Pharmacology Biochemistry & Behavior, Vol. 31, pp. 649–655. © Pergamon Press plc, 1989. Printed in the U.S.A. 0091-3057/88 $3.00 + .00

Alcohol and Marijuana: Comparative Dose Effect Profiles in Humans

STEPHEN J. HEISHMAN,[1] MAXINE L. STITZER AND GEORGE E. BIGELOW

Department of Psychiatry and Behavioral Sciences, Division of Behavioral Biology
The Johns Hopkins University School of Medicine, Baltimore, MD 21224

Received 23 February 1988

HEISHMAN, S. J., M. L. STITZER AND G. E. BIGELOW. *Alcohol and marijuana: Comparative dose effect profiles in humans.* PHARMACOL BIOCHEM BEHAV **31**(3) 649–655, 1988.—This study compared subjective and performance dose effect profiles of oral alcohol and smoked marijuana. Male subjects (N=6) with histories of moderate alcohol and marijuana use received three doses of alcohol (0, 0.6, 1.2 g/kg) and three doses of marijuana (0, 1.3, 2.7% Δ^9-THC) in a double-blind, randomized crossover design. Physiological indices indicated that active drug was delivered to subjects dose dependently. Alcohol produced dose-related elevations on several subjective measures of drug effect. The high dose of alcohol impaired performance on circular lights, tracking and digit-symbol substitution (DSST) tasks, whereas the low alcohol dose impaired only circular lights performance. Marijuana produced elevations on subjective report measures, but effects were similar for the two active doses. Minimal performance impairment was seen with marijuana on only one measure (DSST speed). The subjective and performance effect profiles produced by smoked marijuana were similar to that of the low (0.6 g/kg) dose of alcohol. These data are useful for understanding the relative performance impairment produced by alcohol and marijuana and the relationship between their subjective and behavioral effects.

Alcohol Marijuana THC Subjective effects Performance effects Psychomotor tasks Humans Behavioral pharmacology

ALCOHOL and marijuana are two of the most widely used recreational drugs in the world. Their individual physiological, subjective, and behavioral effects in humans have been well documented. Much of the research on the behavioral effects of alcohol has focused on impaired driving abilities [see (33) for a review]. Additionally, recent studies have shown alcohol-induced impairment on psychomotor laboratory tasks, such as reaction time (19,20), tracking (1), and divided attention (31,35). These performance decrements have occurred over a wide range of blood alcohol levels and generally corresponded to subjective ratings of performance impairment or alcohol intoxication. Similarly, marijuana is known to affect many behavioral responses, especially those requiring complex judgments or discriminations (13,24). Performance decrements have been observed on tracking, divided attention, and circular lights tasks (2, 6, 10, 28). However, correspondence between physiological, subjective and behavioral effects of marijuana has not always been found (7).

Perhaps because of the difficulty in equating drugs with different routes of administration and time courses of action, few studies have systematically compared the effects of alcohol and marijuana. Those studies that have investigated alcohol and marijuana have generally used single active doses of one or both drugs and/or tested drug effects across a limited range of performance, subjective, or physiological measures. Performance decrements in driving skills (11, 21, 39, 44) and cognitive/psychomotor laboratory tasks (3, 4, 8, 9, 23, 25, 30, 40) have been reported for alcohol and marijuana, but none of these studies tested multiple doses of both drugs. Some studies testing a range of doses of alcohol and marijuana have focused on operant task performance (5) or the combined effects of the two drugs (28). In these same studies, subjective and/or physiological measures have been reported for one, but not both drugs (5, 8, 9, 11), or have not been reported (3, 23, 28, 39).

The lack of a systematic approach using multiple doses of both drugs and assessing responses across physiological, subjective, and behavioral indices has hindered a complete understanding of the comparative effect profiles of alcohol and marijuana. The purpose of this study was to determine subjective and performance dose effect profiles for oral alcohol and smoked marijuana under comparable experimental conditions. Such data are useful for understanding the relative performance impairing effects of alcohol and marijuana and the relationship between their subjective and behavioral effects.

METHOD

Subjects

Six healthy male community volunteers with a history of moderate alcohol and marijuana use were recruited through newspaper advertisements to participate in the study. The average age of participants was 26.2 years (SD=5.3). They

[1]Requests for reprints should be addressed to Stephen J. Heishman, Ph.D., NIDA Addiction Research Center, P.O. Box 5180, Baltimore, MD 21224.

reported using alcohol an average of 16 times per month, with an average of 3.3 drinks or beers consumed during each drinking episode. On average, subjects reported using marijuana 10 times monthly, smoking an average of 2.5 joints on each occasion. Four participants were regular cigarette smokers, averaging one pack per day; a fifth subject reported smoking only when he drank alcohol. Three subjects reported daily use of caffeine in the form of coffee, tea, or soft drinks. All subjects reported previous experience with illicit drugs; however, other than alcohol, marijuana, caffeine, and nicotine, cocaine was the only drug reported to be currently used on a regular basis. Four subjects reported intranasal use of cocaine an average of once per month. None of the research volunteers had ever received treatment for alcohol or drug abuse. Prior to participation, they were medically screened and provided a drug free urine specimen. Subjects gave written informed consent about the experiment and its risks prior to the study and were paid $5.00 per hour of participation.

