Psychopharmacology (1994) 115:340–349

Psychopharmacology

Acute and residual effects of alcohol and marijuana, alone and in combination, on mood and performance

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Received: 6 August 1992 / Final version: 8 July 1993

Abstract. The duration of behavioral impairment after marijuana smoking remains a matter of some debate. Alcohol and marijuana are frequently used together, but there has been little study of the effects of this drug combination on mood and behavior the day after use. The present study was designed to address these issues. Fourteen male and female subjects were each studied under four conditions: alcohol alone, marijuana alone, alcohol and marijuana in combination, and no active treatment. Mood and performance assessments were made during acute intoxication and twice the following day (morning and mid-afternoon). Acutely, each drug alone produced moderate levels of subjective intoxication and some degree of behavioral impairment. The drug combination produced the greatest level of impairment on most tasks and "strong" overall subjective ratings. There were few significant interactions between the two drugs, indicating that their effects tended to be additive. Only weak evidence was obtained for subjective or behavioral effects the day after active drug treatments, although consistent time-of-day effects (morning versus afternoon) were observed on several subjective and behavioral measures. In sum, this study provided little evidence that moderate doses of alcohol and marijuana, consumed either alone or in combination, produce behavioral or subjective impairment the following day.

Key words: Human – Marijuana – Alcohol – Drug interaction – Residual effects – Psychomotor effects – Cognitive effects – Subjective effects

There is much evidence that marijuana smoking can produce short-term impairments in human performance on a variety of tasks. The duration of behavioral impairment, however, has not been firmly established. Most studies of marijuana-induced performance effects have not measured behavior beyond 1–2 h after smoking (Chait and Pierri 1992). Of those that have, results have been inconsistent; some report impairments lasting as long as 24 h (Yesavage et al. 1985; Leirer et al. 1991), whereas others fail to find impairment lasting longer than 7 h (Hansteen et al. 1976; Janowsky et al. 1976; Barnett et al. 1985; Cone et al. 1986; Heishman et al. 1989; Leirer et al. 1989).

Our laboratory has conducted two studies attempting to demonstrate behavioral impairment the morning after marijuana smoking (Chait et al. 1985; Chait 1990). Taken together, these two studies found no consistent evidence of either subjective or performance effects the day after use. The present study was designed as a systematic replication of these previous studies. One difference from the previous studies was the inclusion of alcohol, given both alone and in combination with marijuana. Marijuana and alcohol are frequently used together, and the possibility exists that one agent could interact with the other to either potentiate or antagonize next-day effects produced by either drug. In addition, we believed that the alcohol alone condition might serve as a useful positive control, since alcohol, in high doses, is well known to produce "hangover" effects the day after use (Smith and Barnes 1983). Another difference was that in the present study next-day behavior was measured at two different time points: in the morning soon after awakening and in mid-afternoon. The rationale for doing this was evidence that residual effects of sedative-hypnotic drugs can be greater later in the day than in the morning, perhaps due to interactions between drug effects and circadian rhythms (Johnson and Chernik 1982).

Material and methods

Subjects. Volunteers provided a detailed drug and medical history, and received a psychiatric and physical examination before participation. Only those judged healthy with no history of substance use disorder (DSM-III-R criteria, excluding tobacco dependence) were allowed to participate. In addition, volunteers were required to meet each of the following three criteria: 1) current use of marijuana (at least once per month), 2) current use of alcohol (at least once per

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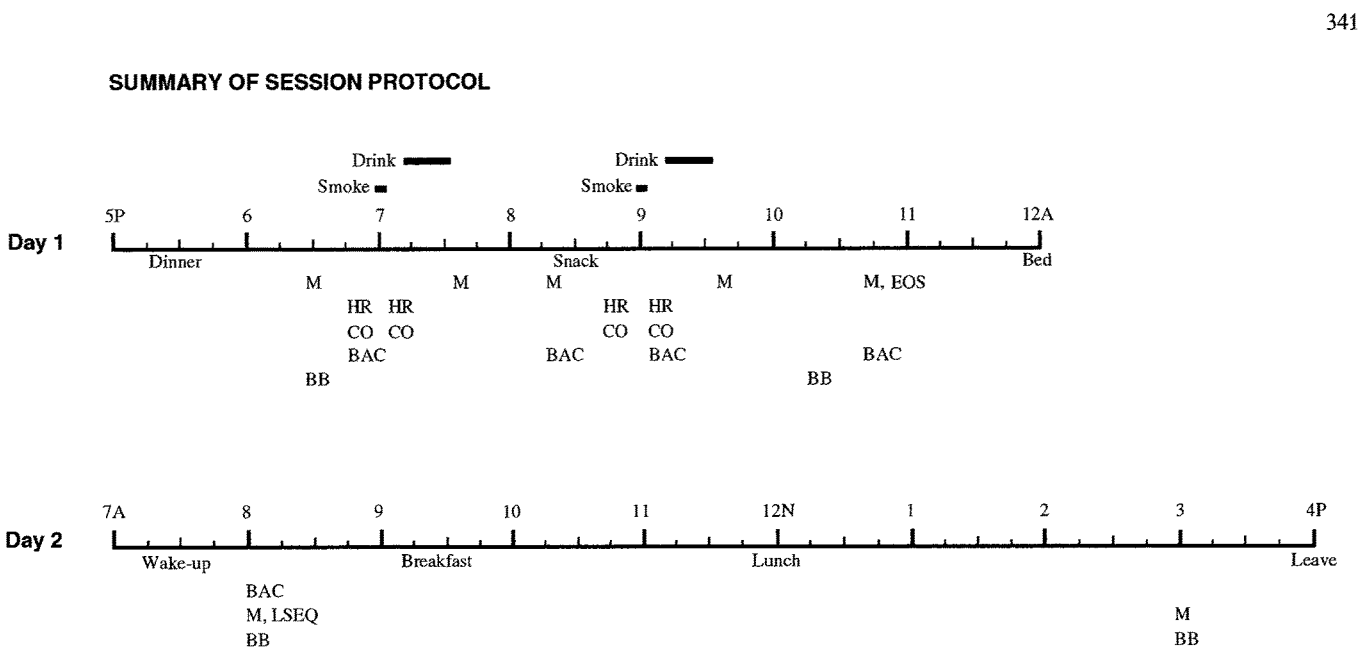

