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Effects of acute marijuana smoking on pulse rate and mood states in women

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Abstract. The effects of marijuana cigarette (1.8% THC) smoking on pulse rate and mood were studied under double-blind placebo-controlled conditions in 28 adult female volunteers during the follicular, luteal, and ovulatory phases of the menstrual cycle. Statistically significant increases in pulse rate, subjective levels of intoxication, and the POMS confusion factor occurred after marijuana smoking. However, no statistically significant differences for any measure were observed following marijuana smoking as a function of menstrual cycle phase. Subjects with a past history of intermittent marijuana use (five or less times weekly) had significantly higher pulse rates, subjective levels of intoxication, and POMS confusion factor scores than did subjects with a past history of regular (six or more times weekly) marijuana use. Persistence of marijuana-induced changes in pulse rate, intoxication, and confusion were also of longer duration for subjects with a past history of intermittent marijuana smoking. The influence of past history of marijuana use on marijuana-induced alterations in pulse rate, intoxication, and mood for females appears to be similar to males. These similarities are not attenuated as a function of the menstrual-cycle phase of females.

Key words: Marijuana – Women – Acute effects – Menstrual-cycle phases – Smoking history – Mood – Intoxication – Heart rate

Although increments in the rate of lifetime prevalence of marijuana smoking appear to have stabilized (Miller et al. 1983), there has been an increased use of marijuana among women (Abelson et al. 1977; Smart et al. 1979; Smart 1983). A household survey conducted during 1982 (Miller et al. 1983) revealed that 60% of women between the ages of 18–25 years had used marijuana at least once, 33% used marijuana daily during the year prior to the survey, 19% used marijuana during the previous month, and 15% had at some time used marijuana daily for at least 1 month. Comparable findings for males were 68%, 58%, 36%, and 27%, respectively.

While there are no specific reasons for the popularity of marijuana use among women (Prather and Fidell 1978), the general appeal of marijuana use has been described as self-inducement of altered mood states, usually described as being 'stoned' or 'high'. Surprisingly there has been no consistent laboratory documentation of purported inducement of euphoric mood states following marijuana smoking.

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Most previous studies of marijuana effects on mood have been carried out with male subjects. One report (Milstein et al. 1974) provided data on increased postsmoking fear and happiness in groups of female naive and experienced marijuana users: Measures assessed anger, arousal, depression, fear, and happiness. However, no pulse-rate data were provided. The major goal of this study was to determine the acute effects of marijuana smoking on pulse rate, subjective levels of intoxication, and mood states in healthy women. The studies were designed to control for expectancy factors by utilizing double-blind smoking procedures of marijuana and marijuana-placebo cigarettes. Studies were also structured to determine if past history of marijuana use or menstrual-cycle phase of female subjects contributed to acute effects of marijuana smoking on mood.

Materials and methods

Research findings reported in this study were obtained within the context of an extensive multidisciplinary investigation of behavioral and biological concomitants of marijuana use by women. Subjects were 28 adult female volunteers who were 21–36 years of age (mean 26.07 ± 4.35 SD years) and recruited via newspaper advertisements. All subjects were selected on the basis of a complete physical and mental status examination to rule out current pregnancy, past or current history of drug or alcohol abuse, physical or mental disorders, or recent history of amenorrhea or menstrual-function disturbance. Subjects were fully informed of the nature of this study, provided informed consent, and were paid for their participation.

This study was conducted in the clinical research ward at the Alcohol and Drug Abuse Research Center at McLean Hospital. The live-in facility consisted of six individual patient bedrooms, a nursing station, examination and testing rooms, and a comfortably furnished dayroom area. Subjects had access to television, high-fidelity equipment, and hospital recreational facilities. Physicians and ward assistants were present 24 h per day.

Subjects were admitted to the live-in facility for four consecutive days. They were instructed to refrain from using marijuana or other drugs on the night prior to admission. On admission day, subjects received a complete physical examination, laboratory studies, and interviews to ascertain mental status, marijuana-use patterns, and menstrual history during the previous menstrual cycle.

Acute studies were conducted on days 2 and 4 following admission to the research ward. Marijuana or placebo was administered on a double-blind basis; half of the subjects

Table 1. Background characteristics and previous drug-taking experience of moderate and regular marijuana smokers

	Intermittent smokers ($N = 10$)	Regular smokers ($N = 9$)	
	Mean ± SD	Mean ± SD	t
Age (years)	25.4 ± 4.5	25.2 ± 3.83	0.09
Years formal education	14.9 ± 1.6	14.4 ± 1.5	0.64
Total years marijuana use	9.9 ± 2.5	8.8 ± 3.7	0.79
Years regular marijuana use	7.1 ± 3.4	7.1 ± 3.4	0.06
Marijuana use (mean daily cigarettes/cycle)	0.4 ± 0.2	1.8 ± 1.0	4.43*
Alcohol use (times/month)	6.6 ± 3.0	5.3 ± 3.8	0.81
Cocaine (lifetime use)	9.2 ± 12.5	16.3 ± 17.9	1.02
Tranquilizers (lifetime use)	2.8 ± 3.2	5.4 ± 13.1	0.62
Hallucinogens (lifetime use)	3.5 ± 2.7	6.3 ± 6.7	1.22
Amphetamines (lifetime use)	10.7 ± 13.6	12.9 ± 16.7	0.31

* $P < 0.001$

received placebo on day 2 and the other half on day 4 to control for possible sequence effects.

Subjects were studied under controlled conditions designed to examine the effects of an acute dose of marijuana (or placebo) on mood and neuroendocrine hormones. Hormonal data will be reported elsewhere. Acute studies coincided with a different phase of the menstrual cycle for each of three groups of women. Menstrual-cycle status of each subject was verified by determination of LH and progesterone levels in blood. One group (ten subjects) was studied during the follicular phase and a second group (nine subjects) was studied during the luteal phase. These subjects served as their own controls for both marijuana and placebo trials. A third group (five subjects) was studied during the ovulatory phase of the menstrual cycle: Because of the very short duration of this menstrual-cycle phase these subjects could not serve as their own controls in the 4-day studies, therefore, a separate control group (four subjects) was utilized for this phase of the study.

