Pergamon

Pharmacology Biochemistry and Behavior, Vol. 49, No. 3, pp. 643-647, 1994

0091-3057/94 $6.00 + .00

0091-3057(94)00192-8

Preference for High- Versus Low-Potency Marijuana

L. D. CHAIT[1] AND K. A. BURKE

Department of Psychiatry, MC3077, The Pritzker School of Medicine, The University of Chicago, 5841 S. Maryland Ave, Chicago, IL 60637

Received 5 January 1994

CHAIT, L. D. AND K. A. BURKE. *Preference for high- versus low-potency marijuana.* PHARMACOL BIOCHEM BEHAV **49**(3) 643-647, 1994.—With many drugs of abuse, humans and other species display a preference for higher doses (or more potent dosage forms) over lower doses (or less potent dosage forms). The present study was designed to determine whether this generalization would hold for marijuana smoking by humans. Twelve regular marijuana smokers participated in two independent and identical choice trials in which, on separate sessions, they first sampled marijuana of two different potencies (0.63% and 1.95% delta-9-tetrahydrocannabinol; THC) and then, on the next session, chose which of the two, as well as how much, to smoke. During sampling sessions, the high-potency marijuana produced a greater heart rate increase and greater subjective effects than the low-potency marijuana. Subjects chose the high-potency marijuana significantly more often than the low-potency marijuana (21 out of 24 choice occasions). These results support the hypothesis that the reinforcing effects of marijuana, and possibly its abuse liability, are positively related to THC content.

Human Marijuana Potency Self-administration Subjective effects Reinforcing effects Abuse liability THC

THERE has been concern expressed in recent years regarding the increased availability of highly potent forms of marijuana, and the greater health risks that might be associated with use of such preparations (18). Self-administration studies with both laboratory animals (8,16) and humans (2,9,10,14,22) have generally found that higher doses of drugs are preferred to lower doses. As dose increases still further, preference for drugs may decrease (perhaps due to toxicity factors), producing an inverted U-shaped function relating dose to preference. It is also often assumed that more potent dosage forms of drugs have a higher liability for abuse than dosage forms of lower potency, due to a faster rate of onset and greater intensity of effects (e.g., coca leaves vs. crack cocaine) (3). Based upon the studies cited above, one might predict that marijuana users would prefer to smoke more potent rather than less potent marijuana. On the other hand, another popular drug, alcohol, is generally preferred in its less potent forms, such as beer and wine. This observation suggests that factors besides the concentration of the psychoactive constituent (e.g., sensory, social, cultural, or toxicity factors) may also be important determinants of the preferred dosage form. In the case of marijuana, it is possible that highly potent forms might be less palatable (e.g., produce harsher smoke). Alternatively, it might be easier for users to adjust their intake (to titrate to their preferred level of "high" or to avoid unwanted toxic effects) with lower-potency preparations. Although many studies have measured subjective "high" after marijuana of different potencies, few of these studies assessed subjects' preference for the marijuana (e.g., by having subjects rate how much they liked each potency), and we are aware of no studies that have directly measured preference by allowing subjects to choose among different potencies of marijuana in a self-administration paradigm. The purpose of the present study was to determine marijuana smokers' preferences for marijuana containing two different levels of the primary psychoactive constituent, delta-9-tetrahydrocannabinol (THC).

METHOD

Subjects

Volunteers provided a detailed drug and medical history, and received a psychiatric and physical examination. Only those judged healthy with no history of substance use disorder (DSM-III criteria, excluding tobacco dependence) were accepted. Twelve subjects, nine males and three females, participated. Informed consent was obtained and subjects were paid

[1] To whom requests for reprints should be addressed.

a base wage at the debriefing held at the end of the study. Subjects ranged in age from 19 to 29 years (mean = 23). All had used marijuana on at least 40 occasions (lifetime), and at the time of the study used the drug from about once a month to four times a week (mean quantity smoked was about one cigarette per week). All but two subjects reported a history of recreational use of other (noncannabinoid) drugs. Four subjects also smoked tobacco cigarettes at the time of the study. Mean alcohol consumption was five drinks per week (range 0–20).

