Comparative Effects of Alcohol and Marijuana on Mood, Memory, and Performance

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HEISHMAN, S. J., K. ARASTEH AND M. L. STITZER. Comparative effects of alcohol and marijuana on mood, memory, and performance. PHARMACOL BIOCHEM BEHAV 58(1) 93–101, 1997.—This study compared subjective and behavioral effect profiles of alcohol and smoked marijuana using technology that controlled puffing and inhalation parameters. Male volunteers (n = 5) with histories of moderate alcohol and marijuana use were administered three doses of alcohol (0.25, 0.5, or 1.0 g/kg), three doses of marijuana [4, 8, or 16 puffs of 3.55% Δ9-tetrahydrocannabinol (THC)], and placebo in random order under double blind conditions in seven separate sessions. Blood alcohol concentration (10–90 mg/dl) and THC levels (63–188 ng/ml) indicated that active drug was delivered to subjects dose dependently. Alcohol and marijuana produced dose-related changes in subjective measures of drug effect. Ratings of perceived impairment were identical for the high doses of alcohol and marijuana. Both drugs produced comparable impairment in digit–symbol substitution and word recall tests, but had no effect in time perception and reaction time tests. Alcohol, but not marijuana, slightly impaired performance in a number recognition test. These data are useful for understanding the relative performance impairment produced by alcohol and marijuana at the delivered doses and the relationship between their subjective and behavioral effects. © 1997 Elsevier Science Inc.

ALCOHOL and marijuana are two of the most widely used psychoactive drugs in the world. When used excessively or chronically, they represent a serious threat to public safety and health. In 1993, alcohol was a factor in 44% of traffic fatalities (39). A study of patients admitted to a trauma center because of injuries sustained in vehicular accidents found that 37% of patients tested positive for alcohol and 34% had plasma concentrations of Δ9-tetrahydrocannabinol (THC) that exceeded 2 ng/ml (53). The adverse consequences of acute marijuana intoxication on driving (7,52) and cognition (6,22) have been documented, and the role of marijuana smoke in the etiology of pulmonary disorders has been established (55,56). Given the widespread use and resultant morbidity of these two drugs, it is surprising that relatively few studies have directly compared the behavioral impairment from alcohol and marijuana in a systematic manner.

Studies conducted in the 1960s and 1970s reported that alcohol and marijuana produced various behavioral effects, including impaired performance; however, firm conclusions about the comparative effects of alcohol and marijuana were limited because of methodological deficiencies. For example, the majority of studies tested only one active dose of either or both drugs (5,17,24,50) or examined the effects of alcohol and marijuana across a limited range of physiological, subjective, and behavioral measures (4,11,13,21,33).

More recent studies have attempted to address the methodological limitations of earlier studies. Marks and MacAvoy (34) investigated the effects of placebo and two active doses of alcohol and smoked marijuana on a 40-min divided attention task requiring responses to central and peripheral light stimuli. The high doses of marijuana (5.2 mg THC) and alcohol [peak blood alcohol concentration (BAC) = 97 mg/dl] sig-

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significantly reduced subjects’ sensitivity to the central signal and produced comparable increases in the number of missed peripheral signals. Perez-Reyes et al. (47) reported that alcohol and marijuana comparably increased ratings of subjective intoxication and impaired performance on a 2-min divided attention test. The combination of a high alcohol dose (0.85 g/kg, peak BAC = 110 mg/dl) and marijuana (2.4% THC, one cigarette) increased the impairment observed with each drug alone. Heishman et al. (18) reported that a moderate acute dose of alcohol (0.6 g/kg, peak BAC = 70 mg/dl) and two doses of marijuana (1.3% and 2.7% THC, 16 puffs) produced comparable subjective effects and minimal psychomotor impairment, whereas a high dose of alcohol (1.2 g/kg, peak BAC = 130 mg/dl) produced much greater subjective effects and behavioral impairment. Similarly, Chait and Perry (9) found that alcohol (0.55 g/kg, peak BAC = 88 mg/dl) and marijuana (3.6% THC, four puffs) administered twice during a 4-h session produced comparable subjective effects, but alcohol impaired performance on motor, psychomotor, and cognitive tests to a greater extent than did marijuana.