Drugs

Alcohol was administered as 95% ethanol mixed with orange juice (480 ml constant volume) in doses of 0.6 and 1.2 g/kg. These doses were selected to produce peak blood alcohol concentrations below and above the generally recognized legally intoxicated limit of 100 mg/dl. Placebo consisted of 480 ml orange juice. Drinks were divided into four equal volumes (120 ml); subjects drank each portion in consecutive 5-minute intervals for a total drinking time of 20 minutes. To mask the immediate smell and taste cues of both alcoholic and placebo drinks, the top half of the cup from which subjects drank was wrapped with an alcohol-soaked wristband, and about 2 ml of 95% ethanol was floated on top of the beverage each time the cup was filled.

Marijuana was provided by the National Institute on Drug Abuse (NIDA) in machine rolled cigarettes weighing approximately 900 mg. Doses were determined by the Δ^9-tetrahydrocannabinol (THC) content of the cigarettes as assayed by NIDA: 0 (placebo), 1.3, and 2.7%, equivalent to 0, 12, and 24 mg THC, respectively. The moisture content of the cigarettes was raised by humidification at room temperature over a saturated sodium chloride solution in a closed humidifier at least 12 hours before smoking. Two marijuana cigarettes were smoked consecutively through a plastic holder 3.5 cm in length according to the following standard procedure: total of 8 puffs per cigarette, ad lib puff duration, 10-second retention of smoke in the lungs, 40-second interpuff interval (timed from the start of each puff). This procedure resulted in nearly complete pyrolysis of each cigarette.

Procedure

Subjects participated in six daily experimental sessions, which began at 8:30 a.m. Each session lasted 5–6 hours and was separated by at least 24 hours. Subjects were instructed to abstain from drug and alcohol use at least 24 hours prior to daily sessions. A breathalyzer reading and urine specimen were obtained before each session to assess and encourage drug abstinence between sessions. Drug positive results were obtained once for each of two subjects. One subject testing positive for alcohol was sent home and that session rescheduled for the following day. Another subject tested marginally positive for cocaine. Because his baseline heart rate and behavioral task data were within his nondrug baseline ranges, the data from that session were included in the report.

Each subject participated in two drug conditions, alcohol and marijuana. To equalize potential carryover effects, drug conditions were counterbalanced such that half of the subjects received three sessions of alcohol dosing followed by three sessions of marijuana, and the remaining half received the opposite order. Within drug conditions, subjects received each dose of alcohol (0, 0.6, and 1.2 g/kg) and marijuana (0, 1.3, and 2.7% THC) once in random order. Drug doses were administered in a double-blind manner.

Experimental sessions began with a battery of predrug physiological, behavioral, and subjective report assessments lasting about 20 minutes. Heart rate was measured as wrist pulse for 30 seconds. Breathalyzer readings were obtained during alcohol sessions by having subjects blow into an alcolmeter (Lion S-D2, National Patent Analytical Systems, Inc., Shrewsbury, NJ). Expired air carbon monoxide (CO) readings were obtained during marijuana sessions by having subjects fully exhale, inhale and hold for 20 seconds, partially exhale, then fully exhale into a plastic bag which was sealed. The CO level of the breath sample was read directly in parts per million (ppm) using a MiniCO Model-1000 (Catalyst Research Corp., Baltimore, MD).

Psychomotor performance was assessed using three automated tasks. Prior to the first experimental session, subjects completed at least 10 trials on each task during a single practice session. The circular lights task has been described previously (17). Briefly, subjects faced a wall-mounted panel consisting of 16 button-lights arranged in a 56-cm diameter circle. For 1 minute, subjects pressed the buttons as rapidly as possible in response to the randomly sequenced illumination of their associated lights. The score was the number of correct responses during the 1-minute session. An automated version of the digit symbol substitution test (DSST) has been described previously (27). Briefly, randomly selected digits appeared in the center of a Commodore 64 computer video screen for 90 seconds. 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. The total number of responses and percent correct responses were recorded during the 90-second session. In the automated tracking task, a continuously moving, vertical path 1.65 cm wide appeared in the center of a black, 8×14 cm background centered in the upper half of the Commodore video screen. The path changed horizontal direction an average of 60 times during the 70-second session. Subjects attempted to guide a diamond-shaped pointer (1.1 cm wide, 1.65 cm tall) through the moving path using a paddle controller, which allowed horizontal, but not vertical, movement of the pointer. The percentage of time the pointer was off the path was recorded.

Seven subjective report questions concerning drug effects appeared individually on the video screen. Subjects answered each question using the numeric key pad to move a pointer along an 18.7 cm line scaled from 0 (not at all) to 100 (extremely). The questions in order of presentation were: 1) Do you feel any drug effect?, 2) How high do you feel right now?, 3) How much do you like the drug effect?, 4) How sleepy are you?, 5) How drunk on alcohol are you?, 6) How stoned on marijuana are you?, and 7) How impaired is your performance?

A 10-minute sample of monologue speech was then obtained. Subjects were asked to speak into a lapel microphone, and "Tell us about something that happened yesterday." Speech samples were recorded on audiocassette tape, fed through a voice operated relay, and scored for number of

seconds of speech during the 10-minute sample by a PDP-8 computer. (These data are not reported here.)