Experimental Design and General Procedures

The study consisted of two independent choice trials. Each choice trial consisted of three sessions—two sampling sessions followed by a choice session. Subjects were given low-potency marijuana (L: 0.63% THC) on one sampling session and high-potency marijuana (H: 1.95% THC) on the other. Subjects then chose which marijuana to smoke during the choice session. The two choice trials were identical except that different color codes were used in the two trials to indicate L and H marijuana (see below). Both experimenter and subjects were blind to the potency administered on sampling sessions. The order in which the two potencies were scheduled on sampling sessions was counterbalanced across subjects and was reversed between trials.

Sampling sessions were held on Mondays and Wednesdays or Tuesdays and Thursdays, with the corresponding choice sessions held on Fridays or Saturdays, respectively. Sessions were held from 1900–2200 h. Subjects were told not to use any drugs, other than caffeine and tobacco, during the 24-h period before sessions. Subjects were studied in pairs in a room with couches, chairs, magazines, a TV, VCR, and radio. They were allowed to interact and participate in recreational activities, but not to study or work during sessions. Neither tobacco smoking nor eating was allowed during sessions until 70 min after each subject's last puff of marijuana, at which time snacks were provided. Following each session, subjects were driven home. Prior to the study, subjects attended a practice session in which they were exposed to the experimental setting and procedures.

Sampling Sessions

Subjects were informed that on Monday and Wednesday (or Tuesday and Thursday) evenings they would sample two different marijuana potencies that would be color-coded. The different marijuana potencies were coded by putting colored tape on the plastic holder used to smoke the marijuana cigarettes and on the mood questionnaires. For each session, one member of the pair received L and the other H marijuana. Subjects were told to remember the effects of the color-coded marijuana, so they could decide which of the two they wished to smoke during the choice session.

Upon arrival at the laboratory, subjects relaxed for 30 min to allow their heart rates to stabilize. Sitting radial heart rate was measured 5 min before and 5, 20, and 60 min after smoking. Expired air carbon monoxide (CO) level, an index of smoke absorption, was determined 5 min before and 5 min after smoking (6). Subjective effects were assessed with the ARCI and VAS (see below) 5 min before and 20 and 60 min after smoking. Immediately after smoking subjects completed a questionnaire (Cigarette Questionnaire; see below), rating the marijuana just smoked on several sensory characteristics. Subjects completed an additional End-of-Session questionnaire 60 min after smoking.

On sampling sessions subjects received four uniform puffs of marijuana smoke at 60-s intervals. Each puff consisted of a 5-s inhalation, followed by a 10-s breathhold and exhalation. The experimenter placed the cigarette in a hollow plastic cigarette holder and lit the cigarette mechanically before handing it to the subject. Two puffs were taken from each half-length cigarette. The experimenter controlled the smoking procedure using a stopwatch and providing verbal prompts.

Choice Sessions

At the beginning of choice sessions, each subject separately examined his/her color-coded End-of-Session questionnaires from the two prior sampling sessions held that week. The subject then informed the experimenter which color-coded marijuana he/she wished to smoke that evening (e.g., blue or yellow). The experimenter then brought in a small plastic tray with 10 half-length marijuana cigarettes, a cup of water, a lighter, and an ashtray for each subject. Subjects were instructed to smoke as little or as much as they wished during the next 60 min. Subjects were allowed to smoke each cigarette freely, with or without a holder, but were permitted to smoke only one cigarette at a time, and were required to finish one cigarette before requesting another. The number of cigarettes requested during each 10-min interval was recorded by the experimenter. Heart rate, CO level, and subjective effects were measured 10 min before and immediately after the 60-min smoking period.

Subjective Effects Questionnaires

Four questionnaires were used: a Cigarette Questionnaire, a 53-item version of the Addiction Research Center Inventory (ARCI), a series of visual analog scales (VAS), and an End-of-Session questionnaire (EOS).

