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Sedative, Stimulant, and Other Subjective Effects of Marijuana: Relationships to Smoking Techniques

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BLOCK, R. I., W. J. ERWIN, R. FARINPOUR AND K. BRAVERMAN. *Sedative, stimulant, and other subjective effects of marijuana: Relationships to smoking techniques*. PHARMACOL BIOCHEM BEHAV **59**(2) 405–412, 1998.—A double-blind, placebo-controlled study assessed subjective effects of smoking marijuana with either a long or short breath-holding duration. During eight test sessions, 55 male volunteers made repeated ratings of subjective "high," sedation, and stimulation, as well as rating their perceptions of motivation and performance on cognitive tests. The major finding of the study was that the long, relative to the short, breath-holding duration increased "high" ratings after smoking marijuana, but not placebo. Marijuana smoking increased sedation and a perception of worsened test performance, and decreased motivation with respect to test performance. Paradoxical subjective effects were observed in that subjects reported some stimulation as well as sedation after smoking marijuana, particularly with the long breath-holding duration. Breath-holding duration did not produce any subjective effects that were independent of the drug treatment, i.e., occurred equally after smoking of marijuana and placebo, such as we previously observed with respect to test performance. © 1998 Elsevier Science Inc.

Marijuana Δ9-Tetrahydrocannabinol Subjective effects Sedation Stimulation Breath-holding Motivation Paradoxical effects

POPULAR accounts and scholarly studies have indicated a plethora of subjective effects from marijuana use, including euphoria, altered perception, openness, passivity, paranoia, changes in sense of time and space, and intensified emotions (20,29). Surveys of subjective effects occurring among marijuana users in the community (29) or controlled studies of such effects following administration of marijuana or its primary active ingredient, Δ9-tetrahydrocannabinol (Δ9-THC), in the laboratory (26) have frequently examined a variety of effects. Few generalizations about marijuana's subjective effects have emerged other than the almost universal finding that the drug produces a euphoric or "high" state in most people most of the time [e.g., (2,10,11)]. This lack of generalizability may reflect inconsistency across studies in the dimensions of subjective effects that were examined, as well as variability in other characteristics, for example, individual differences, marijuana doses, and settings in which the drug was administered.

These sources of variability may have contributed to discrepancies in previous findings concerning marijuana's effects on the dimension of sedation vs. stimulation, a dimension that was a major focus of the current study. Many studies have affirmed the common perception that marijuana or Δ9-THC produce sedation, as reflected by ratings indicating at least one of the following changes: increased sedation, impairment, sluggishness, confusion, or dreaminess; or decreased tension, alertness, clear-headedness, or vigor (1,3,10,16,22,26,34). On the other hand, some of these same studies, as well as others,

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have observed stimulant effects of marijuana or Δ^9-THC, as reflected by ratings indicating at least one of the following changes: increased stimulation, tension, jitteriness, or anxiety; or decreased relaxation (3,10,21,26,34).

One potential source of variability in marijuana's subjective effects that was examined in the current study was breath-holding duration. Marijuana users are commonly advised that holding the smoke in their lungs for a long time increases the drug's psychological effects (20), but laboratory investigations have not provided much support for this notion. Two studies found that a longer, relative to a shorter, breath-holding duration increased plasma or serum Δ^9-THC levels (2,31). These studies failed to demonstrate statistically significant effects of breath-holding duration on subjective effects, although a trend toward greater subjective effects with a longer, relative to a shorter, breath-holding duration was observed in one study (31). Two other studies reported minimal effects of breath-holding duration on subjective or cognitive effects of marijuana (33,34). We previously reported that prolonged breath-holding altered performance on cognitive tests following smoking of both marijuana and placebo; there were a few hints that prolonged breath-holding specifically increased effects of marijuana (in contrast to placebo) under some test conditions, but in general it did not (4). In the present report, we examine whether prolonged breath-holding has a more specific influence on the subjective effects of marijuana, relative to placebo. Subjects made ratings of "high" and sedation vs. stimulation, as well as rating their perceptions of motivation and performance on cognitive tests. Long (15 s) and short (7 s) durations of inhalation and breath holding were compared, with the expectation that the former would produce stronger subjective drug effects than the latter. The long duration was comparable to that spontaneously practiced by many marijuana users (24,25,30,32). The short duration was also realistic, constituting 25% of the rest period between puffs (7 ÷ 28 s), compared to 75% for the long duration (15 ÷ 20 s).