Following these initial baseline measurements, drug or placebo was administered under double-blind conditions. The entire sequence of physiological and behavioral measures was repeated at 15, 45, 75, 105, 135, 195, and 255 minutes after drug or placebo administration with two exceptions: 1) the verbal speech sample was assessed at 15, 45, and 75 minutes postdrug only, with instructions to "Tell us something else that happened yesterday," and 2) on marijuana sessions, a second and final heart rate and CO reading were obtained 2 minutes after the last cigarette. Tobacco smoking was prohibited from the beginning of the session until after the 135-minute assessment period. A light lunch was also served at this time.

Data Analysis

Blood alcohol level (BAL), heart rate and expired air CO data were analyzed using one-way analysis of variance. The BAL measure used was the 45-minute postalcohol value. Heart rate and expired air CO were analyzed as change scores by subtracting premarijuana values from the 2-minute postmarijuana values. Subjective report and performance data for alcohol and marijuana were analyzed separately by two-way, repeated measures analysis of covariance with drug dose and time postdrug as the factors. The predrug baseline score on each measure was used as the covariate. Huynh-Feldt adjustments of repeated measures degrees of freedom were used to correct for violations of the sphericity assumption. Post hoc comparisons between placebo and drug and between different drug doses were conducted using the Tukey method. For subjective and performance data, post hoc analyses used scores averaged across the session. For all statistical tests, effects were considered significant if $p<0.05$.

RESULTS

Physiological Measures

Physiological indices confirmed that active drug was delivered to subjects in a dose dependent manner. As shown in Fig. 1, alcohol produced significant, dose-related elevations in BAL at 45 minutes postdrug, $F(2,10)=31.85$, $p<0.001$. Blood alcohol levels for the 0.6 and 1.2 g/kg doses (70 and 130 mg/dl, respectively) were significantly different from placebo and each other. From the 45-minute measurement, BALs for the low alcohol dose gradually declined to placebo levels within the test session, whereas BALs for the high dose remained elevated throughout the session, averaging 70 mg/dl at the 255-minute assessment.

Expired air CO level and heart rate measured 2 minutes after smoking were used as physiological indices of marijuana exposure. Active and placebo marijuana increased CO levels an average of 17.2 ppm across all dose conditions, indicating significant smoke inhalation. As shown in Fig. 1, the magnitude of the CO boost was inversely related to marijuana dose, $F(2,10)=8.44$, $p<0.01$. The mean CO boost following the 2.7% THC dose (10.7 ppm) was significantly less than that after placebo marijuana (23.2 ppm); no other post hoc comparison was statistically significant. Figure 1 also shows that heart rate was increased by marijuana in a dose dependent manner, $F(2,10)=8.41$, $p<0.01$. Post hoc analysis indicated that both active doses produced increases significantly different from placebo, but not from each other.

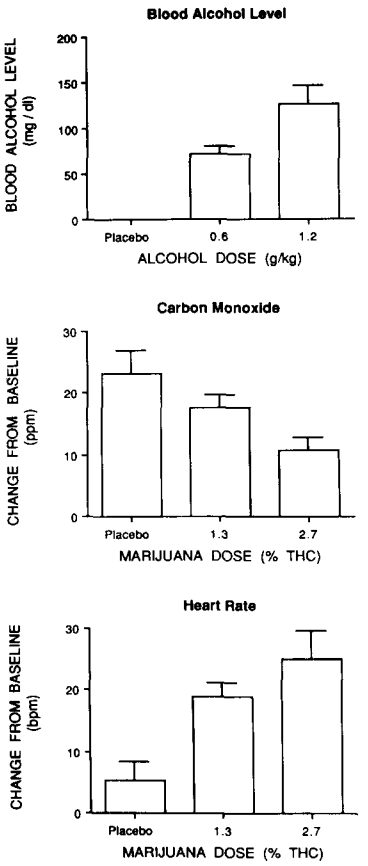

FIG. 1. Physiological verification of dosage delivery after oral alcohol and smoked marijuana administration. Top panel shows blood alcohol levels (mg/dl) obtained 45 minutes after ingestion of three alcohol doses. Middle panel shows expired air carbon monoxide (ppm) increase from presmoking baseline after inhalation of three marijuana doses. Bottom panel shows heart rate (beats per min) increase from presmoking baseline after inhalation of three marijuana doses. Carbon monoxide and heart rate data were measured as change from presmoking to 2-minute postsmoking levels. In all panels for each dosage condition, data represent means of six subjects ±1 SEM.

Subjective Measures

Figure 2 shows average scores for selected subjective report analog questions for each drug as a function of time postdrug. Subjects responded appropriately to the specific drug questions, "How drunk on alcohol are you?," which was elevated selectively only after alcohol ingestion, $F(2,9)=12.58$, $p<0.01$, and "How stoned on marijuana are you?," which was elevated after marijuana administration, $F(2,9)=9.55$, $p<0.01$. Post hoc analysis indicated significant differences between the two active alcohol doses, but not between the two active marijuana doses. The magnitude (i.e., peak scores) and time course of these subjective effect ratings were similar for both active marijuana doses and the low alcohol dose, whereas ratings for the high alcohol dose were clearly greater than the other drug conditions throughout the session.