The Cigarette Questionnaire consisted of four 100-mm horizontal lines that subjects used to rate the marijuana just smoked on four dimensions: taste (0 = very bad to 100 = very good), harshness (very mild to very harsh), heat (no heat to very hot), and freshness (very stale to very fresh).

The ARCI is a true–false questionnaire with empirically derived scales sensitive to the effects of a variety of classes of psychoactive drugs (11). The ARCI items yield scores for six scales: PCAG, a measure of sedation; BG and A, measures of stimulant effects; LSD, a measure of somatic and dysphoric effects; MBG, a measure of euphoria; and M, a measure of marijuana effects (5).

The VAS is a series of six 100-mm horizontal lines, labeled "stimulated," "high," "anxious," "sedated," "down," and "hungry." Subjects were instructed to place a vertical mark on each line indicating how they felt at the moment, from "not at all" to "extremely."

On the EOS, subjects were asked to rate 1) the intensity of the marijuana effect at its peak (on a five-point scale with 1 = "I felt no effect from it at all"; 2 = "I think I felt a mild effect, but I'm not sure"; 3 = "I definitely felt an effect, but it was not real strong"; 4 = "I felt a strong effect"; and 5 = "I felt a very strong effect"); 2) how high they got from smoking at the time of peak effect (on a visual analog scale of 0–100 with 0 = "not high at all" and 100 = "the highest I have ever been from marijuana"); and 3) how much they liked the marijuana effects (on a visual analog scale of 0–100 with 0 = "disliked a lot," 50 = "neutral," and 100 = "liked a lot").

Marijuana Cigarettes

Prerolled marijuana cigarettes (800–900 mg) were supplied by the National Institute on Drug Abuse (NIDA). The ciga-

rettes were assayed for cannabinoid content by GLC analysis (Chemistry and Life Sciences Division, Research Triangle Institute). Cigarettes were stored frozen in airtight containers and were humidified at room temperature for at least 24 h prior to use. Cigarettes were cut in half before use.

Data Analysis

Continuous variables were analyzed with univariate repeated-measures analysis of variance (ANOVA). Huynh-Feldt adjustments of within-factors degrees of freedom were used to protect against violations of sphericity (21). ANOVA factors included trial (first vs. second), potency (L vs. H), time (for variables measured more than once per session), and, for number of cigarettes smoked during choice sessions, interval (first through sixth 10-min interval). No main effects of trial or trial × potency interactions were obtained. Choice results were analyzed with a binomial test comparing the number of consistent H choosers to the number of consistent L choosers. Pearson correlation coefficients were used to assess relationships between selected variables. Results were considered to be statistically significant for $p \leq 0.05$ (two-tailed).

RESULTS

Sampling Sessions

Cigarette questionnaire. Significant effects of potency [$F(1, 11) > 18.0$, $p < 0.0025$ in each case] were obtained on three of the four sensory dimensions: H cigarettes were rated as being harsher (means = 67.2 vs. 43.9), hotter (59.0 vs. 41.7), and fresher (51.8 vs. 39.1) than L cigarettes. Ratings of taste quality did not differ between the two (mean = 45.5 for H vs. 41.4 for L).

Expired air carbon monoxide. Group mean baseline CO level was 4.0 ppm. The postsmoking increase (boost) in expired air CO level did not vary as a function of potency. The mean boost was 4.3 ppm during H sessions and 3.9 ppm during L sessions.

Heart rate. Group mean baseline heart rate was 70.9 bpm. Heart rate increased after smoking both L and H marijuana, but the increase was greater after H marijuana [potency × time interaction: $F(3, 33) = 10.8$, $p < 0.0005$]. Peak heart rate (5 min postsmoking) averaged 92.7 bpm after H marijuana and 84.7 bpm after L marijuana. Heart rates returned to baseline levels by 60 min after smoking.

