Effects of Marijuana Smoking on Subjective Ratings and Tobacco Smoking¹

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NEMETH-COSLETT, R., J. E. HENNINGFIELD, M. K. O'KEEFFE AND R. R. GRIFFITHS. *Effects of marijuana smoking on subjective ratings and tobacco smoking.* PHARMACOL BIOCHEM BEHAV 25(3) 659–665, 1986.—Multiple measures of tobacco cigarette smoking and subjective and physiological effect were collected during 90 minute test sessions in volunteer cigarette smokers who also had histories of recreational marijuana use. Before sessions, subjects smoked one marijuana cigarette (placebo or 1.29%, 2.84%, 4.00%) using a standardized puffing procedure. Each dose and placebo was given four times to each subject in a randomized block sequence. Marijuana smoking produced dose-related increases in heart rate, ratings of dose strength and drug liking. However, marijuana produced no significant alterations in tobacco cigarette smoking: puff duration within each marijuana cigarette varied in a fashion similar to that observed in previous studies of tobacco cigarette smoking: puff duration progressively decreased as the cigarette was smoked. This effect is probably due to progressive decreases in resistance to draw as the cigarette is smoked. Expired air carbon monoxide (CO) levels following marijuana smoking were inversely related to marijuana dose, suggesting the occurrence of some compensatory changes in marijuana smoking in response to dose manipulations. It is concluded that, although marijuana produces dose-related effects on physiological and subjective effects and on marijuana smoking behavior, marijuana differs from a variety of other psychoactive drugs previously studied in this paradigm in that no reliable changes in tobacco smoking were produced.

Marijuana	Smoking	Tobacco	Cigarettes	Nicotine	Self-administration	Humans
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LABORATORY studies have shown that a variety of centrally-active drugs alter patterns of tobacco cigarette smoking. Increases in cigarette smoking have been induced with *d*-amphetamine [14,34] ethanol in alcoholics [7,12] and heroin, methadone, and buprenorphine in persons with histories of opioid use [5, 25, 28]. Pentobarbital also produced increases in cigarette smoking, but only in smokers who had histories of sedative abuse [11]. Caffeine either decreased [22] or produced no significant change [4] in smoking rates.

Two studies have examined the influence of marijuana on tobacco cigarette smoking [26,27]. In both studies, which were conducted on a residential research unit, subjects were permitted to self-administer marijuana during different phases. During the marijuana phase in both studies, there was a temporal correlation between tobacco and marijuana cigarette smoking; however, there was no significant change in the number of tobacco cigarettes smoked on days on which marijuana was available for self-administration when compared to days on which no drug was available. It was concluded that tobacco smoking was not systematically affected by marijuana cigarette smoking [26,27]. However, the generality of the findings were limited since marijuana administration was not controlled and a placebo condition was not employed. Further, since the number and patterns of tobacco cigarettes smoked per day were the only measures of tobacco intake, these studies left open the possibility that subjects may have altered their tobacco intake by other mechanisms (e.g., number of puffs).

The purpose of the present study was to examine the effects of marijuana on tobacco cigarette smoking behavior by assessing a range of marijuana doses on multiple measures of cigarette smoking, subjective response and physiologic change. The study was conducted using an experimental procedure that had been shown to be useful in assessing the effects of a vareity of drugs (d-amphetamine, ethanol, pentobarbital, caffeine, methadone, naloxone, and mecamylamine) on cigarette smoking and subjective responses [4, 5, 11, 12, 14, 32, 33]. Using the same testing apparatus and similar procedures, a range of marijuana doses was given to volunteers with histories of regular tobacco cigarette smoking and recreational marijuana use. During test sessions, a variety of measures of cigarette smoking behavior were collected. Sitting heart rate and blood pressure were also collected to measure the cardiovascular effects of marijuana. In addition, before and after both marijuana and tobacco smoking, samples of carbon monoxide in expired air

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were analyzed to verify exposure levels to marijuana and tobacco smoke. Finally, subject rated measures of dose strength, drug liking and drug effect were obtained after both marijuana and tobacco cigarette smoking.