All subjects tended to be lower-middle class or middle-class single women with some college education. Experience with drugs other than marijuana and alcohol was infrequent. The subjects did not differ significantly on any background variable except prior marijuana consumption. On the basis of interviews and questionnaire data, luteal and follicular subjects were also classified as either regular or intermittent smokers of marijuana ($t = 4.427$, $P < 0.001$). Regular users were persons having at least a 2-year history of marijuana use who smoked six or more times per week during the three menstrual cycles prior to the study. Intermittent users were persons who smoked marijuana more than twice per cycle, but less than five times per week during the three menstrual cycles prior to the study. Information pertinent to background characteristics and previous drug use is summarized in Table 1.

Marijuana was administered in the form of standardized marijuana cigarettes provided by NIDA. Each cigarette contained approximately 1.8% THC. Marijuana placebo provided by NIDA was administered in identical cigarettes containing marijuana leaves from which THC had been extracted. Subjects were instructed to smoke cigarettes via

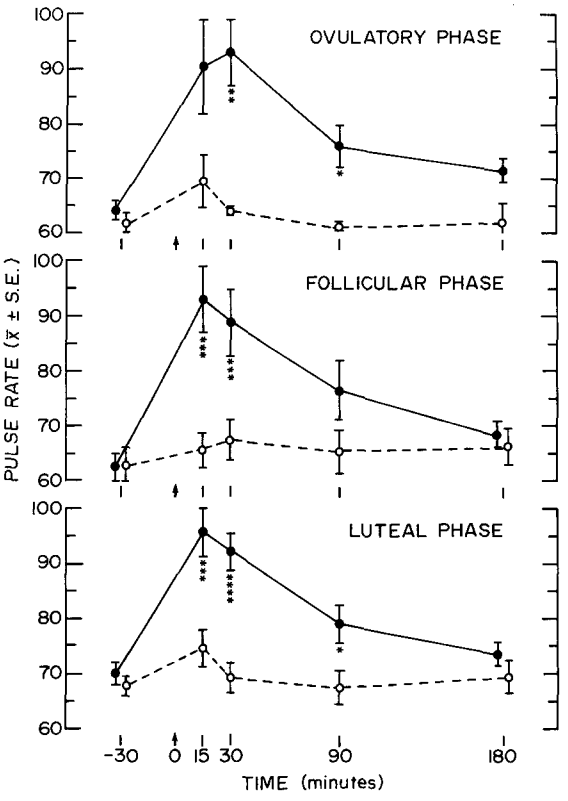


Fig. 1. Mean ± SE pulse rates for ovulatory ($N = 5$ marijuana, 4 placebo), follicular ($N = 10$), and luteal ($N = 9$) subjects at 30 min before and 15, 30, 90, and 180 min after acute marijuana (●) and placebo (○) administration. * $P < 0.05$ ** $P < 0.02$ *** $P < 0.01$ **** $P < 0.001$

controlled inhalation (1 puff/30 s with smoke retention following inhalation of 2–4 s). Subjects also were instructed to inhale using uniform draw practices.

Behavioral assessments were carried out 30 min before and 15, 30, 90, and 180 min after administration of marijuana or placebo. Heart rate was measured by peripheral pulse. Mood was assessed using the Profile of Mood states (POMS, McNair et al. 1971), a simple adjective checklist that includes 72 items grouped into eight factor-analytically derived scales (friendliness, tension, elation, anger, depression, fatigue, confusion, vigor) which have been found to be sensitive to drug effects in a wide variety of populations. Responses to each item were elicited on a 5-point scale ranging from 0 (not at all) to 4 (extremely). Subjects responded to each item in answer to the question, How do you feel right now? In addition, self-ratings of subjective level of marijuana intoxication were obtained. This 11-point scale is based on the instruction, In comparison to the highest you have ever been on marijuana, rate below how you feel right now. Response categories ranged from 0 (no effect, not high at all) through 2 (mildly high), 5 (moderately high), 8 (very high), to 10 (highest ever).

Results

Menstrual-cycle phase and acute effects of marijuana. Figure 1 presents pulse-rate data for subjects studied during the ovulatory, follicular, and luteal phases of the menstrual cycle. Similar changes in pulse rate following marijuana

versus placebo smoking occurred during all three menstrual-cycle phases.

At 30 min before smoking there were no significant differences in mean pulse rate between the marijuana and placebo conditions during the ovulatory phase of the menstrual cycle. At 15 min after marijuana administration, a nonsignificant trend in elevated pulse rate was observed which attained statistical significance at 30 min ($P < 0.02$) and 90 min ($P < 0.05$). A nonsignificant trend also occurred at 180 min after marijuana administration.

For subjects studied during the follicular menstrual-cycle phase, there were no significant differences between marijuana and placebo conditions 30 min before smoking. After marijuana administration statistically significant differences in elevated rates were observed at 15 min ($P < 0.01$) and at 30 min ($P < 0.01$). At 90 min after marijuana administration elevated pulse rates persisted, but the difference between marijuana and placebo did not attain statistical significance. At 180 min, pulse rates for marijuana and placebo conditions were virtually identical.

For subjects studied during the luteal menstrual cycle phase there were no significant differences in pulse rate between marijuana and placebo conditions 30 min prior to smoking. At 15 min after marijuana administration, mean pulse rate increased ($P < 0.01$) and remained significantly elevated ($P < 0.001$) at 30 min. At 90 min after marijuana administration the magnitude of elevation diminished ($P < 0.05$). At 180 min after smoking, a trend persisted that did not attain statistical significance.

