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Acute and Residual Effects of Marijuana in Humans

REGINALD V. FANT, STEPHEN J. HEISHMAN, EDWARD B. BUNKER AND WALLACE B. PICKWORTH

National Institute on Drug Abuse, Intramural Research Program, Addiction Research Center, Baltimore, MD 21224

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FANT, R. V., S. J. HEISHMAN, E. B. BUNKER AND W. B. PICKWORTH. *Acute and residual effects of marijuana in humans.* PHARMACOL BIOCHEM BEHAV **60**(4) 777–784, 1998.—Marijuana continues to be the most commonly abused illicit drug in the United States. Because many people abuse marijuana during the evening and on weekends and then go to work or school the next day, more research is needed on the residual effects of marijuana. The current study sought to examine both acute and residual subjective, physiologic, and performance effects of smoking a single marijuana cigarette. Ten healthy male volunteers who reported recent use of marijuana resided on a residential research ward. On three separate days, subjects smoked one NIDA marijuana cigarette containing either 0%, 1.8%, or 3.6% Δ^9-tetrahydrocannabinol (THC) according to a paced puffing procedure. Subjective, physiologic, and performance measures were collected prior to smoking, five times following smoking on that day, and three times on the following morning. Subjects reported robust subjective effects following both active doses of marijuana, which returned to baseline levels within 3.5 h. Heart rate increased and the pupillary light reflex decreased following active dose administration with return to baseline on that day. A new finding was that marijuana smoking acutely produced decrements in smooth pursuit eye tracking. Although robust acute effects of marijuana were found on subjective and physiological measures, and on smooth pursuit eye tracking performance, no effects were evident the day following administration, indicating that the residual effects of smoking a single marijuana cigarette are minimal. © 1998 Elsevier Science Inc.

Marijuana THC Subjective effects Performance effects Cardiovascular effects Pupillary effects Smooth pursuit eye tracking Cognitive tasks Psychomotor tasks Human behavioral pharmacology

MARIJUANA is one of the most commonly used illicit substances in the United States today (42). Recent evidence indicates that the use of marijuana is on the rise, particularly among young people (43). In 1994, approximately 16.7, 30.4, and 38.2% of 8th, 10th, and 12th graders, respectively, reported having ever used marijuana; an estimated 7.8, 15.8, and 19.0% of these students reported having used within the past month (43). Additionally, marijuana has been cited as the most commonly abused illicit substances with 15% of full-time employed males using the drug within the past month; however, the correlation between positive urine screen and performance impairment is unclear (24). Because many people use marijuana in the evenings or on weekends and then report to school or work the next day, it is important to understand the residual effects of marijuana smoking as well as the acute effects.

The acute effects of marijuana have been well documented. Marijuana has been shown to influence subjective states, performance, and physiological measures. For example, one study found that marijuana produced significant changes on visual analog scale items of high, stoned, impaired, sluggish, confused, clear-headed, and relaxed (2). The same study found performance decrements on digit recall, digit symbol substitution, and divided attention visual search tasks. Another study found similar changes in subjective and performance measures, as well as dose-dependent increases in heart rate (16).

The effects of some other drugs of abuse have been shown to carry over to the next day after dosing. For example, various "hangover" symptoms of alcohol have been reported by a very large percentage of current drinkers (37). Some laboratory studies have shown that performance on the day after drinking is impaired (23,35); however, others have not (8,39).

Requests for reprints should be addressed to Reginald V. Fant, Ph.D., Clinical Pharmacology Branch, NIDA, Intramural Research Program, P.O. Box 5180, Baltimore, MD 21224.

Residual subjective and performance effects have also been reported in laboratory studies the morning after barbiturate (32) and benzodiazepine (25,32) administration.

In contrast, the residual effects of marijuana have been difficult to verify (24). A review of studies on the residual effects of marijuana concluded that a brief "drug residue" effect may be observed up to 24 h after a single marijuana smoking bout (33). For example, studies on the next-day effects of marijuana on airline pilots found significant impairment on flight simulator performance on the day following smoking (20,47); however, a third study failed to replicate this next-day effect (19). Chait et al. (7) found that subjects who smoked marijuana in the evening reported mild subjective "hangover" effects the morning after smoking (about 9 h postsmoking); however, the residual performance effects were minimal. A subsequent study found small decrements in reaction time on a divided attention task as well as substantial decrements in performance on backward digit span on the day following marijuana (6). After smoking two or four marijuana cigarettes, subjective and cardiovascular measures returned to baseline levels on the day following smoking marijuana; however, performance impairment persisted for as long as 24 h after smoking (14).