Fig. 1. Schematic diagram of the sequence of events during experimental sessions. Day 1: drug administration and measurement of acute drug effects. Day 2: measurement of residual drug effects. *BB*, behavior battery; *BAC*, blood alcohol; *CO*, carbon monoxide; *EOS*, End-of-Session Questionnaire; *HR*, heart rate; *M*, Mood Questionnaires; *LSEQ*, Leeds Sleep Questionnaire

week), and 3) consumption of four or more alcoholic drinks on a single occasion at least once in the past month. Informed consent was obtained, and subjects were paid a base wage at the end of the study. Eighteen subjects began the study; three failed to finish (two of these due to adverse drug reactions). Data from one additional subject who did complete the study were not used because preliminary analysis indicated that he was insensitive to the dose of marijuana administered – this subject consistently failed to show an increase in heart rate or subjective "high" after smoking active marijuana. The remaining 14 subjects (10 males, 4 females) ranged in age from 21 to 34 years (mean = 24.5). All but four reported use of marijuana on at least 100 occasions (lifetime). At the time of participation, subjects reported drinking an average of 7 alcoholic drinks per week (range, 2–12) and smoking marijuana an average of 4 times a month (range, 1–16). Four of the 14 subjects also smoked tobacco cigarettes; all smoked less than a pack a day.

Subjects were informed that the purpose of the study was to examine the effects of marijuana and alcohol on mood and behavior. They were told that the marijuana they would receive during the study may or may not contain THC, the active constituent of marijuana, and that the drinks may or may not contain alcohol. Subjects were also instructed not to use any drugs other than tobacco and caffeine outside the laboratory during the 24 h prior to scheduled sessions.

Experimental design and general procedures. The study consisted of five sessions – a single evening practice session and four overnight sessions. The purpose of the practice session, which was conducted in the week just prior to the first overnight session, was to expose subjects to all of the procedures they would encounter during the overnight sessions and to minimize practice effects. All subjects received four puffs of active marijuana and one alcoholic drink during the practice session, and performed the behavioral test battery twice; all of the procedures were the same as those used during the subsequent overnight sessions.

Four treatment conditions were scheduled on the overnight sessions: alcoholic beverage and active marijuana (AM), alcoholic beverage and placebo marijuana (AP), placebo beverage and active marijuana (PM), and placebo beverage and placebo marijuana (PP). Each subject was tested once under each condition and the order of treatments was counterbalanced across subjects. For most subjects the sessions were scheduled 1 week apart on the same day of the week. Subjects were tested in pairs, but treatment condition varied for each member of a pair. Both subjects and experimenter were blind to the treatment conditions.

Subjects were admitted to a private room in the Clinical Research Center (CRC) for the four overnight sessions. They arrived at 5 P.M. and ate dinner (Fig. 1). At 6:30 P.M. subjects left the CRC and were brought to a room in a separate area of the hospital where behavioral testing and drug administration took place. Subjects were returned to the CRC at 11:45 P.M. Nursing staff ensured that subjects were in their rooms with lights out by midnight, and that subjects were awakened at 7:30 the following morning. Subjects were allowed 30 min to wash and dress before behavioral testing began (about 8 A.M.). Eating, smoking, and coffee drinking were not allowed, however, until after the morning testing was completed. Subjects were tested once more in the afternoon at 3:00 P.M. Subjects were discharged at 4 P.M. Both the morning and afternoon testing were conducted in the same room as the evening testing.

Drug administration. There were two identical drug administration periods scheduled 2 h apart in the evening sessions (Fig. 1). Each administration consisted of a 5-min smoking component and a 20-min drinking component. The smoking component consisted of four inhalations ("puffs") of marijuana smoke administered with a standardized puffing procedure (Chait et al. 1988a). The drinking component began 10 min after the final puff. Subjects were given 20 min to consume the beverage. This entire procedure was repeated 2 h later. Thus, during each session subjects received a total of eight puffs of marijuana smoke and two alcoholic beverages. Subjects were not allowed to smoke tobacco cigarettes during the evening. Eating was prohibited as well except for a small snack that was provided around 8:30 P.M. Free access to drinking water was provided during marijuana smoking.

The dose of alcohol and marijuana selected for study was based upon prior research in our laboratory. We attempted to choose a dose of each drug that would produce moderate and comparable levels of subjective intoxication when administered alone, but that were not so large as to produce aversive effects when given in combination. The drugs were administered on two separate occasions during the evening in order to simulate the way the drugs might be used in the natural environment (e.g., at a party). We also

assumed that dividing the dose of alcohol would allow the administration of a larger dose than could otherwise be given in a single sitting.

Marijuana cigarettes. Pre-rolled marijuana cigarettes were supplied by the National Institute on Drug Abuse. The delta-9-THC contents of the cigarettes were 0.0% (placebo) or 3.6% (active). Cigarettes were stored in airtight containers in a cold room, and were humidified for 24 h at room temperature before use.

Alcoholic beverages. Alcoholic beverages consisted of 95% ethanol in diet tonic water and lime juice. The content (v/v) of the placebo beverage was 1% ethanol (as a taste mask), 4% lime juice, and 95% tonic, while the content of the alcoholic beverage was 10% ethanol, 4% lime juice, and 86% tonic. Drink volume was adjusted for gender and body weight so that the dose for the alcohol conditions was 0.6 g/kg for males and 0.5 g/kg for females. Drink volume was 540 ml/70 kg for males and 450 ml/70 kg for females. The beverages were served cold in 1 l plastic containers.

