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Smoked marijuana attenuates performance and mood disruptions during simulated night shift work

Diana R. Keith[a,1], Erik W. Gunderson[b], Margaret Haney[b], Richard W. Foltin[b], Carl L. Hart[a,b,c,*]

[a] Department of Psychology, Columbia University, United States
[b] Division on Substance Abuse, New York State Psychiatric Institute and Department of Psychiatry, College of Physicians and Surgeons of Columbia University, United States
[c] Institute for Research in African-American Studies, Columbia University, United States

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ABSTRACT

Individuals who work nonstandard schedules, such as rotating or night shifts, are more susceptible to workplace injuries, performance decrements, and reduced productivity. This population is also almost twice as likely to use illicit drugs as individuals working a standard day shift. The purpose of this study was to examine the effects of smoked marijuana on performance, mood, and sleep during simulated shift work. Ten experienced marijuana smokers completed this 23-day, within-participant residential study. They smoked a single marijuana cigarette (0, 1.9, 3.56% Δ^9-THC) one hour after waking for three consecutive days under two shift conditions: day shift and night shift. Shifts alternated three times during the study, and shift conditions were separated by an 'off' day. When participants smoked placebo cigarettes, psychomotor performance and subjective-effect ratings were altered during the night shift compared to the day shift: performance (e.g., vigilance) and a few subjective ratings were decreased (e.g., "Self-Confident"), whereas other ratings were increased (e.g., "Tired"). Objective and subjective measures of sleep were also disrupted, but to a lesser extent. Marijuana attenuated some performance, mood, and sleep disruptions: participants performed better on vigilance tasks, reported being less miserable and tired and sleep a greater number of minutes. Limited negative effects of marijuana were noted. These data demonstrate that abrupt shift changes produce performance, mood, and sleep decrements during night shift work and that smoked marijuana containing low to moderate Δ^9-THC concentrations can offset some of these effects in frequent marijuana smokers.

1. Introduction

Drug abuse, if unchecked, could lead to a possible loss to business of more than $200 billion per year due to increased absenteeism, accidents, and medical costs (Slavit et al., 2009). Certain employees are more susceptible to drug use than others. For example, individuals who work nonstandard schedules, such as rotating or night shifts, are almost twice as likely to use illicit drugs as those working standard day shift schedules (SAMSHA, 2008; Frone, 2006). This issue becomes more concerning when one considers the fact that shift-workers account for approximately 20% of all workers in developed countries (Eastman et al., 1995; Beers, 2000). Rotating shift work, particularly night-shift work, requires individuals to alter their normal sleep-wake cycles and perform during times when their circadian rhythms make them least alert (for a review, see Arendt, 2010). Hence, shift-workers have higher rates of workplace-related injuries (Dembe et al., 2008; Stimpfel et al., 2015), performance decrements (Fido and Ghali, 2008; Thompson et al., 2016) and reduced productivity (Akerstedt, 1998).

Many shift workers use stimulants, sedatives or both in an effort to offset shift work-related disruptions. Low to moderate doses of stimulants (e.g., amphetamine, caffeine, modafinil) have been reported to be effective countermeasures for mood and performance decrements caused by sleep deprivation and fatigue (e.g., Hart et al., 2003b, 2006; Schweitzer et al., 2006; Walsh et al., 1990), while sedatives have been demonstrated to improve sleep quality (e.g., Porcu et al., 1997; Hart et al., 2003a, 2005). On the other hand, certain types of drug use by shift workers might exacerbate diminished performance, mood alterations, and sleep disturbances associated with shift work. Cannabis [Δ^9-tetrahydrocannabinol (Δ^9-THC)-containing products including marijuana and hashish], the most widely used illicit drug in the world (UNODC, 2015), is of particular concern. In the United States, 28 states and Washington D.C. have passed ballot initiatives allowing patients to

* Corresponding author at: New York State Psychiatric Institute, 1051 Riverside Dr Unit 120, New York, NY, 10032, United States.
E-mail address: clh42@columbia.edu (C.L. Hart).
[1] Current address: Vermont Center on Behavior and Health, Department of Psychiatry, University of Vermont, 1 South Prospect St, Rm 1415, Burlington, VT 05403, United States.