Because previous studies have shown performance impairment as long as 24 h following two or more marijuana cigarettes, the present study was designed to determine the effects of a single marijuana cigarette on the day of smoking and the day after. To test these effects, a battery of subjective, physiologic, and performance measures was used.

METHOD

Subjects

Ten healthy male subjects participated in this inpatient study. Their mean age was 26.8 years (range: 24–31) and their mean weight was 68.0 kg (range: 59.5–76.4). Inclusion criteria included: age 21–31; current marijuana use of at least twice in the past month but not to exceed three marijuana cigarettes per week. Exclusion criteria included: history or active cardiovascular disease, seizure disorder, addiction to drugs other than caffeine or nicotine. Volunteers resided on the clinical ward of the Addiction Research Center for the 2-week duration of the study. Subjects were paid approximately $550 for completion of the study; they were able to earn up to an additional $50 in incentive bonus for the performance tasks as described below. Before participation in the study, each subject signed an informed consent document that was approved by the local institutional review board and met guidelines developed by the U.S. Department of Health and Human Services.

Procedure

Each of the subjects participated in three experimental sessions; each session was separated by at least 3 days. During each session, subjects smoked a single cigarette containing either 0, 1.8, or 3.6% Δ^9-tetrahydrocannabinol (THC) according to a paced-puffing procedure (15): eight puffs per cigarette, 20-s puff retention, 40-s interpuff interval. The THC content of the cigarettes averaged 0, 15.6, and 25.1 mg, respectively. Because of safety concerns for the volunteers, the order of treatments was force-randomized such that the subjects always smoked the low dose before the high dose. All of the subjects were exposed to all treatment conditions in a double-blind manner. Subjects were trained to a level of performance where their speed and accuracy plateaued as in other experiments (29,38). Specifically, each subject participated in a minimum of 15 trials on each performance task. An individual's performance was regarded as stable when the scores of three successive trials did not differ by more than one standard deviation of the mean of those trials.

Experimental Measures

Physiologic, subjective, and performance measures were collected twice in the hour prior to smoking; at 0.25, 1, 1.75, 3.5, and 5.5 h after smoking to assess acute effects; and at 23, 24, and 25 h after smoking to assess the residual effects.

Physiologic measures. At each measurement time, pulse rate, systolic and diastolic blood pressure, skin temperature, and respiratory rate were recorded. Pupillary diameter was measured using a computer-based video system, EPS-100 Eye Performance System (Eye Dynamics, Inc., Torrance, CA). Pupillary diameter was recorded in the dark (prestimulus) and the responses were recorded to two levels of light stimuli: 8 footcandles (ftcd) for 5 s and 20 ftcd for 8 s. At each level of light stimulus, the following light-reflex measures were recorded from each eye: response latency, minimum diameter, recovery slope, percent of recovery at the end of the light stimulus, and hippus (number of oscillations during the recovery phase of the light reflex).

Subjective measures. The subjective effects of marijuana were quantified using the 17-item marijuana scale of the Addiction Research Center Inventory (ARCI) (12). In addition, seven visual analog scales were presented which measured subjective ratings of: "feel drug effect," "high," "like drug," "sleepy," "drunk," "stoned," and "impaired." Subjects responded to the questions on a computer-delivered 100-mm visual analog scale anchored with "not at all" on one end and "extremely" on the other.

Performance measures. Smooth-pursuit eye movements were measured using a computer-based video system, EPS-100 Eye Performance System (Eye Dynamics, Inc., Torrance, CA). This instrument tests for smooth-pursuit eye movements in each eye as subjects followed a target moving between 0 and 45 degrees of horizontal visual angle. For purposes of analyses, the tracking angle was divided into the central visual field (0 to 22 degrees) and peripheral visual field (22 to 45 degrees). Tracking was recorded twice. In the first instance, the target moved at 15 degrees per second through the entire 45 degree visual field; in the second instance, the target moved at 15 degrees per second in the first 35 degrees, and at 6 degrees per second in the final 10 degrees.