Heart rate. Heart rate was measured just before and after marijuana smoking as an indirect indicator of THC absorption. Radial pulse was measured digitally for 30 s.

Carbon monoxide level. Post-smoking increase in expired air carbon monoxide level (CO boost) served as an index of marijuana smoke exposure. CO was measured just before and after marijuana smoking. Samples were collected according to the procedure described by Chait and Griffiths (1982), and were read immediately with a portable CO meter (Mini CO Model 1000, Catalyst Research, Baltimore).

Blood alcohol concentration. Blood alcohol concentration (BAC) was determined five times during the sessions: just before each drink, 45 min after the first drink, 65 min after the second drink, and in the morning (Fig. 1). BAC was estimated with a breathalyzer (Alco-Sensor, Intoximeters, St Louis).

Subjective measures. Three different subjective effects questionnaires were used to assess mood state: an experimental version of the Profile of Mood States (POMS), a 53-item version of the Addiction Research Center Inventory (ARCI), and a series of six visual analog scales (VAS). These questionnaires were administered as a set seven times during the course of the sessions (Fig. 1).

The POMS (McNair et al. 1971) consisted of 72 adjectives commonly used to describe momentary mood states. Subjects indicated how they felt at the time for each adjective on a 5-point scale ranging from "not at all" (0) to "extremely" (4). Eight clusters of adjectives representing specific mood states (Anxiety, Depression, Anger, Vigor, Fatigue, Confusion, Friendliness, Elation) have been formed using factor analysis. The value of each scale is determined by adding the numbers checked for each adjective in the cluster and dividing the total by the number of adjectives in that cluster.

The ARCI (Haertzen 1974) is a true-false questionnaire with empirically derived scales sensitive to the effects of a variety of classes of psychoactive drugs. The version used consisted of 53 items comprising six scales: MBG, a putative measure of drug-induced euphoria; A, a scale specific for dose-related effects of d-amphetamine; BG, an amphetamine scale consisting mainly of items relating to intellectual efficiency and energy; PCAG, a measure of sedation; LSD, a measure of dysphoria and somatic symptoms; and M, a measure of marijuana effects (Chait et al. 1985).

The VAS consisted of six 100-mm horizontal lines each labelled with an adjective ("stimulated," "high," "anxious," "sedated," "drunk," and "hungry"). The left ends of the lines were labelled "not at all" and the right ends "extremely." Subjects were instructed to place a mark on each line indicating how they felt at the moment.

Subjects completed an End-of-Session (EOS) questionnaire at approximately 11:00 P.M. each evening. This questionnaire asked subjects to rate the strength of the overall drug effect on a 5-point scale (1 = "I felt no effect at all."; 2 = "I think I felt a mild effect, but I'm not sure."; 3 = "I definitely felt an effect, but it was not real strong."; 4 = "I felt a strong effect."; and 5 = "I felt a very strong effect."); and how much they liked the drug effect (on a 100-mm visual analog scale with 0 = "disliked a lot"; 50 = "neutral"; and 100 = "liked a lot").

Subjects also completed the Leeds Sleep Evaluation Questionnaire (LSEQ) in the morning. The LSEQ measures four aspects of sleep: getting to sleep (GTS), quality of sleep (QOS), awakening from sleep (AFS), and behavior following wakefulness (BFW). The instructions for all of the scales ask the subjects to rate their sleep relative to their usual sleep. The LSEQ has been shown to be sensitive to the residual effects of a variety of sedative-hypnotics (Parrott and Hindmarch 1980).

Behavioral tasks. Subjects performed a battery of behavioral tasks four times during each session: twice in the evening (pre- and post-drug administration) and twice the next day (morning and afternoon) (Fig. 1). The battery was designed to include a wide range of motor, psychomotor and cognitive tasks that have been shown in other studies to be sensitive to alcohol and/or marijuana. The tasks were performed in a fixed order. The first was a time production test. After a verbal cue from the experimenter, subjects were instructed to respond "30," "60," and "120" when they believed that 30, 60, and 120 s had elapsed. Next, subjects performed a standing steadiness task. Subjects were required to stand on one leg with their arms outstretched and their eyes closed for as long as they could without touching the raised foot to the floor. Subjects then repeated the task with the other leg. The experimenter recorded the time at which the subject's foot touched the floor up to a maximum of 30 s. Lastly, subjects performed five automated tasks on an Apple IIe computer. The tasks were scheduled in the following order: digit symbol substitution test (DSST), backward digit span (two trials), logical reasoning (Baddeley 1968), visual divided attention, and free recall. For the logical reasoning task subjects were presented with statements describing the relationship between the letters A and B (for example, "A is not preceded by B") followed by the letter pair in either order ("AB" or "BA"). After each statement, subjects responded T (true) or F (false) according to whether they thought the statement was a true description of the letter pair. The divided attention task required subjects to respond as quickly as possible to a primary target stimulus (the digit zero) presented in a continuous string of random digits while at the same time counting (and remembering) the number of occurrences of a secondary target stimulus (the digit five followed immediately by a number larger than five). For the free recall task, 20 common three-letter nouns (randomly selected from a master list of 140) were displayed to subjects one after the other. Subjects then typed in as many of the 20 words as they could recall. The DSST, backward digit span, divided attention and free recall tasks are described in detail elsewhere (McLeod et al. 1988). The entire sequence of computer tasks took 10–15 min to complete.