Subjective level of intoxication. Figure 2 shows subjective intoxication levels for subjects studied during the ovulatory, follicular, and luteal phases of the menstrual cycle. Comparable changes during marijuana and placebo conditions for the three menstrual-cycle phases were found for this measure.

At 30 min before marijuana administration there were no significant differences for subjects studied under marijuana and placebo conditions during the ovulatory phase of the menstrual cycle. A nonsignificant trend can be discerned at 15 min after marijuana administration and a significant difference between marijuana and placebo groups occurred at 30 min after marijuana administration ($P < 0.01$). The magnitude of this difference declined but retained significance 90 min after marijuana administration ($P < 0.01$), and was no longer apparent at 180 min.

For subjects studied during the follicular phase, there were no significant differences between marijuana and placebo conditions 30 min before smoking. At 15 min after marijuana administration subjective level of intoxication was elevated ($P < 0.0005$) and remained elevated at 30 min ($P < 0.005$) and 90 min after administration ($P < 0.005$). At 180 min after administration, differences in subjective intoxication levels failed to attain statistical significance.

A virtually identical pattern was observed for subjects studied during the luteal phase of the menstrual cycle. At 30 min before smoking there were no significant differences in level of intoxication for marijuana versus placebo conditions. At 15 min after marijuana administration a pronounced increase in subjective intoxication levels was reported ($P < 0.0005$). This effect persisted 30 min after marijuana administration ($P < 0.0005$) and continued 90 min after marijuana ($P < 0.025$). At 180 min after marijuana administration some effects remained, but the difference between marijuana and placebo conditions failed to attain significance.

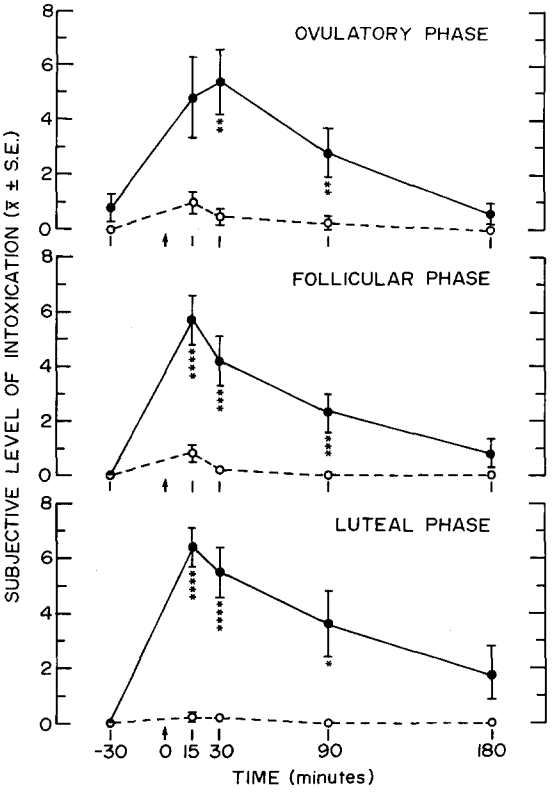


Fig. 2. Mean ± SE subjective level of intoxication ratings for ovulatory ($N = 5$ marijuana, 4 placebo), follicular ($N = 10$), and luteal ($N = 9$) subjects at 30 min before and 15, 30, 90, and 180 min after acute marijuana (●) and placebo (○) administration. * $P < 0.025$ ** $P < 0.01$ *** $P < 0.005$ **** $P < 0.0005$

POMS factor scores. POMS scores during marijuana and placebo conditions were obtained for subjects studied during each menstrual-cycle phase (follicular, luteal, ovulatory). No significant differences between marijuana and placebo were observed 30 min before smoking. Moreover, no POMS factor scores for friendliness, anger, fatigue, depression, tension, vigor, or elation attained statistical significance for any subject group at 15, 30, 90, or 180 min after marijuana administration in comparison to placebo. An increase in the POMS confusion scale (which includes feeling more confused, unable to concentrate, muddled, bewildered, forgetful, uncertain about things, and less able to be efficient) was reported by subjects after marijuana smoking during all phases of the menstrual cycle.

Increased confusion-scale responses were more pronounced in subjects studied during the follicular phase. Significant differences between marijuana and placebo conditions were found at 15 min ($P < 0.02$) and 30 min after administration ($P < 0.05$). At 90 and 180 min after administration, however, mean confusion scores were similar.

Subjects studied during the luteal phase reported increased confusion at 15 min after marijuana administration ($P < 0.01$). Increased confusion persisted 30 and 90 min after marijuana administration, but did not attain statistical significance and returned to near baseline values at 180 min after marijuana administration.

Comparisons of reponses from subjects studied during the ovulatory phase of the menstrual cycle revealed no significant differences between the placebo and marijuana groups at any of the five assessment times.

Subjects studied during the luteal and follicular phases of the menstrual cycle were compared for differences in pulse rate, subjective intoxication level, and POMS confusion factor scores after both marijuana and placebo conditions. There were no significant differences between luteal and follicular subjects at any of the five assessment items (−30 to +180 min) for either subjective level of intoxication or POMS confusion factor scores. Comparison of pulse rates also were not significantly different, with the exception of 30 min before marijuana administration ($P < 0.05$). This appears to be a chance association unrelated to subsequent administration of marijuana 30 min after that measure was obtained. Thus, menstrual-cycle phase appears to have little effect upon pulse rate, subjective intoxication level, or POMS confusion scores associated with either placebo or marijuana smoking.