Psychomotor performance was measured using the circular lights task (14). In this task, subjects were required to rapidly press a single lighted button on a 71 $\times$ 71 cm panel of lights that contained 33 button-lights arranged in three concentric circles. When the illuminated button was pressed, another immediately lighted. Subjects performed the task for 1 min. The number of correctly pressed buttons was the dependent measure. As an incentive for performance subjects were awarded $.01 for each correct response.

Four computer-delivered tasks from the Walter Reed Performance Assessment Battery (PAB) (41) were chosen to measure aspects of cognitive performance. These tasks measured rapid arithmetic skill, digit recall, logical reasoning, and spatial perception as described below. For each task, three dependent variables were analyzed: number of correct responses, percentage of correct responses, and response time. Subjects were awarded $.01 for each correct response.

In the serial addition/subtraction task, two digits appeared sequentially on the screen for 250 ms followed by a plus or mi-

nus sign. The subjects were required to perform mentally the indicated operation and to answer with a single keystroke on the numeric keypad of the computer. If the answer was a two-digit number (e.g., 15), the correct response was the unit digit (e.g., 5). If the answer was a negative number (e.g., −2), 10 was added to the answer and the resulting single positive digit was entered (e.g., 8). The task had a maximum of 50 problems or 120 s.

In the digit recall task, nine digits appeared on the computer screen for 1 s followed by 3 s of blank screen. Then eight of the digits appeared in a different order and the subject was required to enter the single missing digit on the numeric keypad of the computer. Ten problems were presented.

In the logical reasoning task, a statement describing the relationship between two letters (e.g., A precedes B) appeared on the video screen. Below the statement the letters appeared in the order AB or BA. The subject was required to determine with a single keystroke ("Y" or "N") whether the statement accurately described the sequence of the letters (true or false). A total of 32 trials (or 150 s) were presented.

In the mannequin task, a stick figure of a person holding a square-shaped object in one hand and a circular shaped object in the other was presented on the monitor. The mannequin could be facing the viewer or facing away from the viewer and could be upright or inverted. Surrounding the mannequin was a square or circle. The subject was required to determine in which hand (right or left) the mannequin held the object that corresponded to the surrounding shape. A total of 16 trials was presented.

Data Analyses

Each dependent measure was subjected to two-way repeated measures analysis of variance (ANOVA) (46). Data collected at the two baseline time points were averaged. The two factors of each of the ANOVAs were dose (three levels: placebo, 1.8 and 3.6% THC) and time (nine levels: baseline, 0.25, 1, 1.75, 3.5, 5.5, 23, 24, and 25 h postsmoking). Because of the possibility of baseline differences prior to smoking, only significant dose by time interactions were taken to indicate significant drug effect. For all subjective measures, data from one of the subjects were eliminated, and data from two subjects were eliminated for measures of drunkenness and feeling a drug effect because of inconsistencies in ratings. For pupillary measures, data from the two eyes were averaged into a single score. Where there were significant dose by time interactions, post hoc analyses were performed using Tukey's honestly significant difference test to determine time points that were significantly different from baseline and/or placebo.

To examine the possibility that subjects learned to perform the tasks better across subsequent session days because of practice, baseline data for the three experimental session days were examined without regard to the drug administered on that day. To examine the possibility of carry-over effects, baseline data were examined as a function of the drug administered on the previous session. Because of the forced randomization used in the experimental design, the 3.6% THC marijuana dose was administered in the final session for 7 of the 10 subjects; therefore, carry-over comparisons were only made between the placebo and the 1.8% THC marijuana dose.

RESULTS

Subjective

Marijuana smoking produced dose by time interaction effects on six subjective visual analog measures including: "feel drug effect," $F(16, 128) = 14.5$, $p < 0.001$, "high," $F(16, 128) = 16.4$, $p < 0.001$, "like drug," $F(16, 112) = 7.0$, $p < 0.001$), "drunk," $F(16, 128) = 2.3$, $p < 0.01$, "stoned," $F(16, 112) = 7.4$, $p < 0.001$, and "impaired," $F(16, 128) = 3.3$, $p < 0.001$. The pattern of responding was similar for each of these measures; mean response scores on the measure of "high" are representative and are shown in Fig. 1. In general, post hoc analyses showed that visual analog scores were highest at the 0.25-h time point and remained significantly elevated above placebo levels up to 1.75 h postsmoking in the 1.8% THC condition and up to 3.5 h postsmoking in the 3.6% THC condition. While the duration of effects was longer in the 3.6% THC condition, there was no difference in the magnitude of effects between the two active dose conditions. Dose by time interactions were not significant on the visual analog measure of "sleepy" or on the marijuana scale of the ARCI.