METHOD

Subjects and Screening

After obtaining institutional review board approval, 55 subjects were tested. They consisted of 48 subjects whose cognitive test scores, but not subjective ratings, were described in our initial report (4), together with seven additional subjects who were tested in identical fashion shortly after the initial group of 48. Paid male volunteers were recruited through advertisements. After obtaining informed consent, screening assessments were administered as described in our initial report (4). Volunteers classified their average weekly frequency of using marijuana or other cannabis products as "not at all," "less than once," one to four times, five to six times, or seven or more times. Subjects were restricted to adults (age range, 18 to 42 years) who were experienced marijuana users and whose health was adequate for administration of marijuana, based on their medical history information, blood tests, and urinalysis. Individuals who frequently used any illicit drugs other than marijuana or had a history of dependence on any such drugs (27) were excluded. Women were not recruited to provide a homogeneous sample with respect to gender. Institutional concerns about the gender composition of research samples were not prominent when this research was conducted, particularly for studies involving drugs that might conceivably have adverse effects during pregnancy.

Dropouts

In addition to the 55 subjects who completed the experiment, 14 subjects began but quit or were excluded before completion due to moving, becoming too busy with other activities, experiencing adverse reactions to smoking, or other reasons.

Drug

The mean weight of the marijuana cigarettes was 755 mg, and their mean content of Δ^9-THC was 2.57%, or 19 mg. Placebo cigarettes contained inactive, cannabinoid-extracted marijuana with only trace amounts of Δ^9-THC. The cigarettes were provided by the National Institute on Drug Abuse.

Smoking Procedure

Using a stopwatch, the research assistant guided subjects in a paced smoking procedure. The research assistant said "in" every 35 s, cueing subjects to inhale deeply and hold the smoke in their lungs. For the long and short breath-holding durations, which were each used with half the subjects, the research assistant said "out" 15 s and 7 s after "in," respectively, cueing subjects to exhale and pause. Subjects smoked the cigarettes as completely as possible, using a holder while consuming the butts. Numbers of puffs were recorded. At the beginning of the study, all subjects smoked with a long breath-holding duration. Four subjects quit or had to be dropped from the study due to adverse reactions (e.g., nausea, dizziness) following marijuana smoking with a long breath-holding duration early in the data collection period. To help understand these unanticipated effects, a short breath-holding duration was subsequently added. The first 24 subjects were tested with the long breath-holding duration and the next 24 with the short breath-holding duration; seven additional subjects were tested shortly thereafter, four with the long breath-holding duration and three with the short breath-holding duration.

Test Procedure

Subjects were tested individually. Subjective ratings were obtained repeatedly, intermingled with administration of cognitive tests. Because of the number of cognitive tests and their durations, subjects had to participate in four marijuana-smoking sessions to insure that all tests could be completed while the drug's effects remained substantial. To control for placebo effects, subjects had to participate in four corresponding placebo-smoking sessions. So that performance would not be influenced by effects of self-administered drugs, subjects had to promise to abstain from alcohol on the day of each session and after 1800 h on the preceding evening; and to abstain from marijuana and other drugs on the day of each session and the preceding 3 days. Their compliance was verified by questioning during each session. Each subject participated in eight sessions, which were separated by intervals of at least 4 days and commonly 1 week or more.

In each session, subjects smoked a marijuana or placebo cigarette under double-blind conditions. The smoking procedure for each subject was the same in all his sessions. Orders of administering marijuana and placebo were approximately counterbalanced by assigning subjects to four different sequences of drug administration. For all sequences, each successive pair of sessions (sessions 1–2, 3–4, 5–6, and 7–8) involved smoking marijuana once and placebo once. The same subjective ratings and tests were given within each pair of sessions. This procedure made it possible to collect data for each test under marijuana and placebo conditions without interpo-

sition of other tests. Similarly, to provide some consistency over time for subjects with respect to the general nature of the tests, microcomputer-based cognitive and psychomotor tests were administered in the first four sessions, whereas standardized, multiple-choice, pencil-and-paper tests were administered in the last four sessions.