Marijuana smoking history and acute effects of marijuana. The contribution of marijuana smoking history to responses of regular and intermittent marijuana smokers during placebo and marijuana conditions is shown in Fig. 3, 4, and 5. Profiles of responses displayed for each of the measures (pulse rate, subjective level of intoxication, POMS confusion scores) clearly show that, following marijuana smoking, a greater magnitude of change was experienced by intermittent smokers in contrast to regular smokers.

As shown in Fig. 3, both regular and intermittent smokers had significant differences in pulse rates between marijuana and placebo conditions at 15 min ($P < 0.01$ for both regular and intermittent smokers) and 30 min ($P < 0.01$ for regular smokers, $P < 0.001$ for intermittent smokers) after administration. At 90 and 180 min after administration, regular smokers showed no significant differences between marijuana and placebo conditions. Intermittent smokers, however, continued to have significantly increased pulse rates ($P < 0.05$) at 90 and 180 min.

Figure 4 shows that, 15 min after smoking, both regular and intermittent smokers had significant differences in subjective levels of intoxication between marijuana and placebo conditions ($P < 0.001$ for regular smokers, $P < 0.001$ for intermittent smokers). Marijuana effects persisted at 30 min after administration ($P < 0.01$ for regular smokers, $P < 0.001$ for intermittent smokers). At 90 min after administration, effects of marijuana on intermittent smokers continued ($P < 0.01$), but effects on regular smokers failed to attain significance. At 180 min after smoking there were no significant differences between effects of marijuana or placebo for either group.

Figure 5 indicates that, 15 min after smoking, significant differences in POMS confusion factor scores between marijuana and placebo conditions were observed for both groups ($P < 0.02$ for regular smokers, $P < 0.011$ for intermittent smokers). At 30 min after marijuana administration, confusion effects increased in intermittent smokers ($P < 0.05$), but began to decrease in regular smokers. At 90 and 180 min after marijuana administration, confusion effects had diminished and differences failed to reach statistical significance in either group.

Correlation coefficients for changes in pulse rate and subjective level of intoxication, changes in pulse rate and changes in confusion scale scores, and subjective level of intoxication and changes in confusion scale scores for regular and intermittent smokers are shown in Table 2. Differences in these correlations largely reflect past history of marijuana use. In comparison to regular smokers, responses following marijuana smoking (or placebo smoking) were more pronounced and more persistent for intermittent users. At 15, 30, and 90 min after marijuana administration, correlations of ratings obtained for regular smokers range from negligible to low, while those for intermittent smokers range from low to substantial. At 30 min after marijuana

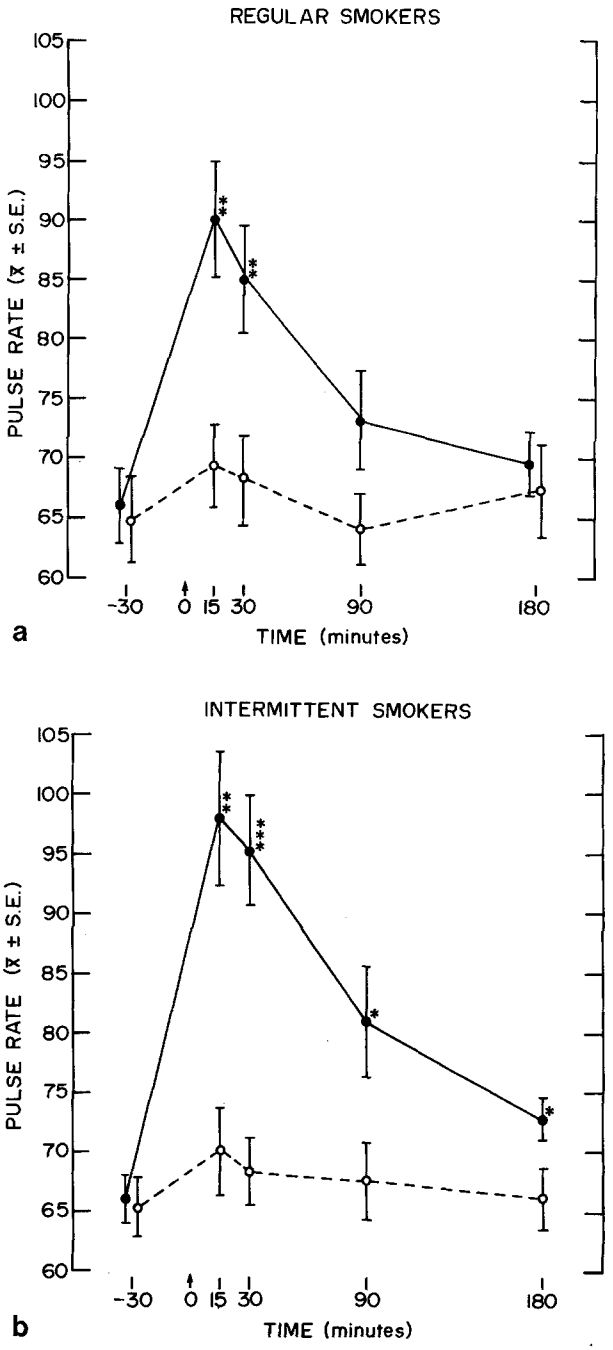
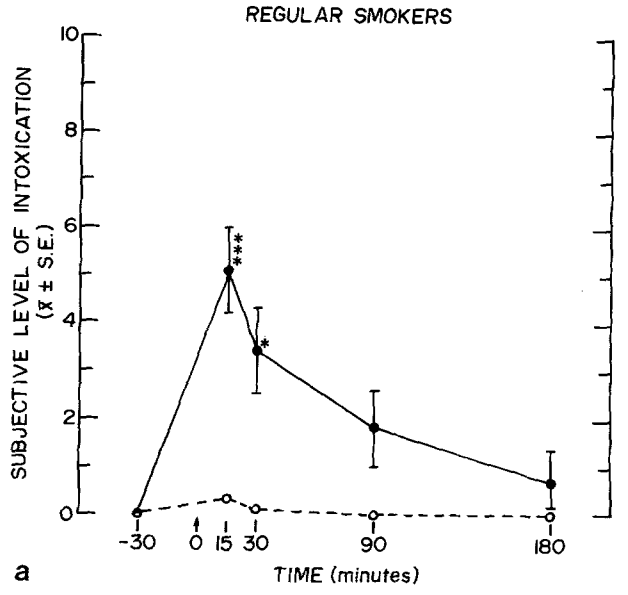
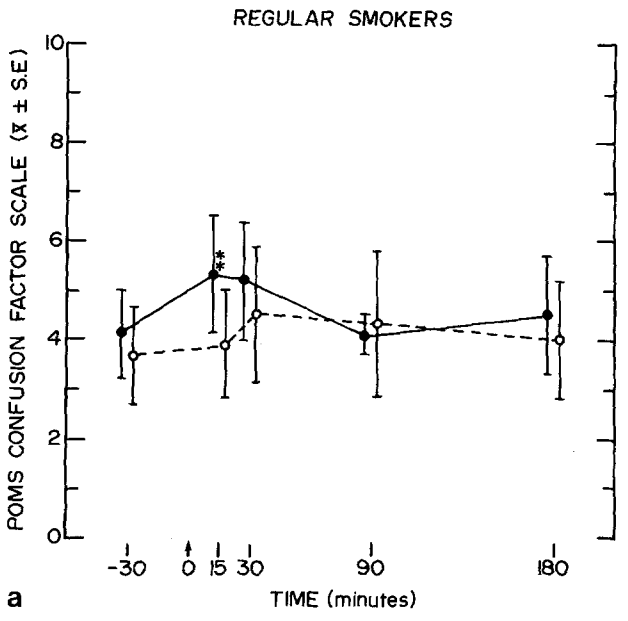
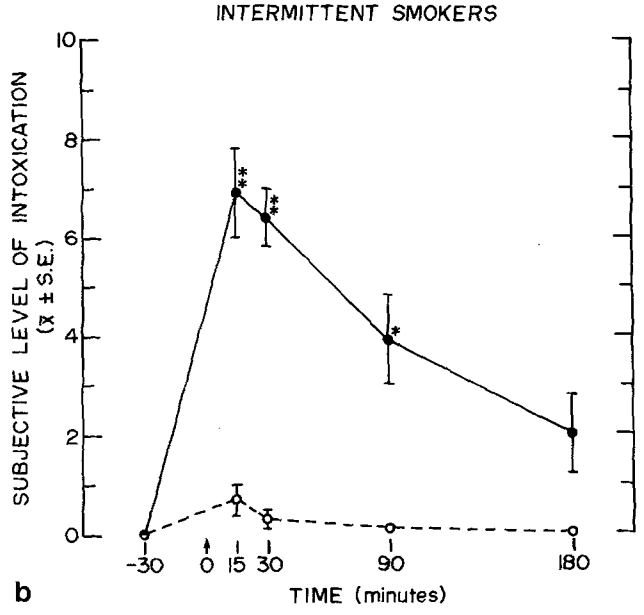