In response to the question, "How high do you feel right now?" (Fig. 2), ratings were significantly increased for alcohol, $F(2,9)=19.07$, $p<0.01$, and marijuana, $F(2,9)=17.04$, $p<0.01$. Post hoc comparisons revealed that the two active

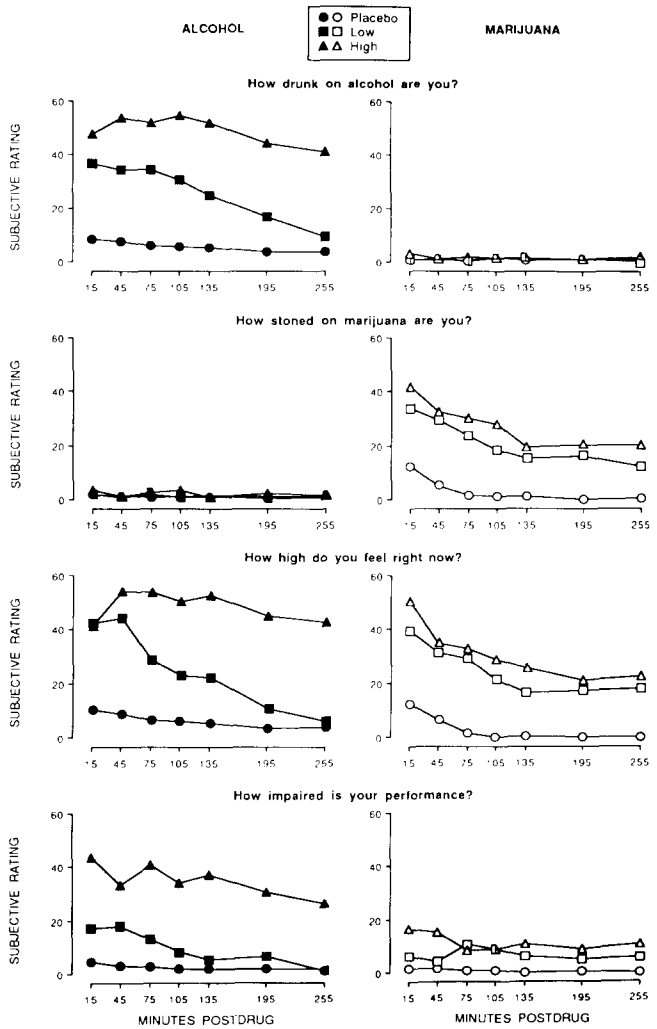

FIG. 2. Time course data for four subjective report questions for three doses of oral alcohol (left column) and three doses of smoked marijuana (right column). Alcohol doses were 0, 0.6, and 1.2 g/kg 95% ethanol. Marijuana doses were 16 puffs from cigarettes containing 0, 1.3 and 2.7% THC. Data points are adjusted for predrug baseline values and represent means of six subjects.

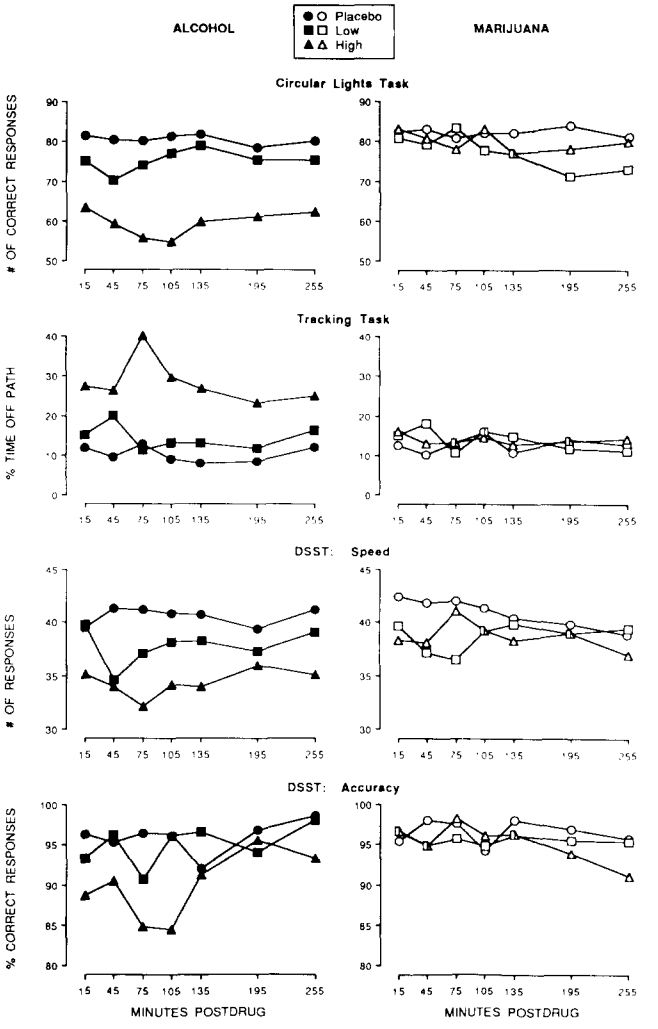

FIG. 3. Time course data for four performance measures for three doses of oral alcohol (left column) and three doses of smoked marijuana (right column). Data points are adjusted for predrug baseline values and represent means of six subjects. See Fig. 2 legend for drug doses.

alcohol doses were significantly different from each other, whereas the two active marijuana doses were not. At the time of peak "high" for each drug (45 minutes postdrug for alcohol and 15 minutes for marijuana), subjective ratings were similar in magnitude for the low doses of alcohol and marijuana and for the high doses of both drugs. However, due to declining ratings during the session, the time course of the marijuana subjective effects was more similar to the low than to the high dose alcohol condition.