The specific tests were as follows: sessions 1–2: Buschke's Test (6), Free and Constrained Associations, and Psychomotor Tests (Critical Flicker Fusion and Discriminant Reaction Time); sessions 3–4: Concept Formation, Text Learning, and Paired Associate Learning; sessions 5–6: Ability to Do Quantitative Thinking and Ability to Interpret Literary Materials; sessions 7–8: Correctness and Appropriateness of Expression, Vocabulary, and Short Test of Educational Ability (Level 5) (28). All tests in sessions 5–8 except Short Test of Educational Ability were components of the Iowa Tests of Educational Development (Level II) (17). Details of all tests and their administration (e.g., use of alternate forms and counterbalancing of orders of administration), as well as effects of marijuana on performance, were described in our previous report (4). In all sessions, the tests were completed within about 1.5 h after smoking, a period during which effects of smoked marijuana remain substantial.

In each session, subjects provided subjective ratings immediately before and immediately after smoking either marijuana or placebo. They also provided subjective ratings after the first, second, and third tests (which were of similar durations) in each of the first four sessions; the final rating was completed about 1 h after smoking. Ratings were not collected after testing in the last four sessions, because these sessions involved some longer tests, which would have made the timing of the ratings more irregular than in the first four sessions. All ratings were made on horizontal scales labeled with numbers from 0 to 10 and with anchors at the left and right indicating the extremes of the dimension to be rated.

At each time of assessment, subjects rated how "high" they felt (with anchors being not at all/highest ever from marijuana) and made 10 ratings of different aspects of stimulation vs. sedation (alert/drowsy, attentive/dreamy, tense/relaxed, interested/bored, capable/incompetent, excited/calm, clear-headed/fuzzy, well-coordinated/clumsy, quick-witted/mentally slow, and energetic/lazy). These were selected from 16 rating scales that Norris (23) originally grouped into four categories—mental sedation; physical sedation; tranquilization; and attitudes or other feelings; the numbers of scales from these categories were 4, 3, 2, and 1, respectively. Minor modifications in anchors were made to avoid difficult vocabulary items. Half the scales had the anchor representing sedation on the left, while the remainder had it on the right.

In addition, after each test in the first four sessions, subjects made ratings in response to three questions concerning the immediately preceding test: "How motivated were you to do well?"; "How did you actually do?"; and, "How did the drug affect your performance?" The anchors for these questions were motivated/unmotivated, well/poor, and improved/impaired, respectively.

Subjects were required to stay in the laboratory for 3 h after smoking to assure that marijuana's effects had abated, and to agree not to drive home from the sessions or later on the days of the sessions.

Statistical Analyses

Prior to analysis, ratings for some scales were subtracted from 10 so that higher values on all scales represented greater "high," sedation, or perception of decreased motivation or worsened test performance (i.e., of doing poorer or being impaired by the drug). To assess effects of marijuana and breath-holding duration, the data were submitted to analyses of variance. Parallel analyses were conducted for the two successive ratings done in all sessions and the five successive ratings done only in the first four sessions. These analyses included within-subjects factors representing drug (marijuana vs. placebo), time (the successive ratings within sessions), and exposures (the successive pairs of sessions for each subject); and between-subjects factors representing breath (long vs. short breath-holding durations), the four sequences of drug administration used with different subjects, and the counterbalancing of alternate forms of the cognitive tests over drugs. The significance level for all F-tests was $p < 0.05$.

RESULTS

Subjects' Characteristics

On average, subjects were 21.1 ± 0.6 (mean ± standard error) years old and had attended school for 13.5 ± 0.2 years. One subject described himself as Hispanic and the remainder described themselves as Caucasian. One subject was unemployed and the remainder were in school (46%), employed (20%), or both (33%). (The percentages do not add to 100 due to rounding error.) One subject had a history of noncurrent major depression and one had a history of noncurrent major depression and atypical bipolar disorder (27). None had a history of schizophrenia. On average, subjects started using marijuana in grade 10.0 ± 0.3. Their median reported frequency of current marijuana use was one to four times weekly. Apart from marijuana and alcohol, the drugs with which subjects had the most experience were stimulants, psychedelics, and amyl or butyl nitrites. Most subjects (73%) had smoked at least one tobacco cigarette in the last 30 days, but considerably fewer (20%) had smoked about one pack per day or more during this period.