These studies suggest that there are certain doses of alcohol and marijuana that may produce comparable behavioral impairment; however, complete knowledge of such comparative drug profiles requires testing a range of behavioral measures and knowing the delivered drug dose. The latter has proven elusive in many studies of marijuana because of lack of control over smoking behavior and failure to measure plasma THC concentration. The purpose of this study was to extend the findings of previous comparisons of alcohol and marijuana by testing a broader range of behavioral and cognitive measures, including memory, which few comparative studies have examined; administering multiple doses of both drugs, including placebo; controlling puffing and inhalation parameters during marijuana smoking; and measuring plasma THC concentration.

METHODS

Subjects

Participants were five healthy, male volunteers who ranged in age from 18 to 26 years (mean = 22, SD = 3.8). Subjects were recruited from the community through newspaper advertising and were paid $10.00 per hour of participation. Before the study, subjects were medically screened, interviewed about past and current drug use, and gave written informed consent about the study. They reported drinking 4–15 alcoholic drinks per week (mean = 8.2), drinking no more than the equivalent of five 1-oz drinks on a typical occasion, and drinking less often than daily. Subjects also reported smoking one to six marijuana cigarettes per week (mean = 4.4), smoking no more than two cigarettes on a typical occasion, and smoking less often than daily. Subjects reported regular use of no other drugs and no history of treatment for drug or alcohol dependence.

General Procedure

Participants were informed that the purpose of the study was to investigate the effects of commonly used drugs on mood and behavior and that they could receive several doses of alcohol, marijuana, or placebo. Before the first experimental session, subjects were trained in the smoking procedure. In an attempt to deliver uniform amounts of marijuana smoke per puff, a computer-based smoking topography system (62) was used that monitored puff volume (PV), inhalation volume (IV), lung exposure duration (LED; sum of inhalation, breathhold, and exhalation durations), and interpuff interval (IPI). Using placebo marijuana cigarettes, subjects were trained using a feedback tone to attain the following target values: PV = 60 ± 4 ml, IV = 25% of vital capacity (≥ 100 ml), breathhold = 10 s, LED = 15 s, IPI = 60 s (timed from the start of the puff). Subjects also practiced the computerized behavioral and cognitive tests until performance was stable, defined as a minimum of 50 correct responses on the digit-symbol substitution test (DSST) and correct recall of 12 words after the third presentation in the word recall test. The other performance tests and the subjective measures were performed once for familiarization.

Subjects participated in seven experimental sessions that lasted 3–4 h and were separated by 1 week. Each session tested one of seven drug conditions: 0.25, 0.5, and 1.0 g/kg alcohol; 4, 8, and 16 puffs of 3.55% THC marijuana; and one placebo (alcohol and marijuana) condition. Drug doses were administered in random order under double blind conditions. Subjects were instructed to abstain from alcohol and drug use for 24 h before sessions. A breathalyzer reading and a urine specimen were obtained at the start of each session to assess and encourage compliance with these rules. Urine specimens tested positive for only cannabinoids.

Drugs and Dosing Protocol

Alcohol was administered as 95% ethanol mixed with orange juice (480 ml constant volume) in doses of 0, 0.25, 0.5, and 1.0 g/kg alcohol; 4, 8, and 16 puffs of 3.55% THC marijuana; and one placebo (alcohol and marijuana) condition. Drug doses were administered in random order under double blind conditions. Subjects were instructed to abstain from alcohol and drug use for 24 h before sessions. A breathalyzer reading and a urine specimen were obtained at the start of each session to assess and encourage compliance with these rules. Urine specimens tested positive for only cannabinoids.

Marijuana cigarettes weighing approximately 800 mg were provided by the National Institute on Drug Abuse (NIDA). Cigarettes measured 85 mm in length × 25 mm in circumference and contained either 0 (placebo) or 3.55% (active) THC by weight, as assayed by NIDA. The moisture content of the cigarettes was raised by placing them above a saturated sodium chloride solution in a closed humidifier for at least 12 h before smoking. Marijuana doses were 0, 4, 8, and 16 puffs from the active cigarettes.

Dosing involved a double dummy procedure such that, during each session, a single active dose of either alcohol or marijuana was administered and the other drug was given in placebo form. During each session, 16 drinks (30 ml each) were consumed, and 16 puffs from four marijuana cigarettes (4 puffs from each cigarette) were smoked. Subjects consumed each drink during the 60-s IPI, such that puffs and drinks alternated during the 16-min drug administration period. To administer the 0- (placebo), 4-, 8-, and 16-puff marijuana conditions, either zero, one, two, or four active cigarettes, respectively, were included in the total of four marijuana cigarettes. When there were one or two active cigarettes, placebo cigarettes were smoked first and active cigarettes were smoked last.