EOS. Ratings of strength of drug effect, peak "high," and liking of drug effect were all higher after H than L marijuana [main effect of potency: $F(1, 11) > 12.0$, $p < 0.005$ in each case]. Mean ratings of strength of drug effect were 4.0 and 3.1, respectively. Mean ratings of peak "high" were 62.3 vs. 36.1, and ratings of liking were 72.8 vs. 59.3.

ARCI. No potency × time interactions were obtained on any of the ARCI scales, but a significant main effect of potency was observed for the LSD, $F(1, 11) = 7.5$, $p < 0.025$, and M scales, $F(1, 11) = 8.8$, $p < 0.025$. At the time of peak effect (20 min after smoking), mean scores on the LSD scale were 5.6 after H vs. 4.7 after L, whereas corresponding M scores were 5.8 vs. 4.4.

VAS. A significant potency × time interaction was obtained for ratings of "high," $F(2, 22) = 17.8$, $p < 0.00025$. Mean peak "high" ratings (20 min after smoking) were 59.5 and 41.8 for H and L marijuana, respectively. A main effect of potency, $F(1, 11) = 6.5$, $p < 0.05$, was obtained for ratings of "stimulated"; peak ratings after H and L averaged 43.4 and 30.8, respectively.

Choice Sessions

All 12 subjects chose H marijuana during the first choice trial, and nine chose H marijuana during the second choice trial (Table 1). Overall, H marijuana was chosen on 21 of 24 occasions (87.5%). Of the nine consistent choosers, all nine preferred H marijuana ($p = 0.004$). The total number of cigarettes smoked during choice sessions ranged from zero to eight (mean = 3.5), and did not differ between trials. One subject chose to smoke no cigarettes during both choice sessions, and another chose to smoke no cigarettes during the second trial only. In all other cases, subjects smoked at least one cigarette during choice sessions. Cigarettes were not smoked at a steady rate throughout the 60-min smoking period [main effect of interval: $F(5, 55) = 14.1$, $p < 0.0001$]—more cigarettes were smoked during the first 10-min interval (mean = 1.4) than during the subsequent intervals (means ranged from 0.3 to 0.6). Positive correlations (ranging from 0.67 to 0.87) were found between total number of cigarettes smoked and other choice session variables (EOS ratings of strength of drug effect, peak "high," liking, ARCI M scores, and CO and heart rate increase). There was no correlation between the number of cigarettes smoked and the frequency of subjects' use of marijuana outside the laboratory.

As a group, subjects smoked more marijuana during choice sessions than they received during sampling sessions. The average CO boost on choice sessions was 11.5 ppm, compared with 4.3 ppm during H sampling sessions. Consistent with this fact, subjects reported stronger effects during choice sessions: for example, mean EOS strength of drug effect and peak

TABLE 1

TYPE AND NUMBER OF CIGARETTES SMOKED BY INDIVIDUAL SUBJECTS DURING CHOICE SESSIONS

			Number of cigarettes smoked 10-min interval						
Subject	Trial	Potency	1	2	3	4	5	6	Total
1	1	H	0	0	0	0	0	0	0
	2	H	0	0	0	0	0	0	0
2	1	H	1	0	0	1	0	0	2
	2	H	0	0	0	0	0	0	0
3	1	H	2	0	1	1	1	1	6
	2	H	2	1	1	0	1	2	7
4	1	H	1	0	1	1	1	0	4
	2	H	2	0	1	1	1	1	6
5	1	H	3	1	0	0	2	1	7
	2	H	3	1	1	1	1	1	8
6	1	H	2	1	0	0	1	1	5
	2	H	2	1	0	1	0	1	5
7	1	H	1	0	1	0	0	1	3
	2	L	1	1	0	0	0	1	3
8	1	H	1	0	1	0	0	1	3
	2	L	1	0	0	0	1	0	2
9	1	H	1	0	1	0	0	0	2
	2	L	1	1	0	0	0	1	3
10	1	H	1	0	0	0	0	0	1
	2	H	1	0	0	0	0	0	1
11	1	H	2	1	1	0	0	1	5
	2	H	2	1	1	0	2	0	6
12	1	H	2	0	1	0	0	1	4
	2	H	1	1	0	0	0	0	2

"high" ratings were 4.4 and 74.8, respectively, compared with 4.0 and 62.3 on H sampling sessions.