Effects of Breath-Holding Duration

If marijuana's effects had been greater when the breath-holding duration was long than short, this would have been reflected in the analyses as a drug × breath × time interaction. This interaction was significant for "high" ratings, $F(1, 39) = 5.4$, $p < 0.05$, as was the drug × breath interaction, $F(1, 39) = 6.7$, $p < 0.05$. (These interactions and both drug × breath × time interactions discussed subsequently occurred in the analyses involving single pre- and postsmoking ratings.) The means are shown in Fig. 1. Ratings were, naturally, near zero before smoking. They increased slightly after smoking placebo and markedly after smoking marijuana. For marijuana but not placebo, this increase was greater with the long than the short breath-holding duration. Follow-up analyses indicated that the difference between the long and short breath-holding durations was significant after smoking marijuana, $F(1, 39) = 6.7$, $p < 0.05$, but not after smoking placebo or before smoking marijuana or placebo.

Two of the individual sedation ratings showed different marijuana effects with the long and short breath-holding durations. Calmness showed a drug × breath × time effect, $F(1, 39) = 6.3$, $p < 0.05$. Marijuana smoking decreased calmness (i.e., increased excitement) relative to placebo overall, but this effect was greater with the long than short breath-holding duration. The difference between the long and short breath-holding durations approached statistical significance after

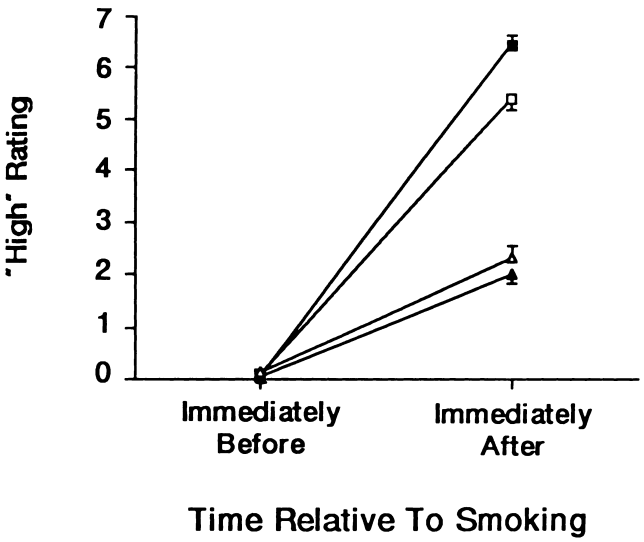

FIG. 1. "High" ratings (means ± standard errors) immediately before and immediately after smoking marijuana and placebo in all sessions. The treatments and breath-holding durations are represented as follows: ■, marijuana, long; □, marijuana, short; ▲, placebo, long; △, placebo, short.

TABLE 1

EFFECTS OF BREATH-HOLDING DURATION ON MEAN SUBJECTIVE RATINGS OF CALMNESS AND RELAXATION IN ALL SESSIONS

			Time	
Rating	Drug	Breath-Holding Duration	Immediately Before Smoking	Immediately After Smoking
Calmness	M	L	6.2 ± 0.2	5.4 ± 0.2
		S	6.5 ± 0.2	6.1 ± 0.2
	P	L	5.9 ± 0.2	6.4 ± 0.2
		S	6.6 ± 0.2	6.6 ± 0.2
Relaxation	M	L	6.4 ± 0.2	6.2 ± 0.2
		S	6.5 ± 0.2	7.0 ± 0.2
	P	L	6.5 ± 0.2	6.7 ± 0.2
		S	7.0 ± 0.2	7.2 ± 0.2

All values are means ± standard errors. M = marijuana; P = placebo; L = long; S = short. All ratings were made on scales from 0 to 10. Higher values represent greater calmness or relaxation. The drug × breath × time interactions in the analyses of variance were significant for calmness and relaxation, indicating that marijuana's effects differed with the long and short breath-holding durations (see text for discussion).

smoking marijuana, $F(1, 39) = 3.2$, $p < 0.10$, but was nonsignificant after smoking placebo and before smoking marijuana and placebo. The mean ratings are shown in Table 1.

