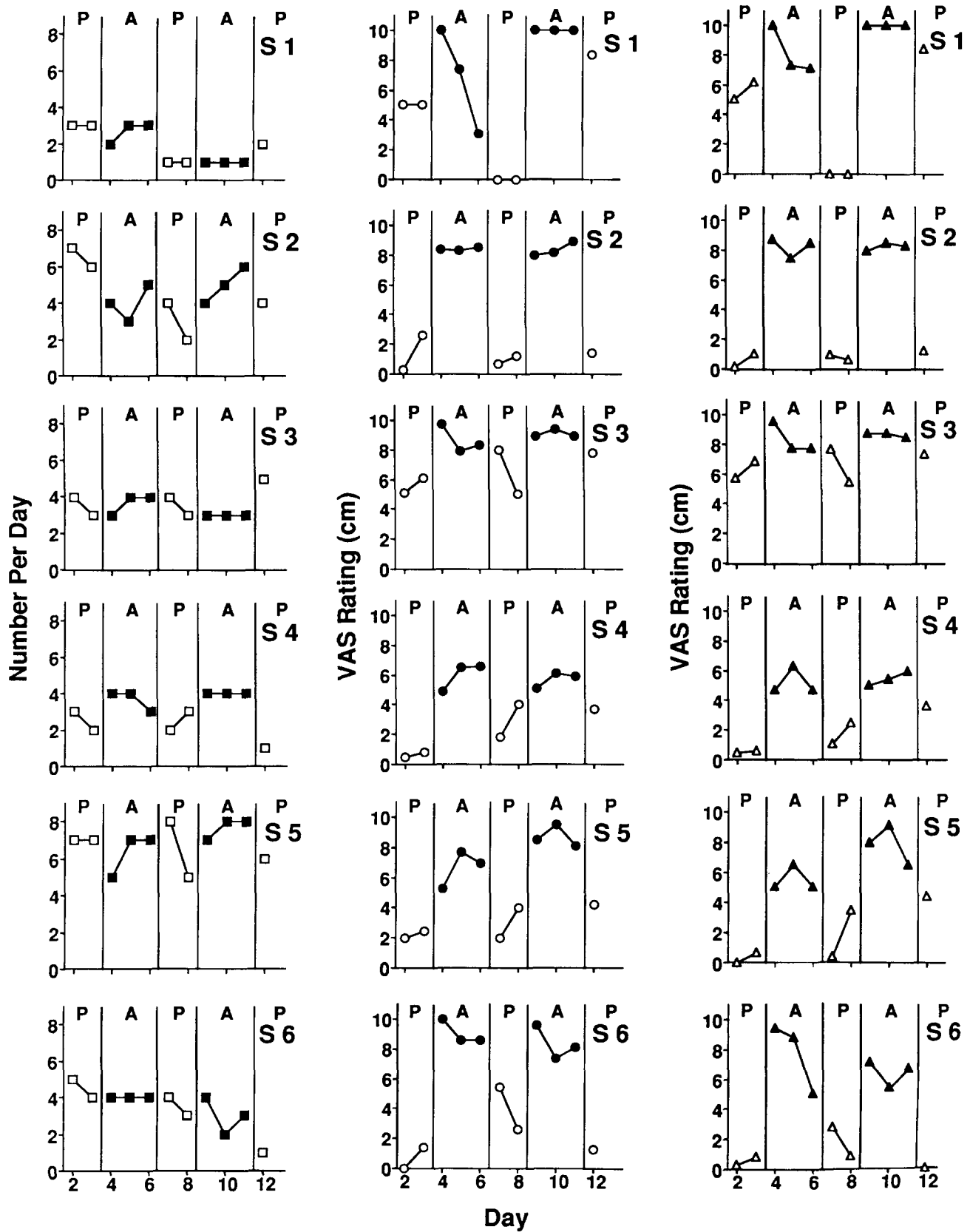


FIG. 1. Number of marijuana cigarettes smoked per day, and self report of drug "Liking" and "Potency" by each subject during placebo (P) and active (A) dose conditions.