Subjects rated their overall performance as impaired under the influence of alcohol, $F(2,9)=17.24$, $p<0.01$, but not marijuana (Fig. 2). Post hoc analysis indicated that high, but not low, dose alcohol ratings of perceived impairment were significantly different from placebo. Again, the subjective ratings for the high dose of alcohol were clearly distinct from the other drug doses.

Data from the remaining three subjective report questions are not shown. Responses to the question, "Do you feel any drug effect?," showed dose and time course effects for alcohol and marijuana which were similar to the responses to "How high do you feel right now?" (Fig. 2). In response to the question, "How much do you like the drug effect?," subjects reported significant liking for marijuana, $F(2,9)=9.20$, $p<0.01$, but not for alcohol. Both active doses of marijuana were significantly different from placebo, but not from each other. Neither alcohol nor marijuana produced any significant responses to the question, "How sleepy are you?."

Performance Measures

In general, the high dose of alcohol significantly impaired all performance task measures, whereas marijuana and the low alcohol dose impaired performance only on selected measures. Figure 3 displays average scores from the three psychomotor tasks for each drug as a function of time postdrug. Eye-hand coordination, assessed in the circular

lights task, was significantly impaired by alcohol, $F(2,9)=92.09$, $p<0.001$. Post hoc comparisons revealed that scores in both active alcohol dose conditions were significantly different from placebo and from each other. Peak performance impairment was observed at 45 minutes postdrug for the low alcohol dose; responding recovered to placebo levels by the 135-minute assessment. The high alcohol dose produced significantly greater impairment than the low dose throughout the session with peak effect occurring at 105 minutes postdrug. Marijuana did not significantly impair performance on the circular lights task.

The percentage of time spent off the path in the tracking task was significantly increased by alcohol, $F(2,9)=38.33$, $p<0.001$. Post hoc analysis indicated that the high, but not low, alcohol dose was significantly different from placebo. Performance was most impaired at 75 minutes postdrug by the high alcohol dose and remained impaired at the end of the session. Marijuana did not significantly affect performance on the tracking task.

Alcohol significantly decreased the total number of responses on the DSST, $F(2,9)=13.69$, $p<0.01$. Post hoc comparisons showed that only the high alcohol dose significantly slowed responding compared to placebo. DSST performance under the high alcohol dose was significantly slower than that of the low dose. For the high alcohol dose, peak impairment occurred at 75 minutes postdrug and remained impaired throughout the session. Alcohol also significantly impaired DSST accuracy, $F(2,9)=9.96$, $p<0.01$. Only the high dose was significantly different from placebo with peak effect occurring 75–105 minutes postdrug. Marijuana slowed DSST performance, indicated by a significant decline in total number of responses, $F(2,9)=7.25$, $p<0.05$. Post hoc analysis indicated that both marijuana doses produced impairment significantly different from placebo, but not from each other. Marijuana did not significantly impair response accuracy on the DSST.

DISCUSSION

This study has demonstrated dose-related effects of oral alcohol (0.6 and 1.2 g/kg) on a variety of subjective report and performance measures. Smoked marijuana (16 puffs from 1.3 and 2.7% THC cigarettes) produced effects on subjective report measures, but minimally affected task performance. Although the two active doses of alcohol produced effects that were very different in magnitude and duration, effects of the two marijuana doses could not be distinguished on most measures. The subjective and performance effect profile produced by smoked marijuana most closely resembled that of the low dose of alcohol.

Subjects were able to differentiate the two alcohol doses in terms of subjective reports at each assessment point (Fig. 2). The high dose of alcohol (1.2 g/kg) was equivalent to about eight 1 oz drinks of 90 proof liquor in a 150 lb man and produced a peak BAL of 130 mg/dl at 45 minutes postdrug, whereas the low dose of alcohol (0.6 g/kg) was equivalent to about four 1 oz drinks and resulted in a BAL of 70 mg/dl at 45 minutes (Fig. 1). By the end of the experimental session, subjects no longer reported being drunk or "high" under the low dose of alcohol; however, scores for the high dose remained elevated at levels not much below peak effects. Subjects judged their performance as significantly impaired under the high, but not low, dose of alcohol, indicating accurate assessment of their actual degree of behavioral impairment. This finding is consistent with previous studies reporting accurate subjective estimates of performance decrements produced by alcohol (15,32) and pentobarbital (41).