METHOD

Subjects

Subjects were eight normal, healthy adults (4 women and 4 men) with an average age of 28 years (range: 18-40). Subjects reported smoking an average of 30 cigarettes per day (range: 20-40) for an average of 13 years (range: 3-20). Subjects smoked cigarette brands which delivered an average of 1.1 mg nicotine per cigarette (range: 0.8-1.3). Detailed subject characteristics are presented in Table 1. Measurement of carbon monoxide (CO) in samples of expired air indicated that all subjects regularly inhaled tobacco smoke (mean CO levels immediately after reporting to the laboratory on experimental days ranged from 16.4 to 28.2 ppm across subjects.) All subjects reported recreational marijuana use, with current use ranging from 5 to 20 times per month. Before beginning the study, subjects received a physical examination and provided informed consent for their participation in accordance with the Department of Health and Human Services guidelines for the protection of human subjects. Subjects were paid for their participation in the study at a rate of approximately \$15/session.

Subjects were instructed not to smoke marijuana, recreationally, for the duration of the study. Compliance was strengthened by the routine collection of fresh urine samples before the start of each test session, and the instructions that earnings would be withheld from the subject if his/her THC level exceed an established limit. Due to individual differences and the limitations of the urine assay results, however, it was not possible to determine to what extent the subjects had restricted their marijuana use, recreationally, over the course of the study.

General Procedure

Subjects were told that the purpose of the study was to investigate how marijuana and cigarettes affect physiology, mood, and behavior; they were not told what experimental outcomes might be expected, or what dependent variables were of particular interest. Each subject was tested individually at the same time on either Mondays, Wednesdays and Fridays or on Tuesdays and Thursdays. Daily procedures involved a period of controlled marijuana smoking followed by a 90 minute ad lib tobacco smoking session. Although the design did not permit control of tobacco smoking prior to experimental sessions, CO levels immediately after reporting to the laboratory showed little variability within subject (Table 1), suggesting that individual subjects, on a day to day basis, tended to report to the laboratory with reasonably similar histories of immediately preceding smoke exposure.

Controlled Marijuana Smoking Procedures

On experimental days subjects reported to the laboratory and were escorted to the test room. A trained research technician measured the subject's sitting heart rate and blood pressure. Also, an expired air CO level was obtained using a standardized procedure [17]. The technician then seated herself behind the subject, placed a marijuana cigarette into a

plastic cigarette holder and lit the cigarette using a 50 cc bulb aspirator. The plastic holder was mounted in a funnel-like apparatus which allowed the subject to hold the marijuana apparatus without seeing the cigarette. The plastic cigarette holder was connected via a 2-m length of flexible tubing (2 mm o.d.) to a pressure sensitive switch (Micro Pneumatic Logic, Inc., Ft. Lauderdale, FL) which operated a relay following a decrease in pressure (3.3 mm Hg) induced by puffing on a cigarette. This system permitted the measurement of the duration of each puff from the marijuana cigarette. A stop watch was started and every 40 seconds the funnel was handed to the subject. The subject took one puff and returned the funnel to the research technician. Subjects were instructed to hold the smoke in their lungs until they heard the exhale command, which was given 10 seconds after inhalation. This procedure was repeated until eight puffs from a single marijuana cigarette had been taken (approximately 7 min). On the infrequent occasion that a subject did not hold the smoke in their lungs due to coughing or premature exhalation, an additional puff was given to ensure that the above procedure was followed for eight full puffs.

Two minutes after marijuana administration expired air CO levels were measured. After marijuana smoking subjects also completed a questionnaire in which visual analog scales (100 mm lines) were used to rate the subjective characteristics of the marijuana cigarettes. Subjects rated each of the following: strength (very weak/very strong); heat (no heat/very hot); harshness (not harsh/very harsh); draw (easy/hard); taste (very bad/very good); satisfaction (very unsatisfying/very satisfying). At this time (approximately 5 minutes after marijuana dose they received that day on a four point scale (1="I feel no effects from the drug at all"; 2="I think I feel a mild drug effect, but I can definitely feel a drug effect").

Fifteen minutes following marijuana administration (immediately before 90 min tobacco smoking sessions), sitting heart rate and blood pressure were measured. Also, at this time, and immediately after tobacco smoking sessions (105 min post-marijuana), subjects completed a Drug Liking scale, a short form of the Addiction Research Center Inventory (ARCI) and the Profile of Mood States (POMS). The Drug Liking scale consisted of a 5-point scale on which subjects reported their liking as: 1="not at all": 2="slight": 3="moderate"; 4="a lot"; 5="an awful lot." The ARCI is a true-false questionnaire with empirically derived scales. Five scales with a total of 49 items were used including the MBG (morphine-benzedrine group or "Euphoria") scale (ARCI No. 464), the A (amphetamine) scale (ARCI No. 446), the BG (benzedrine group) scale (ARCI No. 465), PCAG pentobarbital-chlorpromazine-alcohol group or "Sedative") scale (ARCI No. 452) and the LSD (lysergic acid diethvlamide or "Dysphoria") scale (ARCI No. 454) [9]. The POMS, a mood adjective rating check list, contains empirically derived scales that are sensitive to changes in mood and affect [24]. A 65-item version of the POMS was used and the results from seven scales were analyzed. These were Vigor. Fatigue, Tension, Depression, Anxiety, Confusion, and Friendly.