Cardiovascular

Dose by time interactions were demonstrated on measures of heart rate (Fig. 2), $F(16, 144) = 6.45$, $p < 0.001$, systolic blood pressure, $F(16, 144) = 1.7$, $p < 0.05$, and skin temperature, $F(16, 144) = 1.8$, $p < 0.05$. Post hoc analyses showed that heart rate was increased significantly above placebo levels in both active marijuana conditions at the 0.25-h postsmoking time point and remained significantly elevated through the 1-h postsmoking time point in the 3.6% THC condition. Systolic blood pressure was only increased above placebo levels in the 1.8% THC condition at the 0.25-h postsmoking time point. The effects of marijuana on skin temperature were small in magnitude and did not reach statistical significance over placebo levels in post hoc analyses.

Pupillary

Initial pupil diameter (preceding exposure to the light stimulus) was not significantly affected by marijuana; no significant dose by time effects were noted preceding either the bright or dim light exposure. Pupillary responses to the light stimuli were diminished by marijuana, as shown in Fig. 3. Dose by time interactions were shown on the constriction amplitude measure (the difference between initial and minimum

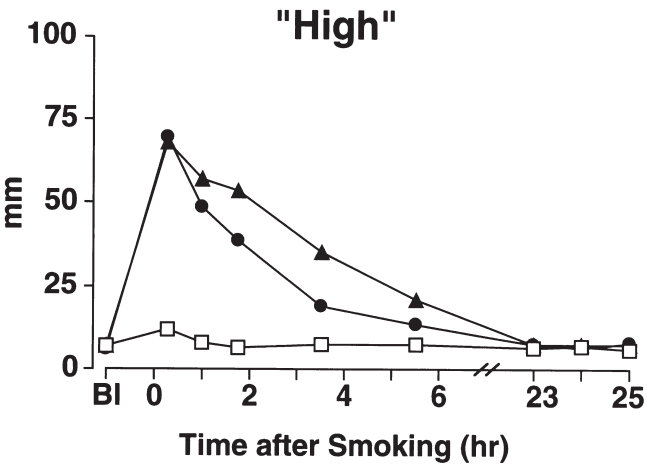

FIG. 1. Mean ratings of self-reported ratings of "high" on a computerized 100 mm visual analog scale before and after smoking one marijuana cigarette containing 0% THC (placebo) -□-, 1.8% THC -●-, or 3.6% THC -▲-.

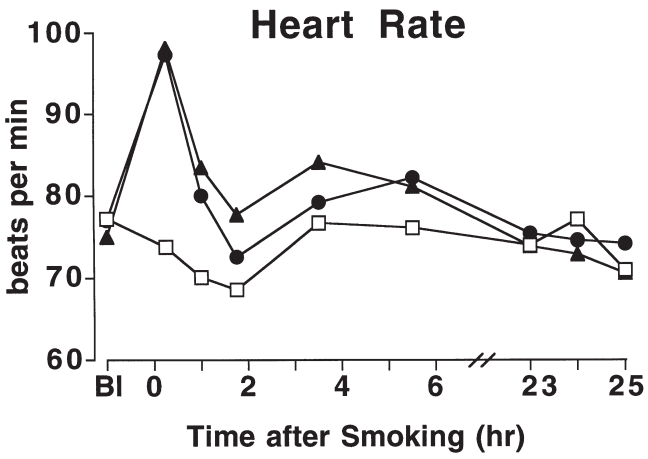

FIG. 2. Mean heart rate before and after smoking one marijuana cigarette containing 0% THC (placebo) -□-, 1.8% THC -●-, or 3.6% THC -▲-.