In this study, the high dose of alcohol produced impairment throughout the testing session on all psychomotor tasks: circular lights, tracking, and DSST (Fig. 3). These results are consistent with past reports of impaired psychomotor performance at comparable BALs (26, 34, 43). This performance impairment, together with the subjective report data, demonstrated that the high dose of alcohol produced debilitating effects from which subjects had not fully recovered 4 hours after drinking. Indeed, at this time, BALs were still elevated at 70 mg/dl. Their extremely impaired performance is a clear example of behavioral effects when BALs rise above legally intoxicated levels [cf. (33)]. Additionally, performance was most impaired under the high alcohol dose during the ascending and early descending phases of the BAL curve (15–105 minutes postdrug),that is during the time of highest blood levels. This correspondence between BAL and degree of impairment is consistent with many other studies assessing the effect of alcohol on task performance [e.g., (35,43)]. In contrast, the low dose of alcohol significantly impaired performance only on the circular lights task, although responding was also somewhat slowed on the DSST. This relative lack of performance impairment with 0.6 g/kg alcohol is consistent with some previous studies testing comparable doses of alcohol (8, 9, 23, 40). For example, MacAvoy and Marks (28) reported no impairment on a divided visual attention task at BALs of 48 and 96 mg/dl. However, the majority of recent research has reported significant performance impairment using comparable or even lower doses of alcohol (1, 4, 21, 31, 32, 35). This suggests that our performance tasks may have been less sensitive to the effects of lower alcohol doses than the tasks used in these recent studies. It is also clear that tolerance to the effect of alcohol plays a role in the degree of performance impairment (32).

The two doses of marijuana were physiologically active, as evidenced by the heart rate measure (Fig. 1) and produced subjective effects that were clearly different from placebo (Fig. 2). However, unlike alcohol, the two active marijuana doses produced subjective effects that did not differ in magnitude or duration. We followed a commonly used dosing procedure by varying the THC content of the marijuana cigarettes while holding smoking parameters constant. This means of dosage variation can produce dose-related differences in plasma THC concentrations (38). However, many researchers have also reported no differences on measures of subjective drug effect across active marijuana doses delivered in this manner (10, 22, 36, 38). This suggests that either the subjective effect of smoked marijuana was not easily discriminable because of subtle differences between doses or that the delivered doses were not very different. The latter alternative may be explained by the possibility that subjects altered their smoking behavior relative to the potency of the marijuana.

That smoking behavior changes occurred in this study was suggested by the observation that CO boosts were inversely related to marijuana dose (Fig. 1). Nemeth-Coslett *et al.* (36) reported similar findings and suggested that compensatory changes in smoking and/or CO yield differences of the placebo and active marijuana cigarettes were responsible for this result. Using an automatic smoking machine, it was shown that the CO generated by active marijuana cigarettes of various potencies (0.9–2.6% THC) was equivalent; however, the CO yield of placebo marijuana cigarettes was about 30% greater than that of active marijuana (42). This could account for the difference in CO boosts between active and placebo cigarettes. However, a difference in CO boost be-

tween the active marijuana doses suggests that some degree of dose regulation was also occurring. That is, in spite of experimenter-controlled puffing procedures, subjects were able to reduce intake of smoke from the higher potency cigarette compared to the lower potency cigarette. This may have contributed to the poor subjective differentiation between active marijuana doses in the present study. Thus, a smoking procedure which controls only puff number and inhalation duration may not be an effective means of accurately varying THC dose. It is possible that better dosage differentiation could be achieved by developing marijuana cigarettes with a wider range of THC concentration and/or utilizing methods that allow greater control of smoking parameters, such as puff and inhalation volumes. Measurement of plasma THC levels would also be desirable to verify delivered dosage.

Marijuana produced minimal performance impairment (Fig. 3). This may be due, in part, to the use of relatively low marijuana doses. Even the highest dose (16 puffs from 2.7% THC cigarettes) may represent light exposure because regular smokers studied in the laboratory have taken twice this number of puffs during ad lib smoking of a single marijuana cigarette of comparable potency (38). Additionally, the systemic availability of THC from marijuana smoke has recently been estimated to be as low as 8–24% of a cigarette's total THC content (37). It is also possible that the tasks employed in this study were not optimal for assessing the effects of marijuana. Other investigators have reported marijuana-induced decrements in tracking performance (12, 16, 21, 29, 45) or tracking combined with a visual search task (2,14). However, the tasks used in these studies were pursuit or compensatory tracking, which may be more difficult than the tracking task reported here. Contrary to the results of this study, circular lights performance impairment has been reported following ad lib smoking of two 2.8% THC cigarettes (10). This amount of marijuana was comparable to the high dose condition in the present study; however, ad lib smoking may have resulted in greater THC plasma levels than our paced smoking procedure, which limited number of puffs. In the present study, the DSST was sensitive to the performance impairing effects of both marijuana doses, which is consistent with its demonstrated sensitivity to other drugs (18, 27, 41). The behavioral effects of marijuana are most clearly observed when rapid, complex responses are required (13,24). Thus, road driving or its simulation (11, 21, 39) and divided attention tasks (2, 6, 14, 21, 28) have also been reported to be sensitive to the performance impairing effect of marijuana. It would be of interest to examine the effects of marijuana on more complex performance tasks.

The majority of past research investigating the effects of alcohol and marijuana has been limited by testing single, rather than multiple, doses of both drugs (4, 25, 30, 40, 44). Additionally, many studies have examined alcohol and marijuana effects across a limited range of physiological, subjective, and performance measures (3, 5, 8, 9, 11, 23, 28, 39). Recent work characterizing the effects and abuse liability of illicit drugs in humans has emphasized the importance of assessing a range of doses on both subjective and performance measures over an appropriate time course to obtain a complete comparative drug effect profile (18,41). This study has compared dose effects of alcohol and marijuana across a range of outcome measures for several hours. We found that 16 puffs from marijuana cigarettes containing either 1.3 or 2.7% THC produced subjective effects similar in magnitude and time course to those reported after 0.6 g/kg alcohol. These doses that elicited comparable subjective ratings also similarly produced minimal psychomotor performance impairment.