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use marijuana on the advice of their physicians. Furthermore, eight states now allow adults to legally purchase and use the substance for recreational purposes. Even before these recent developments, marijuana was the most commonly detected illicit drug in the workplace, accounting for approximately 50% of all positive urine toxicology screens (Quest Diagnostic, 2010). Because it may take several weeks for marijuana to be fully cleared from the system (Ellis et al., 1985; Huestis et al., 1996), a urine toxicology screen that is positive for marijuana metabolites does not provide information about time of use, nor an individual's possible level of intoxication or her/his ability to perform workplace-related operations. The sheer number of marijuana users combined with data showing that 2 million Americans (i.e., 1.6% of the workforce) report being intoxicated on the drug while at work at some point (Frone, 2006), however, suggest the importance of understanding the potential contributions of marijuana use to workplace productivity and safety.

Data from laboratory studies assessing the acute effects of smoked marijuana in experienced users show that the drug produces paradoxical effects; it enhances ratings of alertness and stimulation (e.g., Haney et al., 1999; Hart et al., 2001, 2002) but facilitates sleep (e.g., Vandrey et al., 2011). The drug's effect on performance depends upon the marijuana use history of research participants. That is, infrequent users tend to display marked disruptions during intoxication (e.g., Fant et al., 1998; Curran et al., 2002; D'Souza et al., 2004), whereas frequent users show little performance alterations (e.g., Hart et al., 2001, 2010; Vadhan et al., 2007; Ramaekers et al., 2009; Schwope et al., 2012). One consistent disruptive effect observed in frequent smokers, however, is that marijuana increases the amount of time participants need to complete cognitive tasks (e.g., Hart, 2001). This finding could have important implications in real world settings, such as in the workplace, where rapid decisions may be required.

There is little information about the effects of marijuana on performance or other measures (e.g., mood, sleep) of individuals subjected to work conditions that mimic those in the natural ecology. Thus, the purpose of this study was to examine the effects of smoked marijuana on the daytime and nighttime performance during shift work in current marijuana smokers. We developed a controlled laboratory model of shift work in order to more closely model the real world work environment. Participants live in a residential laboratory and work 3 days on a day shift (0830–1730 h) and 3 days on a night shift (0030–0930 h), with shift condition switching several times during the study. This within-participants model facilitates the examination of abrupt work shift change-related alterations in human behavior and the interactive effects of drugs on these alterations. We hypothesized that marijuana would exacerbate night-shift-related performance decrements but improve mood.

2. Methods

2.1. Participants

Ten healthy research participants (mean age [± SD] 27.2 ± 5.6) completed this 23-day residential study: three were female (two Black, one Hispanic) and seven were male (three Black, one Hispanic, one Native American, and two White). They were solicited via word-of-mouth referral and newspaper advertisement in New York City. Participants' formal education ranged from 10 to 16 years (mean 13.2) and all reported previous experience working irregular shift schedules. Participants reported smoking marijuana an average of 3.5 ± 0.5 days/week and 1.2 ± 0.4 marijuana cigarettes/smoking occasion. Nine reported occasional use of alcohol (1–6 drinks/week), and eight smoked tobacco cigarettes (1–20 cigarettes/day). Participants reported that they used other drugs infrequently: three had used methylenedioxymethamphetamine (MDMA) less than a total of five times, three used illicit prescription opioids less than a total of three times, two used psychedelic mushrooms twice, one used cocaine once, and one reported using d-lysergic acid diethylamide (LSD) once. Urine toxicology analyses during the screening process confirmed the absence of illicit drug use other than marijuana (all participants tested positive for Δ^9-THC only). All volunteers passed comprehensive medical and psychological evaluations and were within normal weight ranges according to the 1983 Metropolitan Life Insurance Company height/weight table (mean body mass index: 25.3 ± 4.0).