diameters) in both dim, $F(16, 144) = 2.0$, $p < 0.05$, and bright, $F(16, 144) = 2.1$, $p < 0.05$, stimulus conditions. These effects were statistically significant from placebo in the 3.6% THC condition only; effects were evident at the 0.25-h time point and lasted for up to 1.75 h after smoking in the dim condition and up to 1 h in the bright condition. Marijuana did not affect the time taken to reach the minimum diameter following either light stimulus. The final diameter (diameter at the end of the stimulus presentation, the measure of pupillary escape) was significantly affected by marijuana in the bright stimulus condition, $F(16, 144) = 2.2$, $p < 0.01$. Post hoc analyses showed that these effects were only significantly greater than placebo following the 3.6% THC dose and were increased significantly as soon as 0.25 h postsmoking, and were the largest at the 1.75-h time point. Final diameter was unaffected by marijuana following dim stimulus presentation.

Performance

Smooth pursuit was significantly impaired by marijuana dosing, particularly in peripheral visual fields (Fig. 4). Significant dose by time interactions were shown for peripheral pursuit measures for trials in which a constant pursuit speed of 15 degrees per s was required, $F(16, 144) = 3.0$, $p < 0.001$). Post hoc analyses showed that pursuit speed was slowed below placebo levels in both the 1.8 and 3.6% THC conditions; however, only speeds in the 3.6% THC condition were significantly slowed. Tracking speed was significantly decreased from baseline levels 1 h after smoking and were largest at the 1.75-h time point, at which time speeds following the 3.6% THC marijuana cigarette were significantly slower than placebo speeds. Similar slowing was noted in the peripheral trial in which a change in pursuit speed from 15 degrees per second to 6 degrees per second was required. In this trial, pursuit speeds after both active doses of marijuana fell significantly below placebo speeds and were most marked at the 1.75-h time point. Similar decrements in pursuit speeds were noted in the central field pursuit trials; the ANOVA performed on data from the second trial showed a dose by time interaction that neared significance ($p < 0.07$). Pursuit speed was decreased primarily in the 3.6% THC dose condition and was slowest at the 1.75-h time point.

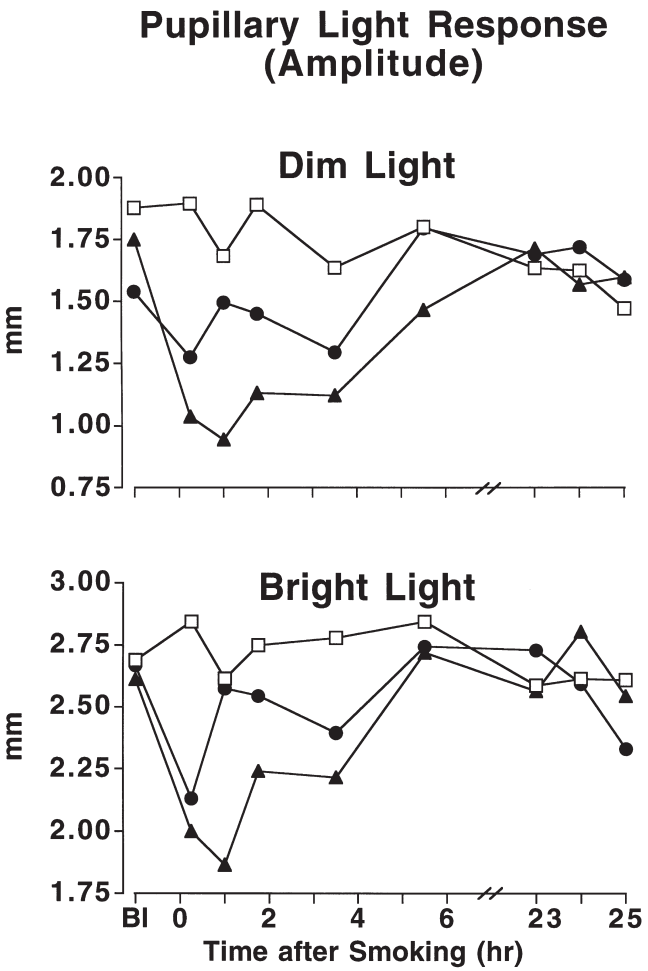

FIG. 3. Mean constriction amplitude in response to a dim (8 ftcd) or bright (20 ftcd) light stimulus before and after smoking one marijuana cigarette containing 0% THC (placebo) -□-, 1.8% THC -●-, or 3.6% THC -▲-.