Ad Lib Tobacco Smoking Procedures

Approximately 30 min after reporting to the laboratory and 15 min following the completion of marijuana smoking.

MARIJUANA AND TOBACCO SMOKING

the 90 minute tobacco sessions began. Expired air CO levels were obtained immediately before and within 10 minutes following sessions. The test room and apparatus for assessing ad lib cigarette smoking have been described in detail [3,13]. Briefly, the test rooms were equipped with two comfortable armchairs; one for the subject and one for the research technician. Additionally, a television set and tobacco smoking console were located in the test rooms as well as a oneway observation window. The console contained a session light, a depository for tobacco cigarette butts, and a pressure transducer. During experimental sessions, subjects smoked all tobacco cigarettes through a plastic cigarette holder. The holder was connected via a 2-m length of flexible tubing to a pressure sensitive switch as previously described in the marijuana smoking procedure section. When a subject finished smoking a tobacco cigarette, he or she extinguished it in an ashtray and then immediately placed it in the depository, which resulted in the activation of a switch located in the console. The pressure transducer and other components of the console were interfaced to a computer that recorded and controlled experimental events.

The ad lib tobacco smoking sessions were 90 minutes in duration unless a tobacco cigarette was being smoked at the end of this time, in which case the session was automatically extended (without informing the subject) to include data from the last cigarette. While in the room, subjects were allowed to watch television or read a newspaper. They were not allowed to eat, drink, write or sleep. Subjects were instructed to smoke tobacco cigarettes as much or as little as desired during the session. Before each session, subjects were given one fresh pack of their usual brand of cigarettes and they were allowed to keep the tobacco cigarettes that they did not smoke during the session. Immediately following sessions, subjects completed a questionnaire which involved rating the characteristics of tobacco smoking. This questionnaire was identical to the marijuana smoking questionnaire described above.

Marijuana Cigarettes

The marijuana cigarettes were supplied by the National Institute on Drug Abuse. Each marijuana cigarette was an average of 80 mm in length and approximately 1 g in weight. Active delta 9-tetrahydrocanabinol (THC) concentration, expressed as percent weight of each marijuana cigarette was 1.29%, 2.84% or 4.00% as assayed by the National Institute of Mental Health (NIMH). Placebo marijuana cigarettes contained no THC. Cigarettes were machine rolled and physically identical except for the 4.0% THC cigarettes which were hand rolled and slightly smaller than the other cigarettes. All drug doses were coded in advance to ensure that the study was conducted under double-blind conditions. The research technician was not aware of the THC levels of any of the cigarettes. Doses were given according to a randomized block sequence in which each dose was given on four occasions to each subject.

Data Analyses

For each subject, data were averaged across sessions under each marijuana dose condition. These means were then used in the statistical analysis of the data according to a one-way analysis of variance for repeated measures. Heart rate was expressed as a change score by subtracting premarijuana values from the 15-minute post marijuana values.

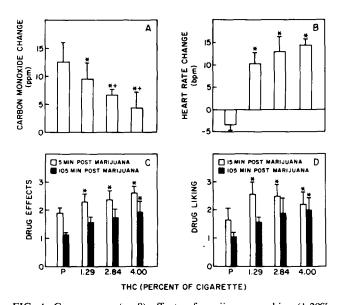


FIG. 1. Group mean (n=8) effects of marijuana smoking (1.29%, 2.84% or 4.0% THC) or placebo smoking (P) on expired air carbon monoxide, heart rate and subject ratings of drug effect and drug liking. Panel A shows carbon monoxide (ppm) change scores (pre-marijuana smoking CO values subtracted from post-marijuana values). Panel B shows heart rate (beats per minute) change scores (pre-marijuana smoking values). Panel C shows the drug effect ratings by subjects 5-minutes post-marijuana smoking (open bars) and again after the tobacco smoking session (solid bars). Panel D shows the drug liking ratings by subjects 15-minutes post-marijuana smoking (open bars), and again after the tobacco smoking session (solid bars). In all panels, asterisks indicate that the value of the point was significantly different from placebo; plus symbols indicate that the point was significantly different from the 1.29% dose.