Volunteers were informed that the purpose of the study was to evaluate the effects of marijuana on cognitive performance and mood of shift workers. Each participant signed a consent form approved by the New York State Psychiatric Institute's Institutional Review Board and was fully informed about experimental and drug conditions at the end of the study. Participants were compensated at a rate of $70 per day.

2.2. Laboratory

Three groups of 3–4 individuals stayed in a residential laboratory in the New York State Psychiatric Institute (Foltin et al., 1996; Hart et al., 2003a). Each participant resided in a private bedroom, equipped with a bed, desk, Macintosh computer system, refrigerator, microwave, toaster, food preparation area, and a barcode scanner (Worthington Data Solutions, Santa Cruz, CA) for food requesting and reporting. The laboratory also included a common area, in which participants were free to engage in social and recreational activities, such as watching videotaped films, playing video games and board games, reading, and exercising. Food and tobacco cigarettes were available *ad libitum* during waking hours. To enable continuous observation of behavior, cameras and microphones are located in the common social area and in bedrooms, but not in bathrooms, showers, or private dressing areas. Communication between participants and research staff was kept to a minimum and primarily accomplished via computers in each participant's bedroom.

2.3. Pre-study training

Prior to beginning the study, participants completed 2 sessions of training (3–4 h per session), during which they were familiarized with laboratory and study procedures and trained on the computerized tasks that would be used in the study. During training sessions, participants were trained in all features of the laboratory. The investigators describe the study in detail, answer questions, and read aloud with the participants a comprehensive manual, available throughout the study for reference, detailing the study and describing laboratory resources.

The purpose of training on the performance battery was to ensure the tasks were well-learned prior to study participation. In this way, the effect of learning on any task performance would be minimized during the study. Indeed, by the end of the second session, none of the participants' performance on any of the tasks varied by more than 10 percent. On a separate day, participants smoked 3 puffs from a single marijuana cigarette (3.56% Δ^9-tetrahydrocannabinol [THC]) to provide them with experience with the study drug and to monitor any potential unusual reactions. No unusual responses were observed.

2.4. Design

Table 1 shows that the study consisted of six 3-day blocks of sessions and all participants experienced six dose/shift combinations: placebo + day and night shift, 1.9% Δ^9-THC concentration + day and night shift, and 3.56% Δ^9-THC concentration + day and night shift. Participants smoked three puffs on marijuana cigarettes, regardless of the dose or shift condition. During the night shift, participants were awakened at 0015, performed computerized tasks (described below) from 0030 to 0930, and went to bed at 1600; during the day shift, they were awakened at 0815, performed computerized tasks from 0830 to 1730, and went to bed at 2400. Shifts alternated 3 times during the study, and shift conditions were separated by an "off" day, during which

Table 1
Study Design.

Study day	Shift condition	Drug Condition (Δ^9-THC%)
1–3	Day	0
*4	Off	Off
5–7	Night	1.9
*8	Night	0
9–11	Night	3.56
*12	Off	Off
13–15	Day	3.56
*16	Day	0
17–19	Day	1.9
*20	Off	Off
21–23	Night	0

Note. *Indicates days that were not included in data analyses; Off = off days.
Shift condition order was varied across participants.
Δ^9-THC order was counterbalanced across participants.
Dosing times: 0915 during the day shift and 0115 during the night shift, i.e., 1-h after waking.

participants were not on a work schedule but were required to go to bed 8.25 h prior to the next shift as they had done during other days. Two groups of participants (N = 7) began on the night shift and one group (N = 3) began on the day shift. Placebo or marijuana (1.9% or 3.56% Δ^9-THC) was smoked once per day, one hour after waking (0915 on the day shift and 0115 on the night shift). Days 8 and 16 were "drug washout" days during which participants smoked placebo marijuana before being switched to another drug condition. In order to minimize potential confounding effects, presentation of Δ^9-THC concentrations were systematically varied between groups of 3–4 participants, although dose order was the same for all subjects in a cohort.