Changes in other performance measures following marijuana smoking were very small. Of the other performance variables examined, only the response time measure of the logical reasoning task showed significant dose by time interactions, $F(16, 144) = 1.8$, $p < 0.05$. However, the effects were not dose dependent, and no post hoc comparisons reached significance at $p < 0.05$.

Practice and Carry-Over Effects

Of the many subjective, physiologic, and performance measures employed in the study, only two of the four computer-delivered cognitive performance measures systematically changed more than 20% across session baselines when examined without regard to drug administration. On the logical reasoning task, performance speed was increased across sessions; mean response times at baseline were 7.9, 5.8, and 4.9 s on the first, second, and third sessions, respectively. Because response times were faster on this task, the number attempted and the number of correct responses were likewise increased; however, the percentage of correct responses was not increased, demonstrating that accuracy was not changed across

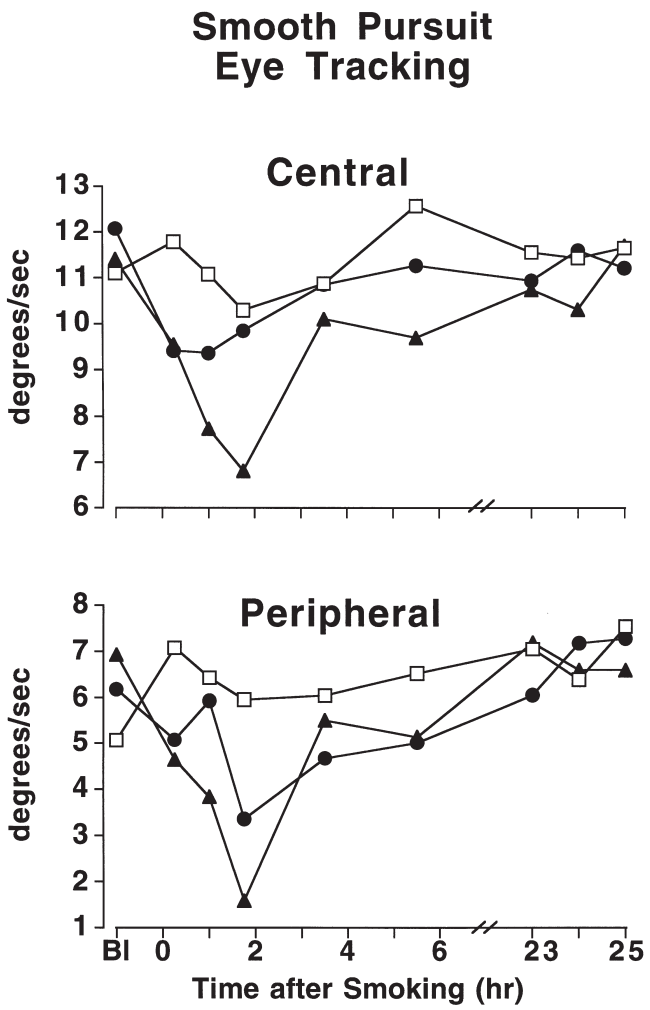

FIG. 4. Mean smooth pursuit eye tracking speeds before and after smoking one marijuana cigarette containing 0% THC (placebo) -□-, 1.8% -●-, or 3.6% THC -▲-. "Central" refers to tracking speeds within 0 degrees to 22 degrees from the center of the visual field; "peripheral" refers to speeds from 22 degrees to 45 degrees from the center.

sessions. Performance speed on the mannequin task was likewise increased with response times decreasing from 4.4 s at baseline on the first session to 3.1 and 3.0 in the second and third sessions, respectively.

With regard to carry-over effects, there were no differences greater than 20% on baseline measures on sessions preceded by placebo or the 1.8% THC marijuana dose.

DISCUSSION

The doses of marijuana smoked in the present study produced pronounced subjective effects (i.e., high, stoned, drug liking), indicating that psychoactive doses of THC were delivered to subjects. These effects peaked at the time point immediately after smoking and lasted up to 3.5 h after smoking in the high dose (3.6% THC) condition. The peak magnitude of effects was similar for both active doses; however, the effects declined at a faster rate in the low dose condition. These subjective effects were of a similar magnitude as those found elsewhere (2).