Experimental Sessions

At the beginning of each session, a breath test to determine BAC and an expired air carbon monoxide (CO) test were conducted. An intravenous catheter was inserted in an antecubital vein for blood sampling, and subjects were connected to a heart rate monitor. A blood sample was collected, baseline heart rate was recorded, and a computerized battery...
of subjective and behavioral measures was completed. Subjects were then connected to the smoking topography equipment. Drug or placebo was administered according to the dosing protocol described above. Midway through dosing, a second blood sample was obtained after eight puffs and drinks. Immediately after dosing, a third and final blood sample was collected. The sequence of measures (BAC, expired air CO, heart rate, subjective, performance) was completed 0 (immediately), 30, 60, 90, and 120 min after dosing. Subjects remained in the laboratory under observation until drug effects had dissipated before they were discharged.

**Biological Measures**

**BAC, CO, and heart rate.** BAC was determined by having subjects breathe steadily for 3 s into the mouthpiece of a hand-held Alco-sensor III (Intoximeters, Inc., St. Louis, MO, USA). Expired air CO was measured by having subjects take a deep breath, hold for 20 s, then breathe steadily for 20 s into the mouthpiece of a Vitalograph-BreatheCO Monitor (Vitalograph Ltd., Lenexa, KS, USA). Heart rate was measured using three silicon EKG electrodes (NDM Corp., Dayton, OH, USA) placed on the right deltoid muscle and second and fifth intercostal spaces. The electrodes were attached to an EKG monitor and Schmitt trigger, which sent a pulse to a computer at the start of an R-wave. The computer timed the interval between pulses and calculated an average rate each minute.

**Plasma THC.** An intravenous catheter was inserted in an antecubital vein of the subject’s nondominant arm. Three blood samples (5 ml each) were collected during experimental sessions, at baseline and after 8 and 16 puffs. No further samples were obtained because previous studies have shown that plasma THC levels peak before or immediately after smoking and decline rapidly thereafter (2,3,23). After each session, plasma was separated and immediately frozen. Plasma samples were subsequently sent to Research Triangle Institute (Research Triangle Park, NC, USA) for radioimmunoassay of THC content (12). The between-run precision of the assay was less than 5% at 8.0 and 30.0 ng/ml THC.

**Subjective Measures**

Twelve visual analog scale (VAS) questions were presented individually on the video monitor. Subjects answered each question by using a joystick to move a cursor along a 15-cm line labeled “Not at all” on the left and “Extremely” on the right. The questions assessed the following: drug high, time perception, energetic, clear-headed, anxious, hungry, sluggish, confused, and relaxed. Similar VAS questions have been shown to be sensitive and reliable subjective measures of alcohol and marijuana intoxication (3,18,26).

**Behavioral and Cognitive Performance**

Five computerized tests were presented in the following order: reaction time, DSST, number recognition, time estimation, and word recall. Subjects were paid for accurate performance on the behavioral tests. Earnings per session averaged $17.80, which was slightly less than half of their total payment.

**Reaction time.** This test consisted of 10 trials, each of which began with subjects depressing and holding the right button of a two-button joystick. After a random latency of 5–15 s from the time the button was depressed, an asterisk was presented in the middle of the video monitor. Subjects responded as rapidly as possible by releasing the right button and depressing the left button. Response time was measured from the presentation of the asterisk to depression of the left button for each trial.

**DSST.** The computerized version of the DSST that was used has been described (36). Briefly, randomly selected digits appeared in the center of the video monitor. Subjects used a numeric key pad to reproduce a geometric pattern associated with the digit by using the digit–symbol code presented continuously at the top of the screen. Each digit–symbol association constituted one response. Subjects were instructed to make as many accurate responses as possible during the 90-s task. Numbers of attempted and correct responses were recorded.

**Number recognition.** This test was adapted from Sternberg (54) and consisted of 20 trials, each of which began with a prompt on the video monitor to “Press and hold both buttons” of a two-button joystick. When subjects were holding both buttons, the monitor went blank for 2 s followed by a 2-s presentation of a set of digits consisting of five to seven single, nonrepeating, randomly selected digits (0–9). After a 2-s delay (monitor blank), a test digit was presented for up to 2 s, during which subjects released the left button if the test digit was included in the original digit set or the right button if the test digit was not included in the original digit set. The size of the digit set and whether or not the test digit was included were randomly determined for each trial. Correct responses when the test digit was present (true positive) and absent (true negative) from the original digit set were recorded. Similarly, incorrect responses when the test digit was present (false negative) and absent (false positive) were recorded. Response time was recorded from the presentation of the test digit to the release of either button.