2.5. Procedure

Participants moved into the residential laboratory the day before the study began to habituate to inpatient living conditions. Study days were highly structured and participants spent the majority of their time during the 9-h work period in their private rooms, where they completed subjective effects and cognitive/psychomotor task batteries (described below). On each day, participants first completed baseline cognitive/psychomotor tasks, a 44-item subjective-effects visual analog questionnaire, and a visual analog sleep questionnaire. Then, they were weighed (but were not informed of their weight) and given time to eat breakfast. Following breakfast, eight 30-min computerized task batteries, composed of the subjective-effects questionnaire and cognitive/psychomotor tasks, were completed. Participants were given a 15-min break between each task battery. From 1000 (0200) to 1245 (0445), participants completed 4 task batteries and, after a 1.5-h lunch break period, they completed 4 additional task batteries from 1415 (0615) to 1700 (0900). Beginning at 1700 (0900), participants had access to activities available in the social area. Two films were shown daily, beginning at 1800 (1000) and 2100 (1300). Lights were turned out at 2400 (1600) for an 8.25-h sleep period.

2.6. Subjective-effects and cognitive/psychomotor battery

The 30-min computerized task batteries consisted of a visual analog questionnaire and cognitive/psychomotor tasks. The 3-min visual analog questionnaire was comprised of a series of 100-mm lines labeled "not at all" at one end and "extremely" at the other end (Hart et al., 2006). The lines were labeled with adjectives describing a mood (e.g., "I feel…" "alert," "depressed," "social"), a drug effect (e.g., "I feel…" "stimulated," "a good drug effect," "a bad drug effect"), or a physical symptom ("I feel nauseous," "I have a headache," "My heart is beating faster than usual"). In addition, 15 min after smoking the marijuana cigarette, participants completed a 2-min drug-effect questionnaire (DEQ) during which they rated "good effects" and "bad effects" on a five-point scale: 0 = "not at all" and 4 = "very much." They also rated how "strong" the drug effect was, as well as their desire "to take the drug again." Lastly, participants rated how much they liked the drug effect on a nine-point scale: −4 = "disliked very much," 0 = "feel neutral, or feel no drug effect," and 4 = "liked very much."

The computerized psychomotor task battery was selected because it had been used in multiple other studies assessing the effects of drugs on performance. This facilitates the comparison of data collected in the current study with previous findings. The battery consisted of five tasks: 1) the Digit Recall Task; 2) the digit-symbol substitution task (DSST); 3) the divided attention task (DAT); 4) the rapid information task (RIT); and 5) the Repeated Acquisition Task (RA).

During the 2-min Digit Recall task, an 8-digit number was displayed for 3 s on the computer screen. Participants were instructed to enter the number correctly while it was on the screen and again after it had disappeared from the screen. They were also told that they would be asked to reproduce and recognize the number near the end of the battery. This task was designed to assess changes in immediate and delayed recall (see Hart et al., 2001).

The DSST is a 3-min task (McLeod et al., 1982) that consisted of nine random three-row, three-column squares (one square blackened/row)

Table 2
Effects of Shift Condition and Smoked Marijuana on Subjective Effects on Day 1.