Relaxation showed a drug × breath × time effect, $F(1, 39) = 4.2$, $p < 0.05$. Marijuana smoking increased relaxation with the short breath-holding duration, but decreased relaxation slightly with the long breath-holding duration. The difference between the long and short breath-holding durations approached statistical significance after smoking marijuana, $F(1, 39) = 3.9$, $p < 0.10$, but was nonsignificant after smoking placebo and before smoking marijuana and placebo. The mean ratings are shown in Table 1.

The overall effect of breath-holding duration was not significant in any of the analyses, i.e., there were no overall differences between ratings with the long and short breath-holding duration. There was one significant breath × time interaction, for "high" ratings in the analysis with four postsmoking ratings, $F(4, 156) = 2.7$, $p < 0.05$. However, this interaction was not independent of drug condition, being primarily attributable to the greater "high" ratings with the long than short breath-holding duration following marijuana smoking.

Overall Effects of Marijuana

Table 2 shows mean ratings of sedation and "high" before and immediately after smoking marijuana and placebo, averaged over all eight sessions. Also shown are means for the 10 individual sedation rating scales. Table 3 shows means of the three ratings of motivation and test performance that were obtained after each test during the first four sessions.

Both Tables 2 and 3 indicate the significant overall effects of marijuana, which were evidenced either by differences between marijuana and placebo in means averaged over all ratings (drug effects) or in the pattern of changes in ratings over time (drug × time effects). These effects indicated that marijuana, in comparison to placebo, produced a greater "high" feeling (Table 2), greater overall sedation (Table 2), and a perception of decreased motivation with respect to performance on the tests, as well as worsened test performance, i.e., doing poorer and being impaired by the drug (Table 3). Changes in the direction of marijuana-induced sedation were evident in 6 of the 10 individual sedation ratings, i.e., drowsy, dreamy, incompetent, fuzzy, clumsy, and mentally slow (Table 2). None of the foregoing ratings showed any tendency for the marijuana-induced changes to decrease relative to placebo over the four postsmoking ratings, i.e., the time course of these subjective effects extended beyond the period covered by these ratings (data not shown). Indeed, the drowsiness produced by marijuana tended, if anything, to increase in ratings following testing (data not shown).

In contrast to the six individual sedation ratings that showed marijuana-induced sedation, the remaining four ratings showed distinctive patterns. As discussed above, stimulant effects of marijuana were more pronounced with the long than the short breath-holding duration for the calmness and relaxation ratings.

Marijuana also produced a distinctive effect on boredom, $F(4, 156) = 2.7$, $p < 0.05$, for drug × time effect in the analysis with four postsmoking ratings. Ratings reflected increasing boredom following the three tests after smoking both marijuana and placebo, but this increase was greater following marijuana. In contrast, marijuana did not increase boredom immediately after smoking, i.e., its effect was contingent on testing. The differences in means (i.e., marijuana minus placebo means) were 0 before smoking, −0.2 immediately after smoking, and −0.1, 0.2, and 0.4 after the first, second, and third tests, respectively. Overall ratings for marijuana sessions also showed greater laziness than for placebo sessions, but this was attributable more to a baseline difference than an effect of marijuana smoking (Table 2).

Number of Puffs

Conceivably, subjects with the long and short breath-holding durations might have differed in number of puffs during