Fig. 3a, b. Mean ± SE pulse rates for **a** regular ($N = 9$) and **b** intermittent ($N = 10$) marijuana smokers at 30 min before and 15, 30, 90, and 180 min after acute marijuana (●) and placebo (○) administration. * $P < 0.05$ ** $P < 0.01$ *** $P < 0.001$







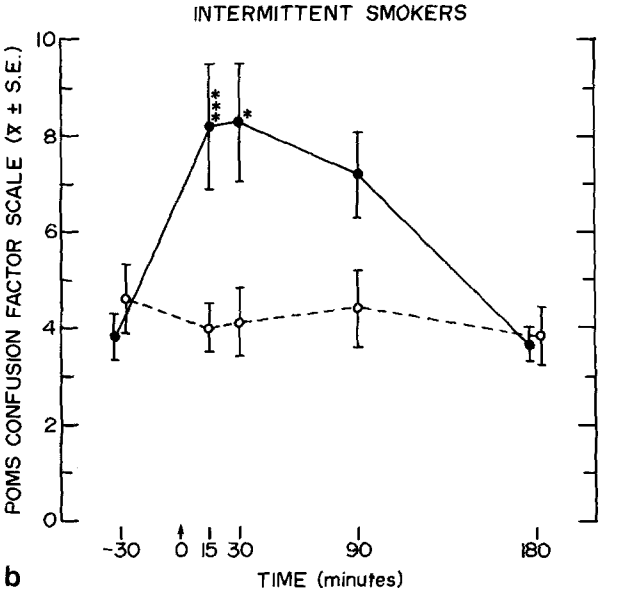


Fig. 4a, b. Mean ± SE subjective level of intoxication ratings for **a** regular ($N = 9$) and **b** intermittent ($N = 10$) marijuana smokers at 30 min before and 15, 30, 90, and 180 min after acute marijuana (●) and placebo (○) administration. * $P < 0.01$ ** $P < 0.001$

Fig. 5a, b. Mean ± SE POMS confusion factor scale scores for **a** regular ($N = 9$) and **b** intermittent ($N = 10$) marijuana smokers at 30 min before and 15, 30, 90, and 180 min after acute marijuana (●) and placebo (○) administration. * $P < 0.05$ ** $P < 0.02$ *** $P < 0.01$

administration, there are statistically significant correlations between increased pulse rates and confusion scale scores for intermittent smokers. In contrast, statistically significant correlations did not occur for regular smokers until 180 min after marijuana administration.