**Time perception.** Three different time intervals (5, 20, and 80 s) were presented in random order. The duration of each interval was signaled by the appearance and disappearance of an asterisk on the video monitor. At the end of an interval, subjects estimated its duration. Subjects then reproduced the interval by pressing a button for the perceived duration. The estimated and produced durations for the three intervals were recorded.

**Word recall.** Lists of 20 concrete nouns were selected from Thorndike and Lorge (57). Word lists were equated for frequency in the language and consisted of common (frequencies greater than 50 per million) and uncommon (frequencies less than 50 and greater than 1 per million) words (29,57). The words were presented on the video monitor at a rate of one every 2 s. Subjects immediately wrote the remembered words during a 2-min free recall period. The same list was presented and words recalled three consecutive times at each trial; new lists were used for each drug condition and assessment.

**Statistical Analysis**

Baseline data for all variables were analyzed across the seven drug conditions using a one-way analysis of variance (ANOVA). No condition main effects were observed, thus postdrug measures only were used in subsequent analyses. Plasma THC data were analyzed using a two-way, repeated measures ANOVA with marijuana dose (4, 8, 16 puffs) and time (mid-smoking, immediately postsmoking) as factors. Data from the word recall test were analyzed using a three-way, repeated measures ANOVA with drug condition (including placebo), list presentation order (1st, 2nd, 3rd), and time postdrug (0, 30, 60, 90, 120 min) as factors. The remaining biological, subjective, and performance data were analyzed using two-way, repeated measures ANOVA with drug condition and time postdrug as factors. Post hoc comparisons between placebo and drug doses and among active drug doses
RESULTS

Biological Measures

BAC and plasma THC. A significant condition × time interaction \( F(24, 96) = 8.26, p < 0.001 \) was obtained for BAC. Figure 1 shows BAC at 30 min postdosing. Post hoc comparisons indicated that BAC for the 1.0-g/kg dose (90 mg/dl) was significantly different from the two lower doses. BAC values in the placebo condition were 0 mg/dl (data not shown). By the end of the session, BAC had declined to 0 mg/dl for the 0.25-g/kg dose; however, BAC remained elevated at 20 and 70 mg/dl for the 0.5- and 1.0-g/kg doses, respectively.

A significant condition × time interaction \( F(2, 8) = 9.04, p < 0.05 \) was also observed for plasma THC concentration. Figure 1 shows THC levels immediately after smoking. Post hoc tests indicated that the 8- and 16-puff marijuana conditions were significantly different from the 4-puff condition, but not from each other. Plasma THC level after 8 puffs in the 16-puff condition averaged 144.0 mg/dl (no active puffs had been smoked after 8 puffs in the 4- and 8-puff conditions).

Heart rate and CO. Post hoc analysis of the condition main effect \( F(6, 24) = 4.31, p < 0.01 \) indicated that marijuana, but not alcohol, increased heart rate. The 4-, 8-, and 16-puff marijuana conditions produced maximal increases immediately after smoking of 97, 109, and 109 beats/min, representing increases over baseline levels of 25, 33, and 34 beats/min, respectively. Heart rate had returned to baseline levels by the end of the session in the 4-puff condition, but remained elevated with the two higher doses.

There was a time main effect for expired air CO \( F(4, 16) = 32.82, p < 0.001 \), but no effect of drug condition. Peak CO increases from baseline were measured immediately after smoking and were 15.6, 13.8, and 17.2 ppm for the 4-, 8-, and 16-puff marijuana doses, respectively; 13.2, 18.0, and 13.8 ppm for 0.25, 0.5, and 1.0 g/kg alcohol, respectively; and 16.2 ppm for placebo. Expired air CO declined to nearly baseline levels across all drug conditions by the end of the session.