	Conditions						
	Pbo Day	Pbo Night		1.9% Δ^9-THC Night		3.56% Δ^9-THC Night	
Measure	Mean (SEM)	Mean (SEM)	*F*-value	Mean (SEM)	*F*-value	Mean (SEM)	*F*-value
Subjective Effects							
Good Drug Effect	47.30 (20.44)	39.00 (25.63)	0.08	198.20 (26.74)	28.40*	287.20 (65.52)	69.04* †
Forgetful	79.80 (35.66)	50.70 (14.07)	1.43	104.70 (28.02)	4.93*	161.60 (48.76)	20.69*
Miserable	26.40 (6.67)	76.20 (20.16)	6.67§	9.70 (4.23)	12.19*	25.56 (13.76)	7.07*
Self-Confident	507.30 (46.12)	454.20 (54.11)	6.55§	535.80 (45.46)	15.25*	541.90 (42.73)	17.76*
Social	478.00 (53.90)	372.80 (48.31)	11.91§	379.60 (37.72)	0.05	504.10 (52.78)	18.56* †
Stimulated	164.20 (63.63)	169.30 (60.49)	0.09	199.70 (54.14)	3.04	253.10 (61.80)	23.11* †
Talkative	436.40 (55.81)	334.20 (46.87)	9.28§	325.80 (48.29)	0.06	445.10 (62.30)	10.92* †
Tired	143.20 (52.23)	175.50 (61.11)	1.06	180.70 (50.27)	0.26	114.20 (29.48)	3.99*
Unmotivated	128.20 (42.10)	213.50 (66.02)	6.71§	136.20 (50.78)	5.51*	127.70 (38.03)	6.79*

Data are represented as AUC values and data for active marijuana conditions are presented for the night shift only df = 1,40.
Pbo = placebo.
§$p < 0.05$, significant difference between the placebo day and placebo night conditions.
*$p < 0.05$, significant difference from the placebo night condition.
†$p < 0.05$, significant difference from the 1.9% night condition.

displayed across the top of the computer screen. Each array was associated with a number (1–9). A randomly generated number appeared at the bottom of the screen, indicating which of the arrays should be reproduced on the nine-key keypad attached to the computer. Participants were instructed to reproduce as many patterns as possible by entering the patterns associated with the randomly generated numbers. This task was designed to assess changes in visuospatial processing.

The 10-min DAT combined concurrent pursuit-tracking and vigilance tasks (Miller et al., 1988). Participants tracked a moving circle on the video screen using the mouse, and also had to signal when a small black square appeared at any of the four corners of the screen. Accurate tracking of the moving stimulus increased its speed proportionately. This task was designed to assess changes in vigilance and inhibitory control.

During the 7-min RIT, a series of digits was presented at the rate of 100 digits per min, and subjects were instructed to press a response button as quickly as possible whenever they detected sequences of three consecutive odd or three consecutive even digits (Wesnes and Warburton, 1983). A point was earned for each correct "hit" and a point was deducted for each "miss" or "false alarm." Participants were instructed to earn as many points as possible during the task. This task was designed to assess changes in sustained concentration and inhibitory control.

At the start of the 3-min RA task, participants were instructed to learn a 10-response sequence of button presses. A position counter incremented by one each time a correct button was pressed, and remained unchanged after an incorrect response. The points counter increased by one each time the 10-response sequence was correctly completed. The sequence remained the same throughout the task, but a new random sequence was generated for each subsequent task battery. Participants were instructed to earn as many points during the task as possible by pressing the buttons in the correct sequence. This task was designed to assess changes in learning and memory (see Kelly et al., 1993).

2.7. Sleep monitoring

Objective sleep was measured using the portable Nightcap sleep systems, which consisted of a headband worn by participants while they slept (Ajilore et al., 1995; Cantero et al., 2002). A miniature electrode attached to the eyelid measured eye movement but did not disrupt sleep, and a body movement sensor in the headband detected and recorded movements. The system provided measures of total sleep time, sleep onset latency, rapid eye movement latency, non-rapid eye movement sleep time, and sleep efficiency (total sleep time as a percentage of time in bed) and has been reported to correspond well to traditional polysomnography and subjective reports of sleep quality (Ajilore et al., 1995). In addition to wearing the portable sleep monitor, participants completed a visual analog sleep questionnaire each morning. This questionnaire consisted of a series of 100 mm lines labeled "not at all" at one end and "extremely" at the other end. The lines were labeled: "I slept well last night," "I woke up early this morning," "I fell asleep easily last night," "I feel clear-headed this morning," "I woke up often last night," "I am satisfied with my sleep last night," and a fill-in question in which participants were asked to estimate the number of hours they thought they slept the previous night (Haney et al., 2001).