Coefficients of partial correlation were calculated to assess the separate contribution of each of the three measures (Table 3). For intermittent smokers, significant correlations occurred at 30 min after marijuana administration. The highest correlations occurred between changes in pulse rates and changes in confusion scale scores. The correlation between changes in pulse rate and subjective level of intoxication also was large and statistically significant. The major contribution of change in pulse rate to ratings of changes in confusion scale scores and subjective level of intoxication in intermittent smokers is shown by absence of a significant correlation between these measures when changes in pulse rate are held constant. For regular smokers, however, partial correlations indicate a minor contribution of changes in pulse rate to ratings for other measures. At 15, 30, and 90 min after marijuana administration, correlations for changes in pulse rate and changes in confusion scale scores

Table 2
Summary of significance levels for correlation coefficients of measures: regular marijuana smokers ($N = 9$) and intermittent marijuana smokers ($N = 10$), marijuana and placebo conditions

	Pulse rate Δ and subjective level of intoxication			
	Regular marijuana smokers		Intermittent marijuana smokers	
	Marijuana	Placebo	Marijuana	Placebo
+ 15 min	−0.19 (NS)	+0.42 (NS)	−0.29 (NS)	−0.31 (NS)
+ 30 min	+0.23 (NS)	−0.02 (NS)	+0.37 (NS)	−0.31 (NS)
+ 90 min	−0.25 (NS)	−[a]	+0.33 (NS)	−0.34 (NS)
+180 min	+0.30 (NS)	−[a]	+0.14 (NS)	−[a]
	Pulse rate Δ and POMS confusion factor scale score Δ			
	Regular marijuana smokers		Intermittent marijuana smokers	
	Marijuana	Placebo	Marijuana	Placebo
+ 15 min	−0.11 (NS)	−0.12 (NS)	+0.36 (NS)	+0.46 (NS)
+ 30 min	+0.10 (NS)	−0.30 (NS)	+0.60 ($P < 0.05$)	+0.76 ($P < 0.005$)
+ 90 min	−0.05 (NS)	−0.44 (NS)	−0.06 (NS)	+0.49 (NS)
+180 min	+0.79 ($P < 0.01$)	+0.57 (NS)	−0.35 (NS)	+0.21 (NS)
	Subjective level of intoxication and POMS confusion factor scale score Δ			
+ 15 min	−0.03 (NS)	+0.35 (NS)	−0.35 (NS)	+0.46 (NS)
+ 30 min	+0.08 (NS)	−0.12 (NS)	−0.17 (NS)	+0.13 (NS)
+ 90 min	+0.04 (NS)	−[a]	−0.14 (NS)	+0.14 (NS)
+180 min	+0.68 ($P < 0.05$)	−[a]	−0.35 (NS)	−[a]

[a] *r* cannot be calculated because of zero values

Table 3. Summary of significance levels of partial correlation coefficients: regular marijuana smokers ($N = 9$) and intermittent marijuana smokers ($N = 10$), marijuana condition

		Regular smokers	Intermittent smokers
+ 15 min	Δ Pulse and level of intoxication, Δ confusion held constant	+0.195 (NS)	+0.188 (NS)
	Δ Pulse and Δ confusion, level of intoxication held constant	−0.118 (NS)	−0.405 (NS)
	Level of intoxication and Δ confusion, Δ pulse held constant	+0.052 (NS)	−0.275 (NS)
+ 30 min	Δ Pulse and level of intoxication, Δ confusion held constant	+0.224 (NS)	+0.599 ($P < 0.05$)
	Δ Pulse and Δ confusion, level of intoxication held constant	−0.084 (NS)	−0.724 ($P < 0.05$)
	Level of intoxication and Δ confusion, Δ pulse held constant	+0.059 (NS)	−0.527 (NS)
+ 90 min	Δ Pulse and level of intoxication, Δ confusion held constant	+0.249 (NS)	+0.325 (NS)
	Δ Pulse and Δ confusion, level of intoxication held constant	−0.041 (NS)	−0.015 (NS)
	Level of intoxication and Δ confusion, Δ pulse held constant	+0.028 (NS)	−0.013 (NS)
+180 min	Δ Pulse and level of intoxication, Δ confusion held constant	+0.528 (NS)	+0.019 (NS)
	Δ Pulse and Δ confusion, level of intoxication held constant	−0.838 ($P < 0.01$)	−0.324 (NS)
	Level of intoxication and Δ confusion, Δ pulse held constant	+0.757 ($P < 0.025$)	−0.324 (NS)

were negligible, and correlations for changes in pulse rate and subjective levels of intoxication were low. Positive significant correlations did not occur until 180 min after marijuana administration.

Table 4 shows that, for intermittent users, there was a high intercorrelation among pulse-rate changes, subjective level of intoxication, and changes in confusion factor scores at 15 and 30 min after placebo smoking. The best interpretation of these findings is that intermittent marijuana smokers were less tolerant and less experienced than regular marijuana smokers and, hence, might be less discriminating of marijuana cigarettes versus placebo cigarettes. An alternative explanation may be that, while THC had been extracted from placebo cigarettes, other residual cannabis compounds could be responsible for apparent placebo responses.

Discussion

Pulse rate. Previous studies have shown that marijuana smoking induces an increased pulse rate in males (Weil et al. 1968; Hollister 1970; Manno et al. 1970; Jones and Stone 1970; Allentuck 1944; Meyer et al. 1971). Female subjects in this study showed an increase in pulse rate following marijuana smoking which attained peak values 15–30 min following cessation of smoking. During the ovulatory phase of the menstrual cycle, statistically significant changes in pulse rate occurred later (+30 min) than changes in pulse rate following marijuana smoking during the follicular and luteal phases of the menstrual cycle (+15 min). The persistence of statistically significant increments in pulse rate were longer during the ovulatory and luteal phases of the menstrual cycle (+90 min) in comparison with persistence

Table 4. Summary of significance levels of partial correlation coefficients: regular marijuana smokers ($N = 9$) and intermittent marijuana smokers ($N = 10$), marijuana condition