DISCUSSION

This study demonstrated a strong preference for self-administration of the higher-potency marijuana. This preference was consistent with the data from the sampling sessions, which indicated that the high-potency marijuana produced stronger effects and that subjects liked the effects of the high-potency marijuana more than the low potency. Thus, the present findings are consistent with other evidence (cited in the introduction) that higher doses of self-administered drugs are generally preferred over lower doses. Of course, because our study was limited to comparison of only two potencies of marijuana, these results do not preclude the possibility that at a high enough level of THC preference for marijuana may decrease due to adverse (toxic) effects (7). A much wider range of marijuana THC concentrations would have to be examined to fully characterize the relationship between preference and potency. It is also possible that the nature of this relationship could vary considerably across individuals, perhaps dependent upon an individual's current or past marijuana use.

Many studies of marijuana smoking in humans have been unable to demonstrate consistent dose-related effects (12,13,15,17,19). One reason for this is that subjects may titrate their smoke intake when smoking marijuana of varying potencies, even if methods to control smoke administration are used (5,12,19). The fact that L and H marijuana both produced the same mean CO boost during sampling sessions indicates that subjects did not titrate their smoke intake in the present study. Another probable reason why other studies have not found consistent dose-related effects of marijuana is that they did not include a wide enough range of doses; there is evidence that the dose-effect function for subjective and behavioral effects of marijuana is rather flat (1,4), and many prior studies have used only two potencies of marijuana that varied over only a twofold range (such as 1.7% and 3.5% THC cigarettes). The present findings suggest that future studies should use a much wider range of doses, because even with the threefold difference in marijuana THC content used here, significant dose-related effects were not obtained on all measures, and the dose-related effects that were obtained were not that dramatic (e.g., a mean peak heart rate increase of about 23 bpm with H compared with 13 bpm with L marijuana).

It is tempting to assume that the preference observed here for the high-potency marijuana was due to greater CNS effects from its higher THC content. This conclusion must remain tentative, however, due to the fact that the H and L cigarettes also differed on several sensory dimensions. It seems unlikely, however, that these sensory differences could have been the primary determinants of the strong preference obtained for H marijuana: although subjects did rate H marijuana as being "fresher" than L marijuana, they also rated H marijuana as being "harsher" and "hotter." The two types of marijuana were not rated differently in how good they "tasted." Other studies have also found that marijuana cigarettes containing different amounts of THC varied in sensory characteristics (19). One experimental approach that could be used in future studies to eliminate these sensory factors as confounding variables would be to use a local anesthetic solution to numb subjects' upper and lower airways before smoking; this approach has been used successfully to study the role of sensory factors in tobacco cigarette smoking (20).

ACKNOWLEDGEMENTS

This research was supported by NIDA grant DA-03517. The authors thank Dr. K. G. Chua, Dr. Ed Senay, Susan Dudish, and Brenda Stalbaum Hsung for subject screening.