TABLE 2

MEAN SUBJECTIVE RATINGS OF "HIGH" AND SEDATION IN ALL SESSIONS

Rating	Drug	Time: Immediately Before Smoking	Time: Immediately After Smoking
Global Rating			
"High"	M	0.1 ± 0.02	5.9 ± 0.2‡¶
	P	0.1 ± 0.03	2.2 ± 0.1
Sedation Ratings			
Alert/drowsy	M	3.2 ± 0.2	4.4 ± 0.1‡¶
	P	3.0 ± 0.2	3.2 ± 0.1
Attentive/dreamy	M	2.7 ± 0.1	4.5 ± 0.2‡¶
	P	2.7 ± 0.1	3.2 ± 0.1
Tense/relaxed	M	6.4 ± 0.1	6.5 ± 0.1*
	P	6.8 ± 0.1	6.9 ± 0.1
Interested/bored	M	3.0 ± 0.1	3.2 ± 0.1
	P	3.1 ± 0.1	3.5 ± 0.1
Capable/incompetent	M	2.1 ± 0.1	3.8 ± 0.1‡¶
	P	1.8 ± 0.1	2.5 ± 0.1
Excited/calm	M	6.4 ± 0.1	5.7 ± 0.2§
	P	6.2 ± 0.2	6.5 ± 0.1
Clear-headed/fuzzy	M	2.6 ± 0.1	4.8 ± 0.1‡¶
	P	2.6 ± 0.1	3.4 ± 0.1
Well-coordinated/clumsy	M	2.4 ± 0.1	4.3 ± 0.2‡¶
	P	2.3 ± 0.1	3.0 ± 0.1
Quick-witted/mentally slow	M	2.8 ± 0.1	4.5 ± 0.1‡¶
	P	2.6 ± 0.1	3.2 ± 0.1
Energetic/lazy	M	4.1 ± 0.1	4.8 ± 0.1†
	P	3.8 ± 0.1	4.3 ± 0.1
Sedation (mean of above 10 individual ratings)	M	3.6 ± 0.1	4.7 ± 0.1‡¶
	P	3.5 ± 0.1	4.0 ± 0.1

All values are means ± standard errors. M = marijuana; P = placebo. Data for the long and short breath-holding durations are combined. All ratings were made on scales from 0 to 10. Higher values represent greater "high" or sedation. Significance levels are based on the effects of drug and drug × time in the analyses of variance described in the text. A significant drug effect indicates that the pooled mean rating before and after smoking marijuana differs from the pooled mean rating before and after smoking placebo. A significant drug × time interaction indicates that the change in ratings immediately after smoking marijuana, relative to before smoking, differs from the change in ratings immediately after smoking placebo, relative to before smoking.

*$p < 0.05$ for drug effect.
†$p < 0.01$ for drug effect.
‡$p < 0.001$ for drug effect.
§$p < 0.01$ for drug × time effect.
¶$p < 0.001$ for drug × time effect.

smoking, and this difference might have contributed to the apparent influence of breath-holding duration on marijuana's effects. In fact, the analysis of number of puffs showed no significant difference between the long and short breath-holding durations, which had means of 15.1 ± 0.2 and 15.7 ± 0.2 puffs, respectively. Because the interval between puffs was the same with both breath-holding durations, this also indicates that the total duration of smoking in the two conditions was comparable.

DISCUSSION

Breath-Holding Duration

The most important finding of the present study was that "high" ratings following marijuana smoking were greater with the long than the short breath-holding duration. This finding is consistent with the advice commonly given to marijuana users to hold the smoke in their lungs for a long time (20). Experimental verification of this phenomenon has proven elusive, with several studies failing to find significantly increased "high" ratings with longer breath-holding durations (2,31,34). However, two of these studies did observe higher blood levels of Δ^9-THC with longer breath-holding durations (2,31). If longer breath-holding durations increase the effective dose, increased "high" ratings would be expected. However, the effects may be relatively small in magnitude, and considerable variability among individuals in "high" ratings may contribute to the difficulty of detecting effects of breath-holding duration on "high" ratings.

TABLE 3

MEAN SUBJECTIVE RATINGS OF TEST PERFORMANCE AND MOTIVATION IN THE FIRST FOUR SESSIONS

Rating	Drug	Time		
		After First Test	After Second Test	After Third Test
Did: well/poor	M	4.4 ± 0.2	4.6 ± 0.2	4.5 ± 0.2*
	P	3.6 ± 0.2	3.6 ± 0.2	3.8 ± 0.2
Drug: improved/impaired	M	6.1 ± 0.2	6.1 ± 0.2	6.4 ± 0.2*
	P	5.3 ± 0.1	5.2 ± 0.1	5.3 ± 0.1
Were: motivated/unmotivated	M	2.6 ± 0.2	2.8 ± 0.2	3.2 ± 0.2†
	P	2.4 ± 0.2	2.5 ± 0.2	2.5 ± 0.2

All values are means ± standard errors. M = marijuana; P = placebo. Data for the long and short breath-holding durations are combined. All ratings were made on scales from 0 to 10. Higher values represent perception of worsened test performance or decreased motivation. Significance levels are based on the effects of drug in the analysis of variance described in the text. A significant drug effect indicates that the pooled mean rating for the three tests after smoking marijuana differs from the pooled mean rating for the three tests after smoking placebo.