Data analysis. Most dependent variables were analyzed with univariate repeated measures analysis of variance (ANOVA). Data collected during evening sessions (acute effects) were analyzed separately from data collected the following day (next-day effects). For analysis of acute effects, ANOVA factors were Alcohol (active versus placebo), Marijuana (active versus placebo) and Time (number of levels varied depending upon the number of determinations during the evening). For the sake of brevity, significant main effects of Alcohol, Marijuana, and Time will not be presented, since they do not reflect drug-induced changes over time, and hence are not of primary interest. For CO and heart rate, post- minus pre-smoking difference scores were used in the ANOVAs, and Drug Administration Period (first versus second) served as an additional factor. For analysis of next-day effects, the ANOVA factors were Alcohol, Marijuana and Time-of-Day (morning versus afternoon). Additional factors were included for some measures (e.g., Target Interval for the time production task, Gender for BAC). Huynh-Feldt adjustments of within-factors degrees of freedom were used to protect against violations of sphericity (Schutz and Gessaroli 1987). Tukey post-hoc

tests were used to compare treatment means when complex interactions were obtained. Ratings of strength of drug effect (ordinal scale) were analyzed with the nonparametric Wilcoxin sign-rank test. Results were considered to be statistically significant for $P \leq 0.05$ (two-tailed).

Results

Acute effects

Blood alcohol concentration. For active alcohol sessions (AP and AM), the mean BAC (mg/dl) was 49 after the first drink, 39 before the second drink, and 88 after the second drink. There was no significant difference in BAC between the AP and AM conditions or between males and females. All BACs were zero at baseline and throughout PM and PP sessions.

Carbon monoxide level. Baseline CO level averaged 6.8 ppm. As expected, the standardized smoking procedure produced reliable CO boosts, ranging from 2 to 11 ppm/4 puffs. Mean CO boost did not differ between the two evening smoke administrations, indicating that subjects did not alter their smoke intake during the second smoking period in response to the initial drug administration. Alcohol condition had no effect on CO boosts. Unexpectedly, greater CO boosts were obtained after active marijuana (mean = 5.1 ppm) than after placebo marijuana (mean = 3.8 ppm) [Marijuana effect: $F(1, 13) = 79.5$, $P = 0.0001$].

Heart rate. Baseline heart rate averaged 71 bpm. As expected, active marijuana increased heart rate; a significant Marijuana × Drug Administration Period interaction indicated that the increase was greater during the first (mean = 18.9 bpm) than during the second (mean = 13.9) smoking period [$F(1, 13) = 6.7$, $P < 0.025$]. The effect of active marijuana on heart rate varied considerably across subjects, from no increase at all to a 56 bpm increase. Neither placebo marijuana nor alcohol significantly altered heart rate, and there was no interaction between marijuana and alcohol.

Subjective effects. End-of-Session questionnaire. The mean overall strength of drug effect ratings for the PP, PM, AP, and AM conditions, respectively, were 1.9, 3.3, 3.5 and 4.1. The means for the three active drug conditions all differed significantly from that of the control (PP) condition (all $P < 0.01$).The fact that the means of the single drug conditions (PM and AP) were virtually identical suggests that we were successful in selecting doses of the two drugs that were equivalent in terms of global discriminative stimulus effects. Ratings of the drug combination (AM) ranged from 3 (definite effect) to 5 (very strong effect).

The only significant effect for ratings of drug liking was a main effect of Marijuana [$F(1, 13) = 9.9$, $P < 0.01$]. Subjects rated liking active marijuana (mean = 64.4) more than placebo (mean = 51.3).

POMS. The POMS was insensitive to the drug treatments, although five of the eight scales did show significant main effects of Time, reflecting more negative mood and greater fatigue as the evening progressed, regardless of drug condition.

ARCI. The only ARCI scale to show significant drug effects was the M (Marijuana) scale [Alcohol × Time: $F(4, 52) = 4.1$, $P < 0.025$; Marijuana × Time: $F(4,$

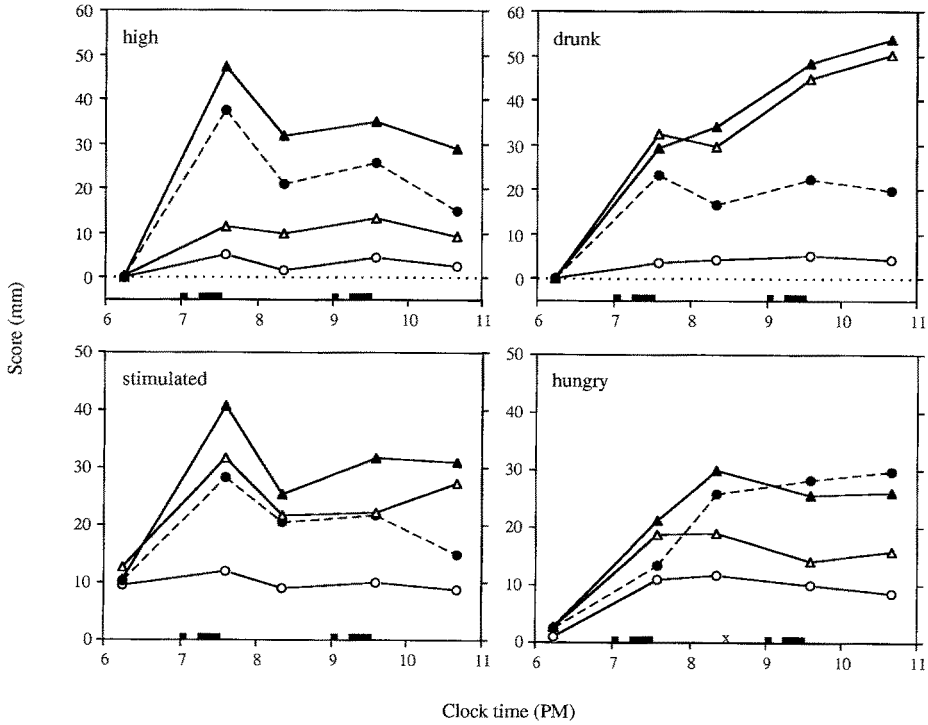

Fig. 2. Group mean ratings on four of the visual analog scales. Ratings could range from 0 to 100. *Thick bars* along the x-axis indicate times and durations of drug administration (*short bars*: smoking; *long bars*: drinking). The "*x*" along the x-axis for "*hungry*" ratings shows the time when a snack was provided. ○, PP; Δ, AP; ●, PM; ▲, AM

52) = 3.8, $P < 0.025$]. Mean scores were increased by 1–2 items on the 12-item scale after each of the active drug treatments relative to control (PP condition).