REFERENCES

1. Azorlosa, J. L.; Heishman, S. J.; Stitzer, M. L.; Mahaffey, J. M. Marijuana smoking: Effect of varying Δ^9-tetrahydrocannabinol content and number of puffs. J. Pharmacol. Exp. Ther. 261:114–122; 1992.
2. Bickel, W. K.; Higgins, S. T.; Stitzer, M. L. Choice of blind methadone dose increases by methadone maintenance patients. Drug Alcohol Depend. 18:165–171; 1986.
3. Busto, U.; Sellers, E. M. Pharmacokinetic determinants of drug abuse and dependence. A conceptual perspective. Clin. Pharmacokinet. 11:144–153; 1986.
4. Chait, L. D. Delta-9-tetrahydrocannabinol content and human marijuana self-administration. Psychopharmacology (Berlin) 98: 51–55; 1989.
5. Chait, L. D.; Fischman, M. W.; Schuster, C. R. "Hangover" effects the morning after marijuana smoking. Drug Alcohol Depend. 15:229–238; 1985.
6. Chait, L. D.; Griffiths, R. R. Smoking behavior and tobacco smoke intake: Response of smokers to shortened cigarettes. Clin. Pharmacol. Ther. 32:90–97; 1982.
7. Domino, E. F.; Rennick, P.; Pearl, J. H. Dose–effect relations of marijuana smoking on various physiological parameters in experienced male users. Observations on limits of self-titration of intake. Clin. Pharmacol. Ther. 15:514–520; 1974.
8. Downs, D. A.; Woods, J. H. Codeine- and cocaine-reinforced responding in rhesus monkeys: Effects of dose on response rates under a fixed-ratio schedule. J. Pharmacol. Exp. Ther. 191:179–188; 1974.
9. Fischman, M. W.; Foltin, R. W.; Nestadt, G.; Pearlson, G. D. Effects of desipramine maintenance on cocaine self-administration by humans. J. Pharmacol. Exp. Ther. 253:760–770; 1990.
10. Griffiths, R. R.; Bigelow, G. E.; Liebson, I. Human sedative self-administration: Effects of interingestion interval and dose. J. Pharmacol. Exp. Ther. 197:488–494; 1976.
11. Haertzen, C. A. An overview of Addiction Research Center Inventory scales (ARCI): An appendix and manual of scales. Washington: U.S. Government Printing Office; 1974.
12. Heishman, S. J.; Stitzer, M. L.; Bigelow, G. E. Alcohol and marijuana: Comparative dose effect profiles in humans. Pharmacol. Biochem. Behav. 31:649–655; 1988.
13. Heishman, S. J.; Stitzer, M. L.; Yingling, J. E. Effects of tetrahydrocannabinol content on marijuana smoking behavior, subjective reports, and performance. Pharmacol. Biochem. Behav. 34: 173–179; 1989.
14. Henningfield, J. E.; Miyasato, K.; Jasinski, D. R. Abuse liability and pharmacodynamic characteristics of intravenous and inhaled nicotine. J. Pharmacol. Exp. Ther. 234:1–12; 1985.
15. Higgins, S. T.; Stitzer, M. L. Acute marijuana effects on social conversation. Psychopharmacology (Berlin) 89:234–238; 1986.
16. Johanson, C. E.; Schuster, C. R. A choice procedure for drug reinforcers: Cocaine and methylphenidate in the rhesus monkey. J. Pharmacol. Exp. Ther. 193:676–688; 1975.
17. Kelly, T. H.; Foltin, R. W.; Fischman, M. W. Effects of smoked marijuana on heart rate, drug ratings and task performance by humans. Behav. Pharmacol. 4:167–178; 1993.
18. Mikuriya, T. H.; Aldrich, M. R. Cannabis 1988, old drug, new dangers, the potency question. J. Psychoactive Drugs 20:47–55; 1988.

19. Nemeth-Coslett, R.; Henningfield, J. E.; O'Keeffe, M. K.; Griffiths, R. R. Effects of marijuana smoking on subjective ratings and tobacco smoking. Pharmacol. Biochem. Behav. 25:659–665; 1986.
20. Rose, J. E.; Zinser, M. C.; Tashkin, D. P.; Newcomb, R.; Ertle, A. Subjective response to cigarette smoking following airway anesthetization. Addict. Behav. 9:211–215; 1984.
21. Schutz, R. W.; Gessaroli, M. E. The analysis of repeated measures designs involving multiple dependent variables. Res. Q. Exerc. Sport 58:132–149; 1987.
22. Stitzer, M. L.; McCaul, M. E.; Bigelow, G. E.; Liebson, I. Oral methadone self-administration: Effects of dose and alternative reinforcers. Clin. Pharmacol. Ther. 34:29–35; 1983.