Measures of expired air CO were also expressed as change scores for both marijuana and tobacco cigarette smoking. Specifically the immediate pre-marijuana smoking CO values were subtracted from the two-minute post-marijuana smoking CO values, and immediate pre-tobacco cigarette smoking values were subtracted from the post-tobacco cigarette CO values. For all statistical tests, effects were considered to be significant if p < 0.05. Post-hoc comparisons between placebo and drug and between different drug doses were accomplished using Newman-Keuls tests [21].

RESULTS

Carbon Monoxide Changes After Marijuana Smoking

Expired air CO levels were elevated when measured two minutes following the smoking of a marijuana or placebo cigarette (mean 8 ppm across all conditions). The magnitude of the CO boost was inversely related to the dose of the marijuana cigarette (Fig. 1, Panel A). As shown in the figure, whereas CO boost was 12.5 ppm following placebo cigarette smoking, CO boost was only 4.0 ppm at the 4.0% marijuana dose. These differences were statistically significant, F(3,21)=13.38, p<0.001.

Marijuana Effects on Heartrate and Blood Pressure

Marijuana produced significant dose-related increases in

Subject	Age (Years)	Years Smoking	Cigarette Brand*	Self-Reported Cigarettes Per Day	Weight (kg)	Baseline CO† (mean ± S.E.)	
01	25 11		Newport (17, 1.2)	30	66	19.2 ± 1.0	
02	40	20	Raleigh Lights 100 (10, 0.8)	40	48	23.6 ± 1.2	
03	24	13	Kool (17, 1.1)	30	74	16.4 ± 0.9	
04	22	13	Marlboro Box (17, 1.1)	20	47	18.0 ± 1.0	
05	23	10	Player Menthol 100 (17, 1.1)	30	60	28.2 ± 1.1	
06	36	18	Kool Mild (11, 0.8)	30	65	17.4 ± 0.9	
07	35	20	Camel (20, 1.3)	30	66	25.5 ± 1.3	
08	18	3	Marlboro Box (17, 1.1)	30	62	19.7 ± 1.1	

TABLE 1SUBJECT CHARACTERISTICS

*Tar (mg) and nicotine (mg) respectively, are presented in parentheses. Estimates are based on a report of the Federal Trade Commission, March 1983.

†Expired air carbon monoxide levels were determined immediately after subjects reported to the laboratory on each experimental day.

	Placebo		1.29%		2.84%		4.00%		F
Number of Puffs	27.5	[4.4]	32.9	[7.8]	29.5	[7.3]	31.1	[7.7]	1.51
Number of Cigarettes	3.3	[0.3]	3.8	[0.4]	3.3	[0.4]	3.4	[0.4]	2.36
Time Alight (sec)	362.0	[28.6]	380.0	[36.7]	362.0	[29.4]	346.0	[20.3]	1.21
Puff Duration (Cigarette)	11.3	[1.4]	11.1	[1.7]	10.9	[1.8]	11.8	[1.4]	0.83
Puff Duration (Puff)	1.4	[0.2]	1.4	[0.2]	1.3	[0.2]	1.4	[0.2]	0.91
Intercigarette Interval (sec)	1437.0	[212]	1367.0	[232]	1440.0	[191]	1616.0	[291]	1.08
Interpuff Interval (sec)	47.0	[6.4]	48.1	[7.4]	45.7	[5.3]	42.6	[4.9]	1.03
Carbon Monoxide (ppm)	5.4	[2.8]	7.0	[2.6]	6.2	[2.8]	8.1	[2.0]	1.23

 TABLE 2

 EFFECTS OF MARIJUANA ON TOBACCO SMOKING*

*Data are means with 1 S.E.M. in brackets. Carbon monoxide data are post-session minus pre-session values.

heart rate, F(3,21)=10.01, p<0.001 (Fig. 1, Panel B). At the 4.0% dose, heart rate averaged 14.7 beats per minute above placebo levels. No significant dose-related changes or trends in blood pressure occurred.