addition, during the social-access period, subjects in group 1 were more likely to smoke under social conditions in the common area than subjects in group 2. This result suggests that the social context may have influenced marijuana smoking in group 1. In contrast, marijuana consumption was clearly related to the time of day in group 2, as higher rates of marijuana smoking occurred during the 1000 period, regardless of whether that period was one of work or social access. Previous studies have also reported time of day influences on marijuana self-administration rates (e.g., 13,14), but this is the first report of increased rates of smoking during the day (i.e., between 1000 and 1530), as opposed to the evening (i.e., between 1630 and 2200). Although these results clearly demonstrate the influence of context on marijuana self-administration, additional studies will be required to determine the relative importance of time of day and environmental context in determining marijuana smoking patterns, or the extent to which these variables influence marijuana smoking in the natural ecology.

Environmental cues associated with marijuana smoking were also examined in the present study. Social-access period cigarettes were often smoked at the beginning or end of the drug-availability interval or of a movie. In contrast, no identifiable cues were associated with marijuana smoking during the work period. In addition, only marijuana smoking by social smokers (i.e., subjects in group 1) was influenced by social context (i.e., social-access period). These results suggest that cigarette smoking in social settings was influenced by environmental cues to a greater extent than was smoking in private settings.

Daily patterns of marijuana smoking were not affected by the presence or absence of THC in the marijuana cigarettes. For subjects in both groups, daily patterns of placebo marijuana cigarette smoking were identical to daily patterns of active marijuana cigarette smoking. These results clearly indicate that variations in the daily patterns of marijuana cigarette smoking observed in this controlled residential laboratory setting were unrelated to THC content.

Previous studies have indicated that marijuana self-administration is unrelated to THC concentration (e.g., 2,16). Similarly, the results of this study, using a rate measure of self-administration, offer no evidence that THC is associated with the reinforcing effects of marijuana. The factors that

maintain rates of marijuana self-administration remain unclear, and could include some combination of marijuana smoking history, cues associated with the smoking process, such as taste and aroma of the smoke, conditions unrelated to the smoking event, such as social context, or conditions associated with the testing environments. Studies have indicated that subject choice of marijuana is influenced by THC concentration (3,14). Additional studies will be required to clarify conditions that modulate the reinforcing effects of placebo and active marijuana.

In contrast to rates of self-administration, subjective reports of "Liking," "Potency," "High," and "Drug" clearly differentiated between placebo and active marijuana cigarettes. Increased ratings were observed when active marijuana cigarettes were smoked, as has been reported in previous studies (e.g., 3,11,16). This result indicates that a pharmacologically active dose of active marijuana was used in the study. The discordant effects of active marijuana on subjective reports of drug effects and marijuana self-administration replicates earlier reports (e.g., 2,3,16), and further strengthens the case for using multiple measures, including direct measurement of drug self-administration or drug choice, in the assessment of the reinforcing effects of drugs (e.g., 4,5).

In summary, the number of marijuana cigarettes smoked was influenced by either time of day or social-access period, indicating the importance of context in determining the rate of drug self-administration. Because smoking patterns were similar for placebo and active marijuana cigarettes, no evidence for a selective reinforcing effect of THC was observed. On the other hand, subjective reports of drug "High" and "Liking" were clearly related to THC content. Although more sensitive to the THC content of marijuana cigarettes than smoking rate, subjective reports did not accurately predict the rate of marijuana self-administration.

ACKNOWLEDGEMENTS

This research was supported by Grant DA-03476 from the National Institute on Drug Abuse. The assistance of Cleve Emurian, Jerry Locklee, Lisa King, and Michelle Woodland are gratefully acknowledged. A preliminary report of these results was presented at the 1991 meeting of the International Study Group Investigating Drugs as Reinforcers, and a portion of these data were published in a festschrift in honor of Joseph V. Brady (9).

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