VAS. Four of the VAS scales were sensitive to the drug treatments (Fig. 2). Ratings of "high" were increased only by marijuana [Marijuana × Time: $F(4, 52) = 17.5$, $P < 0.0001$] whereas ratings of "drunk" were increased only by alcohol [Alcohol × Time: $F(4, 32) = 8.7$, $P = 0.0005$]. With active marijuana, "high" ratings peaked after the first drug administration and showed little further increase after the second drug administration. In contrast, ratings of "drunk" continued to increase throughout the evening when alcohol was given. Ratings of "stimulated" were increased by both drugs [Alcohol × Time: $F(4, 52) = 3.4$, $P < 0.025$; Marijuana × Time: $F(4, 52) = 3.4$, $P < 0.05$]. Marijuana, but not alcohol, also resulted in higher ratings of "hungry" [Marijuana × Time: $F(4, 52) = 6.4$, $P < 0.005$]. Interestingly, the effects of marijuana on "hungry" ratings showed a different time course from the effects of the drug on "high," with "hungry" ratings peaking later in the session (Fig. 2).

Behavioral effects. Time production. Both drugs affected time production [Alcohol × Target Interval: $F(2, 24) = 9.7$, $P < 0.01$; Marijuana × Target Interval: $F(2, 24) = 4.2$, $P < 0.05$]. As shown in Fig. 3, the two drugs produced opposite effects – alcohol administration resulted in subjects producing time intervals longer than the targets (overproduction), whereas marijuana administration occasioned underproduction. When the two drugs were given in combination, (AM condition) the effects canceled each other out, resulting in no effect.

Standing steadiness. Only alcohol impaired performance on this task [Alcohol × Time: $F(1, 13) = 9.9$, $P < 0.01$]. The mean score (time summed for both legs) dropped from 57.7 s before drug to 45.9 s after drug.

DSST. Alcohol impaired performance on all measures of DSST performance: number attempted [Alcohol × Time: $F(1, 13) = 23.3$, $P < 0.0005$], number correct [Alcohol × Time: $F(1, 13) = 22.3$, $P < 0.0005$], and percentage correct [Alcohol × Time: $F(1, 13) = 7.2$, $P < 0.025$]. Number correct decreased from a mean of 43.9 before alcohol to 37.4 after, while mean percentage correct decreased from 96.5 to 91.1. Marijuana affected only percentage correct [Marijuana × Time: $F(1, 13) = 8.3$, $P < 0.025$], which declined from a mean of 96.1 to 91.3.

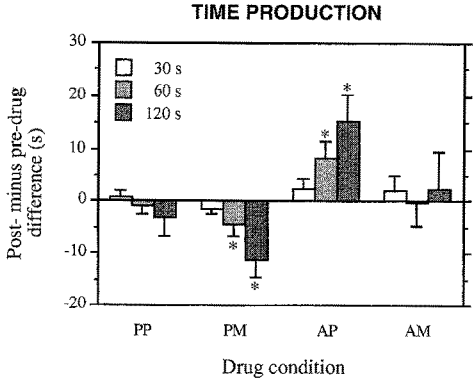

Fig. 3. Group mean (± SE) performance on the time production task during the evening session as a function of drug condition and target interval. *Asterisks* indicate a significant difference from zero (no effect) as determined by one-sample t-tests ($P \leq 0.05$)

Backward digit span. Only alcohol affected this task [Alcohol × Time: $F(1, 13) = 29.0$, $P < 0.0001$]. The average span was 6.5 digits before alcohol, compared with 5.1 digits after alcohol.

Logical reasoning. No significant drug effects were obtained on this task.

Divided attention. There were no effects of the drug treatments on either hit rate or mean reaction time for responding to the primary target. Alcohol increased errors in estimating the number of occurrences of the secondary target [Alcohol × Time: $F(1, 13) = 7.3$, $P < 0.025$], from a mean of 1.0 errors before drug to 1.6 errors after drug. Marijuana increased false alarm responses (responding to the secondary target as if it were the primary target) from 0.9 to 1.6, before and after drug, respectively [Marijuana × Time: $F(1, 13) = 5.9$, $P < 0.05$].

Free recall. Only alcohol affected this task, producing a decrement in the number of words recalled from a mean of 9.3 before drug to 6.6 after drug [Alcohol × Time: $F(1, 13) = 23.5$, $P < 0.0005$].

Next-day effects

Sleep questionnaire. Three of the four factors measured by the LSEQ showed significant drug-related effects (Table 1). Subjects rated it easier to get to sleep (GTS) after both drugs [Alcohol: $F(1, 13) = 15.8$, $P < 0.0025$; Marijuana: $F(1, 13) = 6.4$, $P < 0.025$]. For ratings of quality of sleep (QOS), a significant Alcohol × Marijuana interaction was obtained [$F(1, 13) = 4.9$, $P < 0.05$]. As Table 1 indicates, this interaction was due to higher ratings of sleep quality when alcohol and marijuana were administered alone, but relatively lower ratings after the drug combination. Finally, behavior following wakefulness (BFW) scores were decreased by Alcohol [$F(1, 12) = 7.4$, $P < 0.025$], indicating subjects felt more tired and clumsy.

Blood alcohol concentration. All morning BACs were zero with the exception of two subjects who showed BACs of 10 mg/dl after the AM session.