2.8. Tobacco cigarettes monitoring

The number of tobacco cigarettes smoked was recorded by counting cigarette butts in each participant's ashtray at the end of each experimental day.

2.9. Drug

One hour after waking each morning, participants were given one 1-g marijuana cigarette (0, 1.9, or 3.56% Δ^9-THC: provided by the National Institute on Drug Abuse). Cigarettes were smoked using a cued-smoking procedure, which produces Δ^9-THC concentration-dependent changes in heart rate and subjective-effect ratings (see Foltin et al., 1987a). Colored lights (mounted on the ceiling of the social/recreational area) signaled 'light the cigarette' (30 s), 'get ready' (5 s), 'inhale' (5 s), 'hold smoke in lungs' (10 s), and 'exhale.' Participants smoked three puffs in this manner, with a 40-s interval between each puff. Cigarettes were tightly rolled at both ends and were smoked through a hollow plastic cigarette holder so that the contents were not visible. Twenty-four hours prior to administration, cigarettes were removed from a freezer, where they were stored in an airtight container, and humidified at room temperature.

The examined Δ^9-THC concentrations were selected because they had been previously shown to increase positive subjective-effect ratings and heart rate in a Δ^9-THC concentration-dependent manner (Foltin et al., 1987b; Hart et al., 2001). The goal was to select Δ^9-THC concentrations that would produce euphoria, not disorientation or dysphoria. In this way, we attempted to most closely mimic recreational cannabis use in the natural ecology.

2.10. Data analysis

Data from off and drug washout days (days 4, 8, 12, 16, 20) were not included in the analyses. The area under the curve (AUC) for the subjective effects visual analog questionnaire and the cognitive/psychomotor tasks was determined using the trapezoidal method (Tallarida and Murray, 1981). Peak subjective-effect and cognitive psychomotor data were analyzed similarly. For the sake of brevity, data for the AUC analyses are discussed primarily because significant drug effects were similar for peak and AUC analyses.

Data were analyzed using 3-factor repeated-measures analyses of variance (ANOVA): the first factor was Δ^9-THC concentration (placebo, 1.9, 3.56%), the second factor was shift condition (day, night), and the third factor was day within condition (1, 2, 3). For all analyses, ANOVAs provided the error terms needed to calculate planned comparisons that were designed to answer two questions: (1) are cognitive/psychomotor task performance and subjective-effects ratings disrupted during the night shift, and (2) does marijuana alter night shift-related disruptions? To evaluate night shift-related disruptions, each day of placebo was compared to the corresponding night of placebo (e.g., the first day of placebo during the day shift vs. the first night of placebo during the night shift). To evaluate the effects of marijuana on night shift-related disruptions, each night of each drug condition was compared to a corresponding night of another drug condition (e.g., the first night of 1.9% Δ^9-THC during the night shift vs. the first night of placebo during the night shift). Marijuana-related effects during day-shift work were evaluated similarly. Huynh-Feldt corrections were used when appropriate and p-values < 0.05 were considered statistically significant.

3. Results

3.1. Effects of shift condition

3.1.1. Cognitive performance

The upper panels of Fig. 1 illustrate how selected performance varied between the day and night shift when participants received placebo. Planned comparisons revealed that the number of digits entered in the Digit Recall Task and the number of hits on the RIT were significantly reduced during all three nights that participants worked on the night shift compared to the corresponding days on the day shift ($p < 0.006$). In addition, the number of completed trials on the RA task was decreased on the first and third nights of the night shift ($p < 0.03$). As shown in Tables 3 and 4, other performance measures (e.g., DAT: speed and hit latency; RIT: misses) were also altered significantly as a function of shift condition.