Subjective Measures

Significant condition effects were obtained for six of the VAS questions: drunk \( F(6, 24) = 23.42, p < 0.001 \), stoned \( F(6, 24) = 30.25, p < 0.001 \), impaired \( F(6, 24) = 7.89, p < 0.001 \), clear-headed \( F(6, 24) = 3.04, p < 0.05 \), high \( F(6, 24) = 17.05, p < 0.001 \), and liking \( F(6, 24) = 4.81, p < 0.01 \). A trend toward significance was observed for the item confused \( F(6, 24) = 2.44, p < 0.06 \). Analog questions without significant condition effects were energetic, anxious, hungry, sluggish, and relaxed. Figure 2 shows data averaged over the session from four of the VAS questions as a function of drug dose. Alcohol selectively increased responses to the question drunk on alcohol in a dose-dependent manner. Marijuana produced increases in subjective measures post hoc test (Tukey’s HSD) results; data points not sharing a common letter are significantly different (\( p < 0.05 \)); those with common letters are not significantly different.
in ratings of stoned compared with placebo; however, post hoc analysis indicated that the three doses were not significantly different from each other.

Figure 3 shows time course data for ratings of drunk and stoned. The peak rating of drunk after each alcohol dose was observed at 30 min postdrug; however, ratings were significantly elevated at the end of the session (120 min) for only the 1.0-g/kg alcohol dose. For stoned, maximal effects of marijuana occurred either immediately postdrug (16-puff condition) or 30 min postdrug (lower doses); ratings were significantly elevated over placebo at 120 min postdrug for all marijuana doses.

Subjective ratings of drunk after active marijuana doses and stoned after active alcohol doses were not different from respective placebo responses.

Alcohol and marijuana produced dose-dependent increases in ratings of impaired performance that were comparable in magnitude for the three active drug doses (Fig. 2). The time course for alcohol was very similar to ratings of drunk (Fig. 3), with maximal impairment after each alcohol dose reported at 30 min postdrug. In contrast, the time of peak postdrug impairment ratings after marijuana was dependent on dose: 90 min for low dose, 60 min for moderate dose, and immediately postdrug for high dose. Ratings of perceived impairment remained significantly elevated over placebo at 120 min postdrug for only the high doses of both drugs. Alcohol and marijuana also produced comparable decreases in ratings of clear-headed (Fig. 2). Time course data indicated that maximal decreases occurred either immediately or 30 min postdrug after alcohol and marijuana; effects persisted at 120 min for only the 16-puff marijuana dose.

Marijuana produced increased ratings of drug high that were nearly identical in magnitude and time course to those of stoned (see Figs. 2, 3), whereas alcohol produced small increases that were not significantly different from placebo. Ratings of drug liking were significantly elevated over placebo for all three marijuana doses, but the dose–response function was relatively flat; increases in liking after alcohol were not significantly different from placebo. Only the 16-puff marijuana dose significantly increased ratings of confused.

Behavioral and Cognitive Performance

**DSSST:** Significant condition effects were observed for number of attempted responses \(F(6, 24) = 3.50, p < 0.05\) and number of correct responses \(F(6, 24) = 4.20, p < 0.01\) on the DSSST. Figure 3 shows time course data for correct responses as a function of alcohol and marijuana doses. The 1.0-g/kg dose of alcohol clearly produced the greatest impairment, which nearly returned to placebo levels by the end of the session. In contrast, the 8- and 16-puff marijuana conditions generally impaired DSSST performance throughout the session, but not in an orderly dose-related manner. The mag-
nitude and time course of alcohol and marijuana effects on number of attempted DSST responses were similar to those of correct responding.

**Word recall.** Figure 4 shows effects of alcohol and marijuana on the word recall test averaged over the session as a function of dose and list presentation order. Repeated presentation of the same word list during each trial resulted in an increase in the number of words correctly recalled, and both drugs produced dose-related decreases in the number of words recalled after each list presentation, as revealed by a significant presentation order × drug condition interaction [F(12, 48) = 2.90, p < 0.01]. Post hoc testing indicated that the high doses of alcohol and marijuana consistently impaired recall compared with placebo (Fig. 4). Maximal recall deficits after marijuana generally occurred immediately to 60 min postdrug; however, peak effects following high-dose marijuana were observed at 90 min postdrug on the second and third list presentations. Alcohol consistently produced maximal effects at 30–60 min after drug dosing.

**Number recognition.** There was a significant condition main effect for false positive responses [F(6, 24) = 3.33, p < 0.05]. Post hoc analysis indicated that alcohol, but not marijuana, increased the number of false positives, with the greatest increase occurring at the 0.5-g/kg dose. Mean number of false positive responses averaged over the session was 0.24, 0.12, 0.6, and 0.48 for 0, 0.25, 0.5, and 1.0 g/kg alcohol, respectively. No other response category or response time measure was significantly affected by alcohol or marijuana.