Marijuana smoking also produced cardiovascular effects similar to those reported elsewhere (2,16). Heart rate was significantly increased over placebo levels in both active THC conditions. This effect was evident immediately after smoking and lasted up to 1 h after smoking in the high dose condition.

Pupillary measures have been proposed as a sensitive index of drug-induced performance impairment and as a noninvasive measure to detect recent drug ingestion (28). Marijuana (3.6% THC) significantly reduced the pupillary constriction amplitude and final constriction diameter. These effects were observed in both eyes, after both a low and high light stimulus; the effects were maximal about 1 h after smoking the marijuana cigarettes. These data strongly suggest that marijuana administration diminishes the response to a light flash (phasic response), but the lack of effect on the prestimulus diameter of the pupil indicates that marijuana causes no effects on mechanisms involved in the tonic regulation of pupillary size. The results of the present study are similar to those reported by Waldorf et al. (44). Tennant (40) also reported that marijuana obtunded the light reflex but did not cause a change in the pupil diameter. In another study, a high dose of smoked marijuana diminished the constriction amplitude, constriction, and dilation velocities of the light reflex and caused a small (0.5 mm) decrease in pupil size (28). Taken together, these studies suggest that marijuana smoking consistently affects the phasic response to a light flash; however, the effect on the resting (tonic) diameter is small.

The dissociation between neural mechanisms controlling phasic response to a light stimulus (light reflex) and tonic pupil size has been observed after opiate administration to animals (30,36) and humans (27,31). However, disassociation of tonic and phasic responses are confounded by the profound miosis caused by the opiates. Specifically, it is difficult to determine if the light reflex is obtunded by a direct action of the opiates or because their miotic effect allows less light to stimulate the retina. The marijuana-induced diminution of the light reflex without changes in pupil size observed in the present study support the notion that separate neural mechanisms mediate the tonic and phasic reactions to light in the human pupil.

A new finding of the study was that there were consistent decrements in smooth pursuit eye tracking in the central (0 to 22 degrees) and peripheral (22 to 45 degrees) visual fields. After both doses of marijuana, smooth-pursuit velocity was significantly less than the velocity in the placebo condition. This effect was evident at 0.25 h after smoking and persisted for up to 5.5 h after smoking, although there were no significant residual effects on the day after smoking. Eye movement control is mediated in widely distributed regions of the brain including the cortex, brain stem, and cerebellum (22). Eye movement recordings are extremely sensitive indicators of brain functioning and could be useful markers of drug intoxication and neuropathology. Several studies have shown that saccadic eye movement is adversely affected by centrally acting drugs including opiates, benzodiazepines, barbiturates, and ethanol [review: (11)]. A study on the effects of marijuana on eye movements, however, found no effects on saccadic eye movement or smooth-pursuit velocity (3). The results of the present study indicate that marijuana affects smooth-pursuit eye movement.

Although marijuana affected smooth pursuit eye movements, smoking one marijuana cigarette did not impair performance on any of other the cognitive or psychomotor tests. The lack of impairment found in the present study is consistent with numerous other studies that also reported minimal

or no effects after smoking one or more marijuana cigarettes on a variety of psychomotor and cognitive tests (1,8–10,15). Some other studies that have used comparable dosing parameters (number of puffs, marijuana potencies) have reported marijuana-induced impairment on psychomotor (16,17,45) and cognitive (4,13,18) tests. For example, one study in which the number of puffs of marijuana was varied from 4 to 25, reported that only the 25-puff, high-potency (3.55% THC) condition reliably impaired performance (2). Thus, the performance effects of smoking a single marijuana cigarette may depend upon the drug history of subjects, environmental factors, and performance tests. Because of the effects of marijuana on smooth pursuit eye tracking, it is possible that laboratory tasks in which relevant stimuli are presented in the peripheral area of the visual field (driving and flight simulators) may be more sensitive to the effects of marijuana than those employed in the present study in which the tasks were presented in the central visual field (i.e., on the computer).