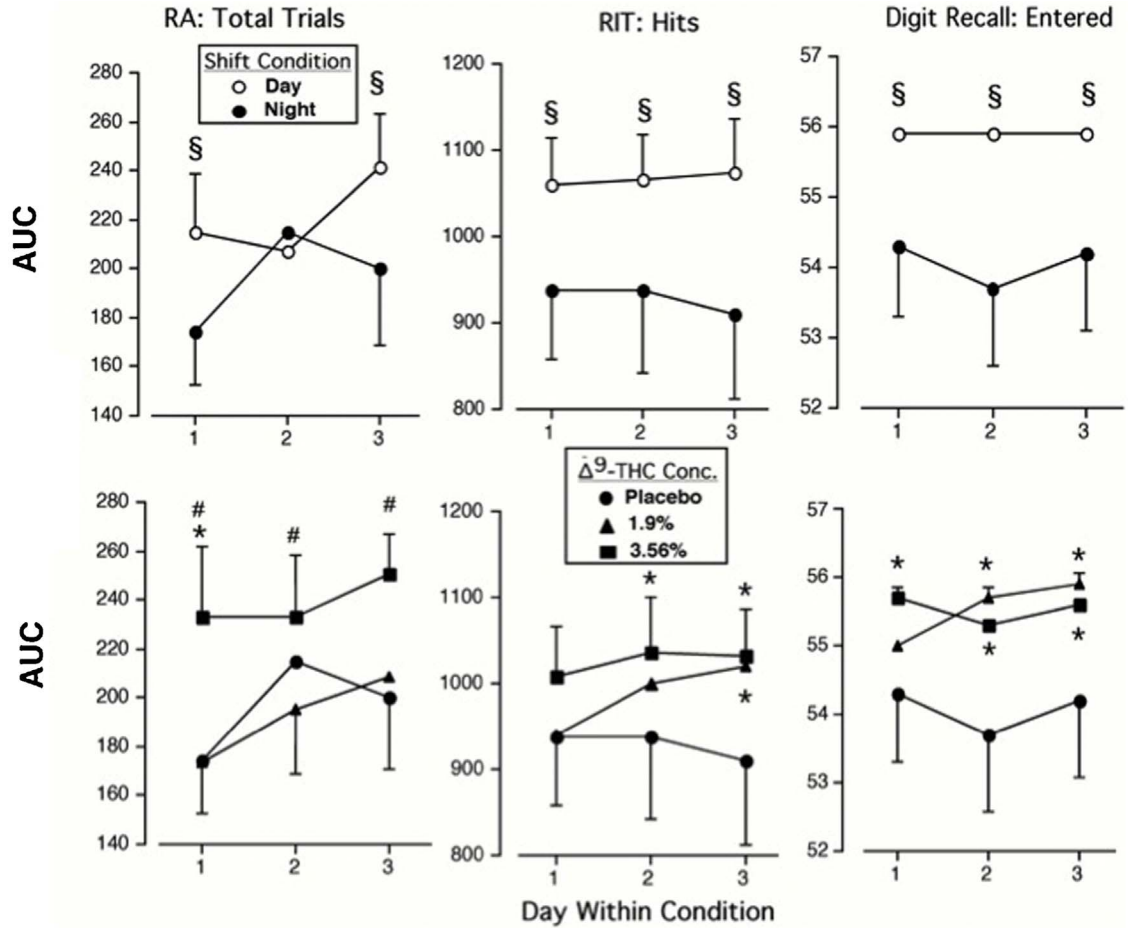

Fig. 1. Upper panel: AUC values for total trials (RA), total number of hits (RIT), and total number of digits entered as a function of shift condition and day within condition. §Significant difference between the day and night shift conditions for that day following placebo administration ($p < 0.05$). Bottom panel: AUC values for total trials (RA), total number of hits (RIT), and total number of digits entered as a function of Δ^9-THC concentration and day of the night shift condition. *Significant difference between placebo and Δ^9-THC concentration for that day ($p < 0.05$). #Significant difference between 1.9 and 3.56% Δ^9-THC for that day ($p < 0.05$). Error bars represent 1 SEM. Overlapping error bars were omitted for clarity.