Subjective effects. Of the 20 mood scales, only 2 showed any significant drug-related effects, and these effects were relatively small (Table 1). On the POMS, Fatigue scores were increased by alcohol in the morning only [Alcohol × Time-of-Day: $F(1, 13) = 5.6$, $P < 0.05$]. For VAS ratings of "stimulated" a complex Alcohol × Marijuana × Time-of-Day interaction was obtained [$F(1, 13) = 10.6$, $P < 0.01$]; in the morning ratings were higher after the

Table 1. Group mean (SE) values for next-day subjective effects

	Morning test session				Afternoon test session				TOD
	PP	PM	AP	AM	PP	PM	AP	AM	
Sleep questionnaire									
GTS	36.4	51.2	60.1	66.8					
	(3.4)	(2.9)	(5.5)	(4.3)					
QOS	38.6	51.0	48.3	44.8					
	(4.0)	(3.0)	(5.2)	(5.4)					
AFS	49.0	48.9	49.2	48.0					
	(4.0)	(3.9)	(4.1)	(4.1)					
BFW	43.4	43.6	35.3	38.1					
	(3.2)	(3.0)	(1.7)	(3.1)					
POMS									
Anxiety	0.36	0.40	0.42	0.54	0.46	0.41	0.60	0.40	–
	(0.05)	(0.06)	(0.05)	(0.13)	(0.06)	(0.07)	(0.18)	(0.04)	
Depression	0.01	0.13	0.07	0.13	0.03	0.08	0.10	0.07	–
	(0.01)	(0.10)	(0.03)	(0.09)	(0.01)	(0.08)	(0.08)	(0.05)	
Anger	0.03	0.16	0.14	0.24	0.05	0.09	0.28	0.07	–
	(0.02)	(0.11)	(0.08)	(0.16)	(0.03)	(0.08)	(0.19)	(0.04)	
Vigor	0.67	0.53	0.41	0.46	1.30	0.96	1.23	1.24	**
	(0.21)	(0.12)	(0.14)	(0.12)	(0.24)	(0.17)	(0.14)	(0.23)	
Fatigue	0.45	0.64	0.79	0.71	0.21	0.29	0.11	0.18	*
	(0.15)	(0.23)	(0.20)	(0.15)	(0.12)	(0.18)	(0.06)	(0.11)	
Confusion	0.56	0.66	0.63	0.70	0.46	0.53	0.51	0.52	**
	(0.06)	(0.10)	(0.07)	(0.12)	(0.05)	(0.09)	(0.10)	(0.05)	
Friendliness	1.20	1.07	0.92	0.93	1.46	1.47	1.42	1.63	**
	(0.23)	(0.17)	(0.20)	(0.16)	(0.20)	(0.20)	(0.18)	(0.22)	
Elation	0.66	0.49	0.42	0.46	1.05	0.95	0.95	1.21	**
	(0.20)	(0.12)	(0.14)	(0.11)	(0.21)	(0.17)	(0.19)	(0.24)	
ARCI									
MBG	1.5	0.8	1.2	0.9	2.4	1.7	3.4	2.9	*
	(0.5)	(0.2)	(0.4)	(0.3)	(0.8)	(0.3)	(1.0)	(0.9)	
A	1.7	1.4	1.6	1.4	2.3	1.7	2.7	2.5	*
	(0.5)	(0.3)	(0.4)	(0.2)	(0.4)	(0.3)	(0.5)	(0.6)	
BG	5.4	4.4	4.5	4.2	5.8	5.7	6.3	5.9	*
	(0.6)	(0.5)	(0.6)	(0.3)	(0.5)	(0.3)	(0.6)	(0.6)	
PCAG	4.8	6.1	6.4	6.3	2.9	3.4	2.4	3.3	**
	(0.8)	(1.0)	(1.1)	(0.7)	(0.8)	(0.7)	(0.4)	(0.7)	
LSD	2.9	3.1	3.3	3.3	3.3	3.4	2.9	2.9	–
	(0.3)	(0.3)	(0.4)	(0.4)	(0.2)	(0.2)	(0.3)	(0.4)	
M	0.4	0.4	0.6	0.6	0.4	0.2	0.6	0.6	–
	(0.2)	(0.2)	(0.3)	(0.2)	(0.2)	(0.1)	(0.3)	(0.3)	
VAS									
stimulated	7.2	10.4	5.1	12.7	7.1	16.3	14.4	16.4	–
	(3.6)	(3.6)	(2.2)	(3.8)	(4.2)	(5.1)	(4.1)	(6.0)	
high	0.1	0.9	1.1	1.4	0.4	0.2	0.3	0.4	–
	(0.1)	(0.7)	(0.6)	(1.0)	(0.2)	(0.2)	(0.2)	(0.2)	
anxious	5.2	7.1	7.4	8.0	12.4	13.6	20.6	13.6	–
	(2.1)	(4.6)	(2.9)	(3.5)	(5.4)	(5.9)	(8.9)	(6.9)	
sedated	6.4	10.6	12.6	11.5	2.1	2.3	2.2	2.6	*
	(3.5)	(4.5)	(6.0)	(5.6)	(1.4)	(1.0)	(1.4)	(1.1)	
drunk	0.3	0.3	5.6	2.6	0.0	0.2	0.2	0.2	–
	(0.2)	(0.2)	(4.0)	(1.6)	(0.0)	(0.1)	(0.1)	(0.1)	
hungry	36.2	36.1	36.6	42.6	6.0	8.5	8.3	8.9	**
	(8.2)	(7.8)	(6.1)	(7.5)	(3.7)	(3.0)	(3.1)	(3.8)	

PP, placebo alcohol-placebo marijuana; PM, placebo alcohol-marijuana; AP, alcohol-placebo marijuana; AM, alcohol-marijuana. TOD, ANOVA Time-of-Day effect: $*P \leq 0.05$; $**P \leq 0.01$; – not significant. GTS, getting to sleep; QOS, quality of sleep; AFS, awakening following sleep; BFW, behavior following wakefulness. Sleep questionnaire and VAS scores range from 0 to 100. POMS scores range from 0 to 4. ARCI scores range from 0 to a maximum of 11 (A) to 15 (MBG and PCAG)