		Regular smokers	Intermittent smokers
+ 15 min	Δ Pulse and level of intoxication, Δ confusion held constant	+0.497 (NS)	+0.662 ($P < 0.05$)
	Δ Pulse and Δ confusion, level of intoxication held constant	−0.314 (NS)	+0.714 ($P < 0.025$)
	Level of intoxication and Δ confusion, Δ pulse held constant	+0.495 (NS)	−0.714 ($P < 0.025$)
+ 30 min	Δ Pulse and level of intoxication, Δ confusion held constant	−0.059 (NS)	−0.634 ($P < 0.05$)
	Δ Pulse and Δ confusion, level of intoxication held constant	−0.305 (NS)	−0.849 ($P < 0.005$)
	Level of intoxication and Δ confusion, Δ pulse held constant	−0.132 (NS)	+0.592 ($P < 0.05$)
+ 90 min	Δ Pulse and level of intoxication, Δ confusion held constant	– [a]	−0.314 (NS)
	Δ Pulse and Δ confusion, level of intoxication held constant	– [a]	+0.475 (NS)
	Level of intoxication and Δ confusion, Δ pulse held constant	– [a]	−0.032 (NS)
+180 min	Δ Pulse and level of intoxication, Δ confusion held constant	– [a]	– [a]
	Δ Pulse and Δ confusion, level of intoxication held constant	– [a]	– [a]
	Level of intoxication and Δ confusion, Δ pulse held constant	– [a]	– [a]

[a] No calculation possible because of zero values of level of intoxication scores

of increments in pulse rate during the follicular phase of the menstrual cycle (+30 min). However, the magnitude of changes in pulse rate following marijuana smoking during all phases of the menstrual cycle were essentially equivalent and there appeared to be no biologically significant differences in pulse rate increments following marijuana smoking as a function of menstrual-cycle phase.

Differences in pulse-rate response following marijuana smoking occurred as a function of past history of marijuana use. Larger and more persistent increases in pulse rate occurred in intermittent marijuana smokers. Differences between intermittent and regular smokers were independent of menstrual-cycle phase. This observation is consistent with data on relationships between frequency of marijuana use and pulse-rate increment following marijuana smoking by male subjects. Jones (1971) reported that males who were frequent users of marijuana (more than seven cigarettes per week) had an approximately 40% lower increment in pulse rate following smoking a 1 g marijuana cigarette that contained 9 mg THC than infrequent users of marijuana (less than two cigarettes per month) studied under the same conditions.

A small increase in pulse rates after smoking placebo cigarettes was within the range of increments (6−8 bpm) previously reported for male subjects (Weil et al. 1968; Manno et al. 1970; Hollister 1970). The pattern of pulse-rate increment following placebo smoking differed from those observed following marijuana smoking as a function of menstrual-cycle phase. At 15 min after placebo smoking, pulse-rate changes were most pronounced in subjects studied during the ovulatory menstrual-cycle phase, less pronounced in subjects studied during the luteal menstrual-cycle phase, and only minimally elevated in subjects studied during the follicular menstrual-cycle phase. In subjects studied during the ovulatory and the luteal phases, pulse rate increments diminished by more than half at 30 min after smoking placebo but, in subjects studied during the follicular phase, pulse-rate increments after smoking placebo persisted at 30, 90, and 180 min. However, consistent patterns in pulse-rate response following placebo smoking occurred as a function of past history of marijuana use. For regular users, pulse-rate increments were observed at 15 and 30 min after smoking placebo but diminished at 90 min, while for intermittent users pulse-rate increments after smoking placebo were observed at 15, 30, 90, and 180 min.

No significant differences in pre-smoking pulse rates were observed for subjects as a function of either menstrual-cycle phase during which the study was conducted or past history of marijuana use. A number of studies with males have pointed out that regular users of marijuana may develop rather slow pulse rates or overt bradycardia (Baker-Bates 1935; Allentuck and Bowman 1942; Gaskill 1945; Williams et al. 1946; Parker and Wrigley 1947; Tayleur-Stockings 1947; deFarias 1955; Chopra and Chopra 1957; Ames 1958; Isbell et al. 1967; Weil et al. 1968; Hollister et al. 1968;; Isbell and Jasinski 1969; Waskow et al. 1970; Weil 1970; Manno et al. 1970; Hollister 1970; Domino 1971; Kiplinger et al. 1971; Forney and Kiplinger 1971; Renault et al. 1971; Johnson and Domino 1971). In contrast to these observations, no statistically significant differences in pulse rate were observed between regular and intermittent female marijuana users. Moreover, there was no evidence of abnormally slow pulse rate or overt bradycardia for any regular or intermittent female marijuana user. Although many factors could account for differences in baseline pulse rate found in males in previous experiments and females observed in this study, it also may be possible that cardiovascular status following long-term marijuana use may vary as a function of gender.

Subjective levels of intoxication. All female subjects reported subjective levels of intoxication in the moderately high range with peak values occurring 15−30 min following marijuana smoking. No statistically significant differences in subjective levels of intoxication were observed as a function of menstrual-cycle phase.

Subjects studied during the luteal phase of the menstrual cycle consistently reported slightly higher subjective levels of intoxication after marijuana administration than subjects studied during the follicular phase. During both the luteal and follicular menstrual-cycle phases, subjects reported peak subjective levels of intoxicaton 15 min after marijuana administration and slight decreases from peak values at 30 min after marijuana administration. In contrast, onset of statisti-

cally significant peak subjective levels of intoxication did not occur until 30 min after marijuana administration during the ovulatory phase of the menstrual cycle. This phenomenon may reflect a smaller number of subjects studied during the ovulatory phase under marijuana conditions in contrast to the larger number of subjects studied during the follicular and luteal phases of the menstrual cycle.