*$p < 0.001$ for drug effect.

†$p < 0.01$ for drug effect.

Stimulation was also somewhat more prominent relative to sedation with the long than the short breath-holding duration in the present study. This difference was evident in the calmness and relaxation ratings, but not in the other eight individual sedation rating scales. Subjects reported decreased calmness (i.e., increased excitement), which tended to be more marked with the long than the short breath-holding duration. Furthermore, relaxation increased with the short breath-holding duration, but decreased with the long breath-holding duration, following marijuana smoking. One previous study (34) found an opposite pattern, i.e., greater sedation with a long, relative to a short, breath-holding duration. The explanation for these differing results is uncertain. They could be related to any of several differences between the studies, for example, the measures of sedation that were used or the characteristics of participants. To whatever extent breath-holding duration is an indirect manipulation of Δ^9-THC dose, this contradictory pattern seems mirrored by some findings with overt manipulations of dose. Some studies have reported dose-related increases in sedative effects of marijuana (1,12,22), while others have reported dose-related increases in stimulant effects (7,8). Perhaps other, nonpharmacological factors, such as the environment in which marijuana is smoked, influence the mixture of sedative and stimulant effects produced by the drug; for example, the stimulant effects might be less prominent when marijuana is smoked alone before bedtime than at an animated recreational gathering.

Comparison With Cognitive Effects

Breath-holding duration, although it influenced the subjective effects of marijuana, did not produce any effects that were independent of the drug treatment, i.e., occurred equally after smoking of marijuana and placebo. In contrast, we previously reported that breath-holding duration affected performance on tests of memory, associative processes, and reaction time equally after smoking of marijuana and placebo; and exerted only minimal effects on cognitive test performance that were treatment-specific, i.e., specifically associated with smoking of marijuana, relative to placebo (4). We speculated that either physiological or psychological factors—for example, exposure to carbon monoxide in smoke or subjects' expectations (18)—might have produced the cognitive effects of prolonged breath-holding that were independent of the drug treatment. The present findings seem more consistent with a physiological than a psychological explanation of this previously observed pattern. Subjective effects would seem more likely to be influenced by expectancies than cognitive test performance, but the subjective effects of breath-holding duration that we observed were treatment specific, and, therefore, more likely to have been pharmacological than nonpharmacological in nature. For example, one could argue that "high" ratings following marijuana smoking were greater with the long than the short breath-holding duration because the subjects were experienced marijuana users who were probably accustomed to smoking with a long-breath holding duration and expected mild effects when instructed to smoke with a short breath-holding duration. However, such an argument would predict that the pattern following placebo smoking would be similar to that following marijuana smoking, contrary to the observed results.

Sedation vs. Stimulation

Marijuana increased overall sedation in the present study. This is consistent with previous studies, for example, Zacny and Chait (34). The specific sedation rating scales reflecting marijuana-induced sedation in the present study also showed some agreement with previous studies of marijuana or Δ^9-THC, i.e., with respect to the present findings of increased ratings of incompetence and mental slowness (3), fuzziness (3,10,16), drowsiness (1,22), and dreaminess (26).

Paradoxically, our subjects experienced some stimulant effects from smoking marijuana, as discussed above. Other studies have also reported some limited stimulant effects from marijuana or Δ^9-THC (3,10,21,26,34).

The mixture of sedative and stimulant effects of marijuana has been noted in other studies (10). Sedation and stimulation are usually regarded as opposite extremes of a single dimension. In a recent review, de Wit and Kirk (13) suggested that

the mixed sedative and stimulant effects of marijuana are more consistent with a multidimensional interpretation of these domains of experience. The results of the present study support this view. The 10 sedation rating scales used in the present study were derived from 16 scales that were originally grouped into four categories by Norris (23). The six ratings that showed changes in the direction of marijuana-induced sedation were categorized as reflecting "mental sedation" or "physical sedation." In contrast, the two ratings sensitive to marijuana-induced stimulation were categorized as reflecting "tranquilization." A subsequent factor analysis provided somewhat consistent results, with the former six ratings all loading on a "sedation" or "alertness" factor, while the latter two ratings constituted an "anxiety" or "calmness" factor (5,14). Based on these interpretations of the rating scales, the results of the present study suggest that there may be a dissociation between marijuana's effects on the dimension of sedation and the related dimension of tranquilization.