Table 2. Group mean (SE) values for next-day behavioral effects

	Morning test session				Afternoon test session				TOD
	PP	PM	AP	AM	PP	PM	AP	AM	
Time production									
Interval (s)									
30	34.3	34.4	31.8	32.6	31.8	31.6	32.6	31.9	**
	(1.6)	(1.5)	(1.0)	(1.2)	(1.0)	(1.2)	(2.0)	(2.3)	
60	71.9	71.3	67.7	66.3	64.7	64.3	66.3	66.8	**
	(3.7)	(2.8)	(2.4)	(2.6)	(2.6)	(2.3)	(3.6)	(5.5)	
120	144.1	137.4	136.5	127.2	129.1	126.3	130.6	128.9	**
	(6.9)	(4.2)	(5.2)	(5.7)	(5.0)	(5.3)	(6.8)	(6.9)	
Standing (s)	59.4	57.5	56.6	56.1	59.5	58.9	59.6	58.6	–
	(0.6)	(1.3)	(2.6)	(2.4)	(0.5)	(0.6)	(0.4)	(1.4)	
DSST									
Attempts	46.4	46.3	46.6	44.8	48.6	49.0	48.2	47.4	**
	(2.0)	(1.4)	(1.5)	(2.0)	(1.9)	(1.4)	(1.6)	(2.0)	
# correct	44.2	44.9	44.9	43.6	45.6	47.4	46.8	45.5	**
	(1.6)	(1.4)	(1.2)	(1.7)	(1.9)	(1.5)	(1.6)	(1.6)	
% correct	95.7	97.1	96.4	97.7	94.1	96.6	97.1	96.5	–
	(1.5)	(0.8)	(0.9)	(1.0)	(1.9)	(1.4)	(0.8)	(1.4)	
Back digit span	6.8	6.9	7.2	6.6	7.0	6.6	6.6	7.0	–
	(0.3)	(0.3)	(0.4)	(0.4)	(0.3)	(0.3)	(0.4)	(0.4)	
Logical reasoning									
Attempts	55.6	58.1	52.4	52.6	56.0	58.4	55.5	55.6	–
	(5.0)	(4.7)	(4.5)	(5.5)	(5.3)	(4.3)	(5.4)	(5.1)	
# correct	52.1	55.4	49.6	50.1	52.2	54.9	52.6	52.6	–
	(4.9)	(5.0)	(4.5)	(5.2)	(5.3)	(4.6)	(5.1)	(4.8)	
% correct	93.5	94.1	94.4	94.8	92.3	92.9	94.9	94.4	–
	(2.1)	(1.7)	(1.1)	(1.5)	(2.7)	(1.9)	(1.3)	(1.7)	
Word recall	10.1	10.6	9.9	9.3	9.7	9.7	9.3	9.9	–
	(1.0)	(1.0)	(0.8)	(0.6)	(0.8)	(0.8)	(0.8)	(0.6)	
Divided attention									
RT (ms)	963	978	987	954	923	931	958	927	*
	(15)	(20)	(37)	(21)	(17)	(15)	(14)	(22)	
# "5" errors	0.6	0.8	0.7	0.8	0.8	1.0	0.6	1.1	–
	(0.3)	(0.3)	(0.2)	(0.3)	(0.3)	(0.3)	(0.2)	(0.3)	
Hit rate (%)	96.3	94.2	96.5	97.2	95.8	96.0	95.5	94.2	–
	(1.1)	(1.8)	(1.0)	(1.1)	(1.1)	(0.9)	(0.9)	(1.6)	
# false alarms	1.0	0.7	0.7	0.9	0.9	0.9	0.6	0.6	–
	(0.3)	(0.2)	(0.2)	(0.3)	(0.5)	(0.3)	(0.3)	(0.2)	

"5" errors for the divided attention task is the number of errors made in estimating the number of occurrences of the secondary target stimulus. See Table 1 for further details

active marijuana conditions, whereas in the afternoon ratings were higher after all three active drug conditions compared with the PP condition.

Although most of the mood scales were not sensitive to the next-day effects of the drug treatments, they were sensitive to morning-afternoon differences: 11 of the 20 scales showed significant main effects of Time-of-Day (Table 1). These effects indicated that subjects reported themselves to be more aroused and in a more positive mood in the afternoon compared with the morning.

Behavioral effects. Only two behavioral tasks showed statistically significant drug-related after-effects (Table 2). A significant Alcohol × Marijuana × Time-of-Day interaction was obtained for backward digit span [$F(1, 13) = 5.6$, $P < 0.05$], while on the divided attention task, an Alcohol × Time-of-Day interaction was obtained for hit rate [$F(1, 12) = 6.4$, $P < 0.05$]. However, the validity of these interactions is questionable since post-hoc tests showed no significant differences among the conditions for either behavioral measure.

As was the case with subjective effects, behavioral effects were more influenced by time of day than by drug condition (Table 2). Subjects produced longer time intervals during the time production task in the morning than in the afternoon [Time-of-Day: $F(1, 13) = 13.1$,

$P < 0.005$]. DSST performance was better in the afternoon than in the morning [Time-of-Day: $F(1, 13) = 63.0$, $P < 0.0001$ for number of attempts; $F(1, 13) = 38.4$, $P < 0.0001$ for number correct]. Finally, reaction time to the primary target stimulus on the divided attention task was faster in the afternoon than in the morning [Time-of-Day: $F(1, 12) = 8.3$, $P < 0.025$].