In testing multiple doses of each drug on a repeated battery of physiological, subjective report, and performance measures, the present study represents a methodological improvement in comparing the effect profiles of alcohol and marijuana. We view this as a first attempt in identifying dose ranges and developing a sensitive test battery for a systematic comparison of these two widely used and abused drugs. However, to characterize fully the dose response effects of alcohol and marijuana, future studies should develop more drug-sensitive behavioral tasks, use methods that allow greater control over marijuana dosage via the inhalation route, and measure plasma THC levels to verify delivered dose.

ACKNOWLEDGEMENTS

This research was supported by USPHS Research Grant DA-03891, Research Training Grant DA-07209, and Research Scientist Development Award DA-00050 from the National Institute on Drug Abuse and by National Patent Analytical Systems, Inc. A preliminary report of these findings was presented at the 1987 meeting of the Eastern Psychological Association.

REFERENCES

1. Annear, W. C.; Vogel-Sprott, M. Mental rehearsal and classical conditioning contribute to ethanol tolerance in humans. Psychopharmacology (Berlin) 87:90–93; 1985.
2. Barnett, G.; Licko, V.; Thompson, T. Behavioral pharmacokinetics of marijuana. Psychopharmacology (Berlin) 85:51–56; 1985.
3. Bech, P.; Rafaelsen, L.; Rafaelsen, O. J. Cannabis and alcohol: Effects on estimation of time and distance. Psychopharmacologia 32:373–381; 1973.
4. Belgrave, B. E.; Bird, K. D.; Chesher, G. B.; Jackson, D. M.; Lubbe, K. E.; Starmer, G. A.; Teo, K. C. The effect of (−) Trans-Δ^9-tetrahydrocannabinol, alone and in combination with ethanol, on human performance. Psychopharmacology (Berlin) 62:53–60; 1979.
5. Cappell, H.; Webster, C. D.; Herring, B. S.; Ginsberg, R. Alcohol and marihuana: A comparison of effects on a temporally controlled operant in humans. J. Pharmacol. Exp. Ther. 182:195–203; 1972.
6. Casswell, S.; Marks, D. Cannabis induced impairment of performance of a divided attention task. Nature 241:60–61; 1973.
7. Chait, L. D.; Fischman, M. W.; Schuster, C. R. 'Hangover' effects the morning after marijuana smoking. Drug Alcohol Depend. 15:229–238; 1985.
8. Chesher, G. B.; Franks, H. M.; Hensley, V. R.; Hensley, W. J.; Jackson, D. M.; Starmer, G. A.; Teo, R. K. C. The interaction of ethanol and Δ^9-tetrahydrocannabinol in man: Effects on perceptual, cognitive and motor functions. Med. J. Aust. 2:159–163; 1976.
9. Chesher, G. B.; Franks, H. M.; Jackson, D. M.; Starmer, G. A.; Teo, R. K. C. Ethanol and Δ^9-tetrahydrocannabinol: Interactive effects on human perceptual, cognitive and motor functions. II. Med. J. Aust. 1:478–481; 1977.
10. Cone, E. J.; Johnson, R. E.; Moore, J. D.; Roache, J. D. Acute effects of smoking marijuana on hormones, subjective effects and performance in male human subjects. Pharmacol. Biochem. Behav. 24:1749–1754; 1986.