**Other tests.** There were no significant condition or condition × time effects on reaction time or time estimation and production tests.

**DISCUSSION**

This study documented that oral alcohol and smoked marijuana produced dose-related subjective effects and impairment of psychomotor and cognitive abilities in volunteers with histories of moderate alcohol and marijuana use. The effects of both drugs were remarkably comparable in magnitude. Because we also obtained measures of BAC and plasma THC concentration, it was possible to relate delivered dose with observed outcomes and to make direct dose–response comparisons between alcohol and marijuana.

The doses of alcohol (0.25, 0.5, and 1.0 g/kg) resulted in BACs at 30 min postdosing of 10, 30, and 90 mg/dl, respectively, which span the range of BACs typically achieved during adult social drinking situations (60). The average THC content of confiscated commercial grade marijuana in the United States (1992–1994) was 4.0% (14), slightly greater than the 3.55% used in this study. Thus, it is likely that the subjective and behavioral effects of alcohol and marijuana observed in this study were produced by doses that are comparable to those achieved during recreational use of these drugs.

Because of large individual variability in delivered dose of marijuana via the smoking route (23), the relatively low bioavailability of THC (14–18%) during ad lib smoking (44,48), and the ability of individuals to adjust their smoking behavior as a function of marijuana potency (19), we have been using a computerized smoking topography system to control puffing and inhalation parameters. This technology has allowed the investigation of the relationship between measured volumes and exposure durations of marijuana smoke and plasma THC concentration. In the present study, THC levels immediately after smoking were 63.1, 150.9, and 188 ng/ml in the 4-, 8-, and 16-puff conditions, respectively. Our previous research (23) has shown that 10 puffs (PV = 60 ml) from 3.55% THC cigarettes produced a mean peak THC level of 147.9 ng/ml, and Huestis et al. (23) reported a peak concentration of 162.2 ng/ml after one 3.55% THC cigarette (8 puffs). The immediate-postsmoking THC level of 150.9 ng/ml in the 8-puff condition in this study is consistent with these previously reported values.

Marijuana, but not alcohol, produced tachycardia, which is the most reliable physiological sign of acute marijuana ingestion (9,19,26). The increase in heart rate was not entirely dose-related, because the 8- and 16-puff conditions produced comparable effects. A possible explanation is that THC concentration between the two dose conditions was not significantly different (Fig. 1). The finding of no difference in expired air CO across the alcohol and marijuana conditions was expected because the same number of puffs was administered in all conditions and because expired air CO is a measure of smoke inhalation, independent of THC content or dose. The consistency of the CO data also verifies the control maintained over smoking behavior by the computerized topography feedback system.

Alcohol and marijuana produced decrements on two performance tests: DSST and word recall. Both drugs slowed responding and decreased accuracy in the DSST. The high doses of alcohol (peak BAC = 90 mg/dl) and marijuana (immediate-postsmoking THC level = 188 ng/ml) produced equivalent mean decreases in number of correct responses (7.4 responses for alcohol and 6.8 for marijuana). Dose-related impairment in the DSST has been reported for alcohol (9,18,27,51) and marijuana (19,26,61). In this study, only the high alcohol dose impaired DSST performance, and marijuana-induced decrements were not dose related, which has been reported (18). The DSST measures a constellation of neuropsychological functioning, including recognition of sensory information, visual–motor coordination, response speed, attention, and memory (30,35). Kaplan (25) has modified the DSST such that these functions can be studied separately to...
determine which are responsible for impaired performance. Psychopharmacological research has not adopted this testing approach; however, it may provide a means by which differential mechanisms underlying drug-induced DSST impairment can be elucidated.

Alcohol and marijuana produced dose-related impairment on the word recall test (Fig. 4). As expected, under placebo conditions, subjects recalled more words over the three repetitions of each list. Interestingly, for each list presentation, the active doses of both drugs produced nearly equivalent decreases in number of words recalled, with the exception that the high alcohol dose (BAC = 90 mg/dl) caused slightly greater impairment than the high marijuana dose (THC level = 188 ng/ml) on the second and third list presentations. To our knowledge, this is one of the few studies to compare directly the effects of alcohol and marijuana on memory and the first to report the plasma concentration at which both drugs significantly decreased free recall. Chait and Perry (9) found that alcohol, but not marijuana, impaired word recall. However, their dose of marijuana was equivalent to the 8-puff condition in the present study, which impaired free recall only on the third list presentation (Fig. 4).