Subject Rating of Marijuana

Subject ratings of magnitude of the marijuana drug effect are shown in Fig. 1, Panel C. At 5-minutes following marijuana administration, ratings of drug effect tended to be dose related; all doses produced significant effects when compared to placebo, F(3,21)=8.35, p<0.001. At 105minutes post marijuana (immediately after the tobacco smoking session) the drug effect ratings were lower and only the 4.0% THC dose was significantly different from placebo, F(3,21)=3.81, p<0.05.

Ratings on the 5-point Drug Liking scale at 15-minutes and 105-minutes following marijuana smoking are shown in Fig. 1, Panel D. Although there were no significant differences among doses at 15-minutes, Drug Liking scores were significantly elevated for all doses of marijuana when compared to placebo, F(3,21)=7.07, p<0.001. As with drug effect ratings, the magnitude of these effects were consistently lower at the 105-minute time point.

Scores on two scales on the POMS were inversely related to marijuana dose: Friendliness, F(3,21)=4.45, p<0.01, and Vigor, F(3,21)=5.63, p<0.01. Scores on the remaining POMS scales and ARCI scores were not significant.

Subject-rated characteristics of marijuana cigarettes showed some significant dose effects. Both the placebo and low dose were rated as significantly "hotter" than either the middle or the high marijuana doses, F(3,21)=6.06, p<0.01; the middle and high marijuana doses were not significantly different from each other on this measure. The high dose marijuana cigarettes (4.0% THC) were rated as harder to draw than were the other doses or placebo, F(3,21)=8.33, p<0.01. Ratings of strength, taste, harshness and satisfaction did not vary as a function of marijuana dose or placebo.

Marijuana Smoking Topography

Several parameters of the smoking of marijuana cigarettes

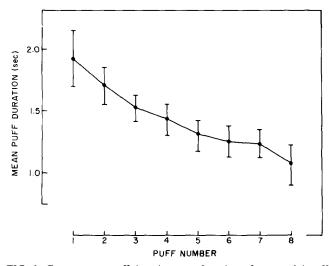


FIG. 2. Group mean puff duration as a function of sequential puff number collapsed across marijuana doses and placebo. Data points represent means and brackets show 1 S.E.M. for mean data from the eight subjects (n=8).

were controlled by the experimental procedure which specified number of puffs, interpuff interval, total time alight, etc. However, whereas subjects were instructed to take eight equal sized puffs, no explicit effort was made to control puff duration. Mean puff durations of the eight subjects during marijuana smoking are presented in Fig. 2. As shown in this figure, puff durations decreased with successive puffs on the marijuana cigarette. These decreases were significant across all doses and placebo, F(7,63)=21.54, p<0.001.

Marijuana Effects on Tobacco Smoking

Marijuana administration did not affect tobacco cigarette smoking consistently across subjects (as shown in Table 2), or significantly within any subject as determined by withinsubject analysis of variance. Carbon monoxide levels were reliably elevated following tobacco smoking sessions (CO boosts after tobacco smoking sessions averaged 6.4 ppm), but these boosts did not systematically vary as a function of marijuana dose. Marijuana did not reliably alter subject ratings of tobacco cigarette smoking (strength, taste, heat, harshness, draw or satisfaction).

DISCUSSION

Marijuana administration produced dose-related effects on several physiological and subjective measures. However, marijuana did not systematically alter tobacco cigarette smoking or subjective responses to tobacco cigarettes. As noted in the introduction, several other drugs systematically altered patterns of cigarette smoking under experimental conditions similar to those used in the present study (i.e., *d*-amphetamine, ethanol, methadone, mecamylamine). In two instances, drug-induced changes in cigarette smoking appeared to be related to the subject's previous experience with the drug. For instance, pentobarbital increased tobacco smoking only in subjects with histories of sedative abuse [10] and the facilitation of smoking by ethanol appeared only in subjects with histories of moderate to heavy alcohol drinking [7,12]. Other drugs produced weak or inconsistent effects on tobacco smoking; e.g., caffeine, [4,22] and naloxone [20,33] Marijuana seems to fall in this latter category, at least with the population of moderate marijuana smokers used in this study. These results are consistent with those of Mello et al. [26,27] who showed that the number of tobacco cigarettes smoked was not systematically affected by marijuana in male and female subjects with histories of moderate and heavy marijuana use. The present study significantly extends the Mello et al. findings by including a placebo-controlled, multi-dose design in which physiological and biochemical measures of marijuana smoking (i.e., heart rate and carbon monoxide) confirm that active doses of marijuana were administered, while behavioral and biochemical measures of tobacco smoking (i.e., puffing and carbon monoxide) suggest that previously unmeasured mechanisms by which tobacco smoke exposure could vary (e.g., puff and inhalation topographies) were probably not affected by marijuana.