Discussion

The present study yielded little evidence for next-day effects after any of the active drug treatments. Regarding marijuana, none of the apparent after-effects obtained in our previous studies was replicated here, despite the fact that the dose of marijuana administered was sufficient to produce substantial subjective intoxication, increases in heart rate, and acute impairment on several of the behavioral tasks. In our first study (Chait et al. 1985) we found increased scores on the A and BG scales of the ARCI, and overproduction on the time production task, the morning after active marijuana. In the second study (Chait 1990), we observed underproduction on the time production task, impaired performance on backward digit span, and slowing of reaction time on the divided attention task the morning after active marijuana. Taking all three studies together, the most parsimonious interpretation of the results would be that marijuana did not produce reliable effects the day after smoking, and that, given the number of tasks and measures employed, the statistically significant effects obtained in the separate studies represent type I errors. One effect of marijuana that did replicate here, although not strictly speaking a next-day effect, was its effect on subjective sleep: in both the present and the previous study in which the LSEQ was used (Chait 1990) active marijuana increased subject ratings of ease of getting to sleep (Table 1); the mean increases in the two studies were of comparable magnitude (12–15 units).

There was evidence that the evening alcohol treatment resulted in some subjective effects the following morning: POMS Fatigue scores were increased, and scores on the LSEQ BFW scale were decreased, indicative of feelings of being tired and clumsy. Nevertheless, there was no evidence for behavioral impairment the morning after alcohol. The total dose of alcohol administered during the evening (1.2 g/kg for males, 1.0 g/kg for females; roughly equivalent to six 12-oz beers) was enough to produce substantial increases in subjective ratings of "drunk" (Fig. 2), impaired performance on several of the behavioral tasks, and BACs just below the legal limit in most states (100 mg/dl). Our failure to find significant behavioral impairment the day after this dose of alcohol is not surprising, since most studies that have reported impairment the day after drinking used doses higher than 1.2 g/kg (Seppala et al. 1976; Myrsten et al. 1980), and some studies using higher doses found no reliable evidence of impairment (Takala et al. 1958).

It is noteworthy that both mood and performance the day after drug administration were more influenced by the time-of-day factor (morning versus afternoon) than by drug condition. The improved performance on the behavioral tasks observed in the afternoon test session are consistent with results found by Blake (1967) and reviewed by Folkard (1990).

It was not the primary purpose of this study to characterize the acute interaction between alcohol and marijuana; acute effects were assessed mainly to demonstrate that effective doses of the two drugs were being administered. Nevertheless, the effects of the drug combination we observed agree well with prior studies. We observed few interactions between the two drugs: on most measures their effects appeared to be additive (Manno et al. 1971; Chesher et al. 1976, 1977; Belgrave et al. 1979; Bird et al. 1980; Perez-Reyes et al. 1988; Marks and MacAvoy 1989). Our finding that THC does not affect blood alcohol levels also confirms previous findings (Hansteen et al. 1976; Chesher et al. 1977; Belgrave et al. 1979; Bird et al. 1980; Perez-Reyes et al. 1988).

Although not an interaction from a statistical standpoint, the acute effects of the drug combination on the time production task were unexpected and worthy of comment. On this task, the two drugs produced opposite effects when given alone, and these effects canceled out when the drugs were given in combination (Fig. 3). Underproduction of time on this task is a well established effect of marijuana (Chait and Pierri 1992), and overproduction of time after alcohol has also been observed before (Jones and Stone 1970; Tinklenberg et al. 1976), but to our knowledge this is the first study that has examined the effects of this drug combination on a measure of time perception. This interesting phenomenon should be further explored in studies utilizing several dose combinations of these two drugs and other techniques for studying time perception (Fraisse 1984).

The doses of alcohol and marijuana chosen for this study produced comparable subjective ratings of overall strength of drug effect, as rated by subjects at the end of the session. Despite this equivalence, alcohol produced greater behavioral impairment than marijuana on most of the tasks. This apparent difference, however, may be an artifact of the procedure: we measured performance only once after the two drug administration periods, about 1 h after subjects finished the second drink. At this time, subjects' ratings of "drunk" during the AP session were at their maximum, but ratings of "high" during the PM session had declined from their peak, which occurred soon after the first drug administration (Fig. 2). Most studies have found that behavioral impairment after marijuana peaks within 30 min of smoking (Chait and Pierri 1992). Therefore, it is likely that the behavioral effects of marijuana were not measured at their peak in this study. This might explain why some commonly observed effects of marijuana (such as impaired performance on free recall; Chait and Pierri 1992) were not observed here.

During the evening sessions, heart rate increased more after marijuana smoking during the first compared with the second smoking period. Similarly, ratings of "high" increased sharply after the first, but not the second smoking period (Fig. 2). Since CO boost did not differ between the two smoking periods, these results provide strong evidence for acute tolerance to these effects of marijuana,

a phenomenon that has been observed by others (Cocchetto et al. 1981; Perez-Reyes et al. 1981).

Finally, we observed significant increases in ratings of "hungry" after marijuana but not after alcohol (Fig. 2). This is of interest because it has been difficult to show reliable increases in subjective ratings of hunger after marijuana smoking (Chait et al. 1985, 1988a,b; Zacny and Chait 1989, 1991; Zacny and de Wit 1989, 1991; Chait and Zacny 1992), despite the fact that cannabis preparations do increase food intake in humans (Hollister 1971; Greenberg et al. 1976; Foltin et al. 1986, 1988). The present results suggest that the inability to show marijuana-induced increases in hunger in at least some of these prior studies may have been because the effect is delayed, not reaching a peak until 1 h after smoking.

In summary, acute administration of marijuana, either alone or in combination with alcohol, did not have effects on mood or psychomotor/cognitive performance the following day. Although this negative outcome should not be generalized to higher doses of these drugs, or to more complex, highly skilled behaviors (e.g., flying or driving), the present results suggest that, for most individuals, moderate doses of these two commonly used substances have little effect on mood or performance the day after use, and that at least equal attention should be paid to time of day as an important influence upon human behavior.

Acknowledgements. This research was supported by NIDA grant DA-03517 and USPHS grant MO1 RR-00055. The authors thank Drs. Stan McCracken, K.G. Chua and Ed Senay for subject screening, and Karin Kirulis for technical assistance.

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