11. Crancer, A.; Dille, J. M.; Delay, J. C.; Wallace, J. E.; Haykin, M. D. Comparison of the effects of marihuana and alcohol on simulated driving performance. Science 164:851–854; 1969.
12. Dalton, W. S.; Martz, R.; Lemberger, L.; Rodda, B. E.; Forney, R. B. Effects of marihuana combined with secobarbital. Clin. Pharmacol. Ther. 18:298–304; 1975.
13. Dewey, W. L. Cannabinoid pharmacology. Pharmacol. Rev. 38:151–178; 1986.
14. Evans, M. A.; Martz, R.; Brown, D. J.; Rodda, B. E.; Kiplinger, G. F.; Lemberger, L.; Forney, R. B. Impairment of performance with low doses of marihuana. Clin. Pharmacol. Ther. 14:936–940; 1973.
15. Evans, M. A.; Martz, R.; Rodda, B. E.; Kiplinger, G. F.; Forney, R. B. Quantitative relationship between blood alcohol concentration and psychomotor performance. Clin. Pharmacol. Ther. 15:253–260; 1974.
16. Evans, M. A.; Martz, R.; Rodda, B. E.; Lemberger, L.; Forney, R. B. Effects of marihuana-dextroamphetamine combination. Clin. Pharmacol. Ther. 20:350–358; 1976.
17. Griffiths, R. R.; Bigelow, G. E.; Liebson, I. Differential effects of diazepam and pentobarbital on mood and behavior. Arch. Gen. Psychiatry 40:865–873; 1983.
18. Griffiths, R. R.; McLeod, D. R.; Bigelow, G. E.; Liebson, I. A.; Roache, J. D. Relative abuse liability of diazepam and oxazepam: Behavioral and subjective dose effects. Psychopharmacology (Berlin) 84:147–154; 1984.
19. Gustafson, R. Alcohol and vigilance performance: Effect of small doses of alcohol on simple visual reaction time. Percept. Mot. Skills 62:951–955; 1986.
20. Gustafson, R. Effect of moderate doses of alcohol on simple auditory reaction time in a vigilance setting. Percept. Mot. Skills 62:683–690; 1986.
21. Hansteen, R. W.; Miller, R. D.; Lonero, L.; Reid, L. D.; Jones, B. Effects of cannabis and alcohol on automobile driving and psychomotor tracking. Ann. NY Acad. Sci. 282:240–256; 1976.
22. Higgins, S. T.; Stitzer, M. L. Acute marijuana effects on social conversation. Psychopharmacology (Berlin) 89:234–238; 1986.
23. Hollister, L. E.; Gillespie, H. K. Marihuana, ethanol, and dextroamphetamine. Arch. Gen. Psychiatry 23:199–203; 1970.
24. Jones, R. T. Human effects: An overview. In: Petersen, R. C., ed. Marijuana research findings: 1980. NIDA Research Monograph. 31. Washington, DC: U.S. Government Printing Office; 1980:54–80.
25. Jones, R. T.; Stone, G. C. Psychological studies of marijuana and alcohol in man. Psychopharmacologia 18:108–117; 1970.
26. Klein, R. H.; Jex, H. R. Effects of alcohol on a critical tracking task. J. Stud. Alcohol 36:11–20; 1975.
27. McLeod, D. R.; Griffiths, R. R.; Bigelow, G. E.; Yingling, J. An automated version of the digit symbol substitution test (DSST). Behav. Res. Methods Instrum. 14:463–466; 1982.
28. MacAvoy, M. G.; Marks, D. F. Divided attention performance of cannabis users and non-users following cannabis and alcohol. Psychopharmacologia 44:147–152; 1975.
29. Manno, J. E.; Kiplinger, G. F.; Haine, S. E.; Bennett, I. F.; Forney, R. B. Comparative effects of smoking marihuana or placebo on human motor and mental performance. Clin. Pharmacol. Ther. 11:808–815; 1970.
30. Manno, J. E.; Kiplinger, G. F.; Scholz, N.; Forney, R. B. The influence of alcohol and marihuana on motor and mental performance. Clin. Pharmacol. Ther. 12:202–211; 1971.
31. Mills, K. C.; Bisgrove, E. Z. Body sway and divided attention performance under the influence of alcohol: Dose-response differences between males and females. Alcohol.: Clin. Exp. Res. 7:393–397; 1983.
32. Mills, K. C.; Bisgrove, E. Z. Cognitive impairment and perceived risk from alcohol: Laboratory, self-report and field assessments. J. Stud. Alcohol 44:26–46; 1983.
33. Mitchell, M. C. Alcohol-induced impairment of central nervous system function: Behavioral skills involved in driving. J. Stud. Alcohol [Suppl.] 10:109–116; 1985.
34. Moskowitz, H.; Burns, M. Effects of rate of drinking on human performance. J. Stud. Alcohol 37:598–605; 1976.
35. Moskowitz, H.; Burns, M.; Williams, A. F. Skills performance at low blood alcohol levels. J. Stud. Alcohol 46:482–485; 1985.
36. Nemeth-Coslett, R.; Henningfield, J. E.; O'Keeffe, M. K.; Griffiths, R. R. Effects of marijuana smoking on subjective ratings and tobacco smoking. Pharmacol. Biochem. Behav. 25:659–665; 1986.
37. Ohlsson, A.; Lindgren, J-E.; Wahlen, A.; Agurell, S.; Hollister, L. E.; Gillespie, H. K. Plasma delta-9-tetrahydrocannabinol concentrations and clinical effects after oral and intravenous administration and smoking. Clin. Pharmacol. Ther. 28:409–416; 1980.
38. Perez-Reyes, M.; Di Guiseppi, S.; Davis, K. H.; Schindler, V. H.; Cook, C. E. Comparison of effects of marihuana cigarettes of three different potencies. Clin. Pharmacol. Ther. 31:617–624; 1982.
39. Rafaelsen, O. J.; Bech, P.; Christiansen, J.; Christrup, H.; Nyboe, J.; Rafaelsen, L. Cannabis and alcohol: Effects on simulated car driving. Science 179:920–923; 1973.
40. Rafaelsen, L.; Christrup, H.; Bech, P.; Rafaelsen, O. J. Effects of cannabis and alcohol on psychological tests. Nature 242:117–118; 1973.
41. Roache, J. D.; Griffiths, R. R. Comparison of triazolam and pentobarbital: Performance impairment, subjective effects and abuse liability. J. Pharmacol. Exp. Ther. 234:120–133; 1985.
42. Rosenkrantz, H.; Fleischman, R. W. Effects of cannabis on lungs. In: Nahas, G. G.; Paton, W. D. M., eds. Marijuana: Biological effects. Oxford: Pergamon Press; 1979:279–299.
43. Sidell, F. R.; Pless, J. E. Ethyl alcohol: Blood levels and performance decrements after oral administration to man. Psychopharmacologia 19:246–261; 1971.
44. Sutton, L. R. The effects of alcohol, marihuana and their combination on driving ability. J. Stud. Alcohol 44:438–445; 1983.
45. Weil, A. T.; Zinberg, N. E.; Nelsen, J. M. Clinical and psychological effects of marihuana in man. Science 162:1234–1242; 1968.