Unlike previous studies using this same methodology to investigate the effects of drugs on cigarette smoking [4, 5, 11, 12, 14, 32, 33], tobacco smoking deprivation was not explicitly controlled in the present study by preloading subjects with tobacco cigarettes a fixed period of time before the tobacco smoking session. Instead, the procedures in the present study specified a minimum tobacco deprivation period of approximately 30 minutes (the time from first reporting to the laboratory to the beginning of the tobacco smoking session). It seems unlikely that the absence of a specific tobacco preloading procedure affected the results. Carbon monoxide levels at the time that subjects reported to the laboratory showed little variability within subject (Table 1). This suggests that individual subjects, on a day to day basis, tended to report to the laboratory with reasonably similar histories of immediately preceding tobacco smoke exposure. Also, the results of the present study were consistent with those of Mello et al. [26,27] who used a different methodology in which tobacco deprivation was irrelevant.

In the present study, the magnitude of the marijuanainduced CO boosts were inversely related to dose. This result is noteworthy because it occurred despite experimental efforts to control biological exposure to marijuana smoke by controlling number of puffs and inhalation duration. Although the finding suggests that some compensatory changes in marijuana smoking may have occurred in response to manipulations of dose (i.e., dose titration), the possibility that this finding may reflect inherent differences in the CO delivery of the different marijuana dose cigarettes cannot be excluded. If dose-related compensatory smoking did occur, it is consistent with previous studies of ad lib marijuana smoking [1,2] and tobacco smoking [8, 10, 15] and suggests that regulation of drug intake in response to dose variation may represent a common feature of human drug selfadministration via smoking.

The finding that puff duration progressively decreased across successive puffs on the marijuana cigarette extends analogous observations made previously with tobacco cigarettes. In a series of tobacco smoking experiments undertaken to investigate this phenomenon, it was shown that puff duration was not appreciably controlled by visual stimulus control, satiation, distance from the burning ember to the smoker's mouth, nicotine delivery, particulate build-up during smoking, subjective acceptability of cigarette smoke, smoke temperature, and filtration of the smoke stream [3, 29–31]. In the present study, the progressive decreases in puff duration across the marijuana cigarettes were not under visual stimulus control since the decrease occurred under conditions in which subjects smoked cigarettes they could not see. Given the results of the tobacco cigarette smoking experiments, it is probable that the decreases in puff duration in the present study were due to decreases in resistance to draw that occurred as the marijuana cigarette rod became progressively shorter.

Increases in measures of drug liking and euphoria are characteristics of drugs known to be abused. Relative to placebo, all doses of marijuana in the present study produced significant increases on the subject-rated drug liking scale. These data are consistent with previous research [16, 18, 19, 23]. The absence of elevation of scores on the MBG or Euphoria scale of the ARCI in the present study is consistent with the results of another study in which subjects without histories of drug dependence, other than their tobacco and marijuana cigarette smoking, were tested [16].

As discussed by Mello and Mendelson [26], the finding that marijuana did not influence the rate of tobacco cigarette smoking has the implication that there may be an increased health risk associated with concurrent tobacco and marijuana smoking. Impaired pulmonary function is a welldocumented adverse consequence of both tobacco smoking and marijuana smoking [6, 35–37]. The fact that marijuana does not decrease tobacco smoking suggests that tobacco smoking marijuana users may be at even greater risk for pulmonary damage than tobacco smokers or marijuana smokers alone.

The present study showed that a standardized procedure could be used to administer marijuana smoke to human volunteers and thereby produce dose-related changes in subjective and physiologic responses. These dose-related effects occurred despite the possibility that amount of smoke inhaled per marijuana cigarette may have varied so as to partially compensate for changes in THC concentration of the marijuana smoke. These findings are consistent with those obtained in other laboratory studies of the effects of marijuana on human volunteers as discussed above. The findings show that the effects of marijuana differ from the effects of a variety of other psychoactive drugs on tobacco cigarette smoking (cf. introduction) in that subjectively and physiologically active doses, administered via smoking, did not alter rate or pattern of tobacco cigarette smoking. Since delivery of both marijuana and tobacco via smoke inhalation may have resulted in unknown route-specific interactions, future research should extend the present findings by systematically replicating the study under conditions in which marijuana or THC is administered via a non-inhalation route.

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