Although there has long been interest in developing nonsedating tranquilizers, the mixture of sedative and stimulant effects produced by marijuana in the present study is not characteristic of typical central nervous system depressants or stimulants. However, psychedelic drugs such as LSD reportedly produce paradoxical combinations of coexisting, seemingly contradictory mood states (19). To the extent that marijuana produces, albeit with limited intensity, some of the subjective effects characteristic of psychedelic drugs, the occurrence of both sedative and stimulant effects following marijuana smoking seems consistent with the paradoxical effects of psychedelic drugs on mood.

Verification of the present results and clarification of the sedative and stimulant effects of marijuana should be sought using other methodologies and instruments for assessing subjective effects of drugs, such as visual analog scales, the Addiction Research Center Inventory (15), and the Subjective Drug Effects Questionnaire (19). The present study used scales with anchors at both ends specifying the extremes of sedation and stimulation. It would be desirable to verify that similar effects are observed using scales with single anchors, which specify sedation for some scales and stimulation for others. It would also be desirable to attempt to replicate the pattern of results that we observed using all 12 of Norris' scales (23) for mental sedation, physical sedation, and tranquilization.

Boredom

Marijuana smoking produced a distinct effect on boredom. The drug did not increase boredom immediately after smoking, but only after two or three tests had been administered during the first pair of sessions. Although the possibility that this finding was attributable solely to a change in drug effects over time cannot be excluded, a more plausible explanation is that marijuana's effects on boredom were contingent on testing, i.e., that the environment influenced the drug's effects. Boredom with testing would be consistent with other effects produced by marijuana, i.e., subjects' perception of worsened test performance and decreased motivation with respect to test performance.

Limitations of the Present Study

The present study lacked some features that would have helped clarify the influence of prolonged breath holding, primarily because this influence was not a focus of the original study design, but was addressed after four subjects experienced adverse reactions following smoking with a long breath-holding duration. These features included: manipulation of breath holding duration within subjects; quantitation of plasma Δ^9-THC concentrations; measurement of smoke exposure, for example, alveolar carbon monoxide levels; and measurement or control of additional parameters of smoking topography, for example, puff volume. We did not include any measurement of actual breath-holding duration, for example, respiratory inductive plethysmography; nor did we examine more than two breath-holding durations or compare the effects of breath-holding duration for differing doses of marijuana. Our manipulation of breath-holding duration did not separate inhaling from breath-holding, as do some paced smoking procedures (9,10), and was much less controlled than other techniques for administering marijuana smoke, for example, syringe methods (33,34). On the other hand, our smoking procedure was more naturalistic than those used in previous studies that failed to detect any influence of breath-holding duration on "high" ratings (2,31,34). Other modifications of smoking topography may covary with breath-holding duration and contribute to its effects on "high" ratings under naturalistic conditions. These modifications may have been operative in the present study, but not in previous ones, and may have been responsible for the differing results.

CONCLUSION

We found that prolonged breath holding increased the "high" produced by marijuana, as many marijuana users believe. This is important, because results of previous studies have called this belief into question. The greatest difference between the subjective effects of marijuana observed in the present study and the drug's effects on test performance described previously (4) concerned the influences of breath-holding duration. In the present study, breath-holding duration influenced subjective experiences after subjects smoked marijuana more than after they smoked placebo, whereas the influences of breath-holding duration on test performance described previously were generally similar after smoking of marijuana or placebo. The present findings also provided some insights into marijuana's paradoxical combination of sedative and stimulant effects, as well as the drug's effects on subjectively rated motivation. Although many researchers prefer to emphasize objectively measurable drug effects relative to subjective drug effects, the present findings illustrate the importance of including subjective, as well as objective, assessments when trying to understand the full spectrum of activities of a drug.

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