Given the lack of acute effects on performance measures other than smooth-pursuit eye tracking, it is not surprising that we found no evidence of impaired cognitive or psychomotor performance 24 h after marijuana smoking. A review supported by the National Research Council (24) could not conclude occasional marijuana use produces measurable next-day performance effects. Lack of evidence for a residual effect occurred in other studies that used doses of marijuana comparable to those used in the present study. For example, Chait et al. (7) found no residual impairment in tests of card sorting, free recall, and digit symbol substitution; however, performance on a time estimation task was impaired. Similarly, Chait and Perry (8) reported minimal next-day impairment on a test battery that included digit symbol substitution, backward digit span, logical reasoning, divided attention, and free recall. However, in studies with larger dose of marijuana, residual impairment was more likely to be observed. When subjects smoked the equivalent of one marijuana cigarette (eight puffs) in the afternoon and in the evening, they were impaired the next morning on tests of time estimation, backward digit span, and divided attention (6). Heishman et al. (14) found evidence for residual impairment on tests of arithmetic and digit recall after subjects had smoked two or four marijuana cigarettes the day before. It appears that observance of residual marijuana-induced behavioral impairment is a function of dose, and that one marijuana cigarette is not sufficient to produce next-day impairment on relatively simple laboratory tests. On complex tasks, such as a flight simulator, studies have reported impairment 24 h after smoking one marijuana cigarette (20,47). However, another study failed to replicate this finding (19). More research using complex "real-world" performance measures is needed to expand the scope of investigation of drug-induced residual behavioral effects.

Another factor that may influence the likelihood of observing next-day effects is the drug history of subjects tested. In the present study, subjects with moderate marijuana use (<3 times weekly) were tested. Block and Ghoneim (5) have shown that heavy (≥ 7 times weekly) marijuana users exhibited deficits in mathematical and verbal abilities on standardized educational tests compared with matched subjects who did not use marijuana. Such deficits were not observed in subjects who used marijuana less frequently. A recent study reported that daily marijuana users were impaired in their ability to sustain and shift attention after at least 19 h of marijuana abstinence compared to infrequent marijuana users (34). Thus, heavy use of marijuana may predispose an individual to exhibit residual behavioral impairment.

The forced randomization procedure used in this study may have confounded some of the performance measure results. Because the 1.8% THC marijuana dose was always administered before the 3.6% THC dose, it is possible that subjects may have done better after the larger dose because of the additional day(s) of practice. To test for the presence of a practice effect, baseline data were compared across the three sessions. Only 2 of the 13 cognitive performance measures showed changes across the sessions. Both of these changes were related to speed of performance rather than accuracy. This indicates that performance was stable across session days at baseline and that there was no evidence of a practice effect.

Because the low-dose THC condition always preceded the high THC condition, some THC may have been in the circulation at the time of high-dose delivery. To test for "carry-over" effects, baseline session data were examined with regard to the drug administered in the prior session. There were no baseline differences greater than 20% on days preceded by administration of the placebo vs. the 1.8% THC dose, suggesting that carry-over effects were not evident following the 1.8% dose. However, because the 3.6% THC marijuana dose was administered in the final session for seven of the subjects and because the 1.8% THC condition never followed the 3.6% condition, comparisons could not be made between baseline data preceded by this dose vs. the 1.8% and placebo doses. Thus, a completely randomized experimental design may have yielded slightly different results because of the possibility that the effects of the 3.6% THC dose may have still been evident if followed by other doses.

Finally, there is the possibility that subjects learned to perform the tasks under the influence of marijuana in the 1.8% THC condition, which may have aided them while under the influence of the higher marijuana dose. Dissociation, or state-dependent learning, refers to the fact that information learned while drug free may not be easily recalled while on a drug and, conversely, that information learned while on a drug may not be easily recalled while drug free (21). This phenomena has been demonstrated using a variety of drugs and tasks (26). Thus, in the present study, the practice obtained while subjects were under the influence of the low dose of marijuana may have influenced performance while under the high dose. Without this practice, marijuana-induced performance impairment in the 3.6% condition may have been more evident.

In summary, the results of the present study and others suggest that the dose of marijuana, the complexity of the task, and the drug history of the subject are important determinants for the residual effects of marijuana. Although acute administration of marijuana caused subjective, physiologic, and performance changes, these effects were short-lived, and none were present 24 h later. Extremely sensitive psychomotor and cognitive testing will be needed to verify potential residual effects of a single marijuana cigarette.

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