In general, one of the most consistently reported behavioral effects of marijuana in humans is disruption of free recall and other memory processes (16). Animal studies have also documented the memory-imparing effects of THC [e.g., (38,42)]. Recent research utilizing radial arm maze and delayed match to sample tasks has implicated cannabinoid receptors in the hippocampus as mediating short-term memory deficits produced by cannabinoids (20,31). There is also an extensive literature documenting the impairing effect of alcohol on subsequent learning and memory [e.g., (32,43,49)]. Interestingly, several studies have shown that alcohol enhances memory of information learned before alcohol was administered (41,45,59). The mechanisms by which this retroactive facilitation occurs are currently being debated (59) and would appear to be an area worthy of future research. In contrast to marijuana, the effects of alcohol are mediated through multiple mechanisms, including cAMP production, adenosine transport, dopamine release, and several ligand-gated ion channels associated with GABA/benzodiazepine, N-methyl-D-aspartate (NMDA), serotonin, and opioid receptors (1,28).

In this study, alcohol increased the number of false positive responses on the number recognition test, but not in a dose-related manner. That marijuana had no effect on number recognition is consistent with one previous study (15); however, Kelly et al. (26) reported that marijuana decreased test accuracy and slowed response time. In the present study, alcohol and marijuana had no effect on reaction time or time estimation and production. Marijuana produces inconsistent effects on simple reaction time tests, with some studies reporting modest impairment and others showing no effect (10). Alcohol has been shown to slow reaction time at doses comparable to those used in this study, but only after 15 min on task in an auditory vigilance task (16) or under complex stimulus conditions (40). A commonly reported effect of marijuana is to increase the subjective passage of time relative to clock time. Thus, many studies have shown that subjects either overestimate an experimenter-generated time interval or underpredict a subject-generated interval (10). Alcohol has been shown to cause the opposite effect, either underestimation or overproduction (9,24,58). Methodological differences may account for the lack of effect of alcohol and marijuana on time perception in this study. In previous studies [e.g., (9,58)], subjects interacted directly with the experimenter, using verbal commands and responses, whereas our subjects interacted with visual stimuli on the computer video monitor, using a motor response.

In this study, alcohol and marijuana produced dose-related changes in several subjective measures. Although drugs were administered using double blind and double dummy procedures, subjects were able to identify the active drug by responding appropriately to the drug-specific questions: drunk on alcohol and stoned on marijuana (Fig. 2). The 1.0-g/kg alcohol dose, equivalent to about five 1-oz drinks of 100-proof liquor consumed in 1 h by a 70-kg man, produced a robust increase in ratings of drunk that remained significantly elevated above placebo at 2 h postdrug, when BAC was 70 mg/dl. In contrast, the dose–response curve for ratings of stoned was relatively shallow given the steep dose–THC concentration function (Fig. 1). This lack of subjective differentiation between active marijuana doses has been reported by others (8,46,61), and it has been suggested that it may be difficult to discriminate marijuana doses producing THC levels in the 90–170-ng/ml range (3).

Interestingly, although relative potency of effect was not directly assessed in this study, alcohol and marijuana produced changes in ratings of impaired performance and clear-headed that were comparable, and at some doses nearly identical, in magnitude. In general, subjective effects produced by the high dose of each drug were significantly different from the low dose or placebo. This same dose–effect pattern was also observed for some of the performance tests, which suggests that subjects were accurately monitoring their psychomotor and cognitive abilities. This finding is consistent with other studies reporting accurate subjective ratings of actual behavioral impairment (18,37).

In summary, we have demonstrated that a range of alcohol and marijuana doses produced comparable subjective effects and performance impairment. The high doses of alcohol (1.0 g/kg, 30-min BAC = 90 mg/dl) and marijuana (16 puffs, 3.55% THC, immediate-postsmoking THC level = 188 ng/ml) produced identical subjective ratings of perceived impairment and very similar degrees of actual impairment on the DSST and a test of word recall. The use of multiple drug doses, technology to control the delivered dose of smoked marijuana, and a battery of behavioral tests measuring different aspects of human performance provided a solid methodology with which to compare the dose–effect profiles of alcohol and marijuana, two of the most widely used and abused drugs in our society.

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