Comparison of subjective levels of intoxication revealed that regular smokers reported lower levels of intoxication than intermittent users at 15, 30, and 90 min following marijuana smoking. This observation is consistent with the development of behavioral tolerance as a consequence of regular marijuana use and with data obtained in studies of male marijuana smokers (Jones 1971). Infrequent male marijuana users studied by Jones (1971) reported subjective ratings of intoxication following marijuana use analogous to those reported by intermittent female smokerrs examined in this study.

In previous studies with male subjects, regular marijuana users reported a mean level of intoxication of 5.8 at 15 min after marijuana smoking, with the instrument used to measure subjective levels of intoxication identical to the one employed in this study (Rossi et al. 1974). Virtually identical mean levels of intoxication (5.1) were reported by regular female marijuana smokers in this study. However, in contrast to studies with males, the subjective level of intoxication declined much more rapidly for females (Rossi et al. 1974). It should be noted, however, that the studies carried out with males involved marijuana smoking within peer-group situations and during conditions where no continuous blood sampling was carried out analogous to procedures used in this study with females. Thus, the rapid decline in subjective level of intoxication observed for females in this study may have been, in part, attributable to the fact that subjects were studied singly and under conditions of continuous blood sampling.

Mood states. Earlier laboratory studies with male subjects have failed to demonstrate consistent mood changes associated with marijuana smoking (Mendelson et al. 1976; Rossi et al. 1977), and revealed considerable complexity in postsmoking mood effects (Rossi et al. 1974). Marijuana smoking has not consistently changed pre-smoking levels of euphoria or dysphoria (Siler et al. 1933; Bromberg 1934; Walton 1938; Allentuck and Bowman 1942; Williams et al. 1946; Ames 1958; Bloomquist 1968; Hollister et al. 1968; Weil et al. 1968; Melges et al. 1970; Pillard 1970; Meyer et al. 1971; Pillard et al. 1974; Hollister et al. 1975; Mendelson et al. 1976; Rossi et al. 1977).

Variables, such as size of dose and previous marijuana experience, appear to interact with expectancy and social modeling effects (Weil et al. 1968; Grinspoon 1971; Hollister 1971; Tart 1971; Meyer et al. 1971; Carlin et al. 1972, 1974). Experienced marijuana users may undergo a socialization process that both enhances discrimination of selected pharmacological drug effects and facilitates labeling of specific cognitive and affective experiences associated with marijuana smoking (Schacter and Singer 1962; Cappell and Pliner 1974; Rossi et al. 1974).

Results in several studies of chronic marijuana administration to groups of three or four male subjects in laboratory settings revealed that one important determinant of subjective mood states is the prevailing mood of others in the environment (Rossi et al. 1974, 1977; Babor et al. 1974; Mendelson et al. 1976). Analysis of variance of changes in mood following chronic marijuana administration to 15 male subjects (Rossi et al. 1977) revealed a small increase in ratings of euphoria before smoking and an additional small increment 30 min after smoking. However, because no linear relationship was found between level of intoxication and mood ratings, it was concluded that marijuana effects could not be solely attributed to a specific pharmacologic action of the drug. However, marijuana use may facilitate expression of pleasant moods among individuals when smoking occurs in a group setting.

Comparison of findings from studies of males using similar mood assessments (Rossi et al. 1974, 1977; Babor et al. 1975; Mendelson et al. 1976) suggest that women resemble men insofar as postsmoking reports of elation and friendliness may be influenced by peers in the environment, while dysphoric changes (such as increased confusion) may be less influenced by peer and social factors.

This interpretation may in part further explain seemingly paradoxical findings from one prior study of marijuana effects on mood in women (Milstein et al. 1974). Changes in mood (anger, arousal, depression, fear, and happiness as measured by an affect scale) were examined in small groups (two or three women) of either experienced or inexperienced marijuana useres at approximately 40 min after acute marijuana (600 mg, 1.3% THC) or placebo administration. For both experienced and naive women, marijuana smoking, in contrast to placebo, was associated with comparable statistically significant increases in happiness and fear. It was concluded that increased happiness was a specific marijuana effect unlikely to be an artifact of the experimental setting, but that increased fear was a paradoxical finding not in keeping with predicted postsmoking tension reduction. Postsmoking anxiety and hilarity are known to co-occur (Paton and Pertwee 1973). However, peripheral pulse rate was not reported by Milstein et al. (1974) and any possible relationship between tachycardia and increased fear responses in the subjects studied remains unknown.

Marijuana induced pulse rate changes and mood effects in a study of an older cohort of females utilizing a protocol identical to this study are consistent with data presented in this paper. Older women had prompt and sustained pulse-rate increments at 15 and 30 min, elevated confusion factor scores at 30 and 90 min, and increased subjective levels of intoxication at 15, 30, 90, and 180 min after marijuana smoking. Statistically significant differences between marijuana and placebo conditions found with older women closely resemble results obtained in our study of young female intermittent marijuana smokers.

Correlation between marijuana induced changes in pulse rate, subjective levels of intoxication, and mood states. Female intermittent smokers had increased pulse rates which were significantly correlated with increased subjective levels of intoxication and confusion scores. This finding is consistent with results reported in earlier studies of male marijuana smokers (Babor et al. 1975; Mendelson et al. 1976). Males who were heavy (daily) or moderate (less than daily) marijuana smokers showed a high intercorrelation among marijuana dose, pulse rate change, and rating of subjective level of intoxication. Pulse rate change was an important predictor of subjective level of intoxication and psychological effects (Babor et al. 1975; Mendelson et al. 1976). Male heavy smokers had a smaller increase in pulse rate and

subjective level of intoxication in contrast to moderate smokers. Data obtained in this study indicates that female marijuana smokers are similar to male marijuana smokers with respect to the influence of marijuana smoking history on both physiological and psychological responses following marijuana use.

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