3.1.2. Subjective-effects ratings

The upper panels of Fig. 2 show how selected subjective-effect ratings varied between the day and night shifts when participants received placebo. Ratings of "Self-Confident" were significantly decreased during all three nights of the night shift compared to the corresponding day shift days ($p < 0.05$). Conversely, ratings of "Tired" and "Miserable" were significantly increased during two of the three nights of the night shift ($p < 0.04$). Tables 2–4 show that several other subjective-

Table 3
Effects of shift condition and smoked marijuana on psychomotor performance and subjective effects on Day 2.

	Conditions						
	Pbo Day	Pbo Night		1.9% Δ^9-THC Night		3.56% Δ^9-THC Night	
Measure	Mean (SEM)	Mean (SEM)	*F*-value	Mean (SEM)	*F*-value	Mean (SEM)	*F*-value
Performance Effects							
RIT: no. of misses	243.10 (46.11)	355.60 (96.41)	12.16§	320.70 (39.42)	1.17	269.40 (56.50)	7.14*
RIT: false alarms	322.10 (59.60)	448.80 (79.57)	13.52§	372.10 (53.96)	4.95*	357.90 (62.44)	6.96*
Subjective Effects							
Good Drug Effect	1.90 (1.51)	19.20 (13.21)	0.34	177.70 (35.10)	28.15*	224.70 (34.64)	47.33*
Can't Concentrate	95.50 (37.85)	89.80 (40.44)	0.02	196.30 (72.43)	7.88*	214.40 (71.61)	10.78*
Forgetful	107.30 (59.22)	52.80 (32.36)	5.00§	92.00 (36.66)	2.59	182.60 (58.05)	28.35* †
Self-Confident	535.20 (48.28)	486.90 (53.25)	5.76§	540.40 (50.23)	6.98*	545.50 (41.48)	8.07*
Stimulated	147.70 (63.01)	183.70 (63.78)	4.27§	231.30 (66.82)	7.46*	223.50 (59.99)	5.21*
Talkative	355.80 (67.34)	439.80 (52.78)	6.63§	354.60 (56.63)	6.45*	439.80 (51.92)	0.00 †
Tired	67.10 (31.93)	147.20 (49.13)	6.79§	126.80 (45.33)	0.45	116.60 (36.92)	1.01

Data are represented as AUC values and data for active marijuana conditions are presented for the night shift only df = 1,40.
Pbo = placebo; RIT = rapid information task.
§$p < 0.05$, significant difference between the placebo day and placebo night conditions.
*$p < 0.05$, significant difference from the placebo night condition.
†$p < 0.05$, significant difference from the 1.9% night condition.

Table 4
Effects of shift condition and smoked marijuana on psychomotor performance and subjective effects on Day 3.

	Conditions						
	Pbo Day	Pbo Night		1.9% Δ^9-THC Night		3.56% Δ^9-THC Night	
Measure	Mean (SEM)	Mean (SEM)	*F*-value	Mean (SEM)	*F*-value	Mean (SEM)	*F-value*
Performance Effects							
RIT: no. of misses	248.90 (58.82)	360.30 (82.59)	11.93§	283.20 (47.83)	5.71*	320.80 (75.54)	1.50
Digit: Imm. Recall	47.50 (1.40)	44.50 (1.80)	5.64§	46.40 (1.67)	2.26	47.80 (1.01)	6.83*
Digit: Del. Recall	4.00 (0.21)	3.50 (0.27)	2.09	3.8 (0.20)	0.75	4.40 (0.22)	6.77*
DAT: no. of misses	0.40 (0.22)	3.00 (1.27)	18.78§	0.30 (0.15)	20.25*	1.20 (0.47)	9.00*
DAT: speed	61.10 (0.80)	52.40 (2.93)	26.54§	58.60 (1.31)	13.48*	58.40 (1.96)	12.62*
DAT: hit latency	6666.30 (338.72)	8996.40 (842.68)	24.49§	6563.30 (350.13)	26.70*	7724.90 (534.15)	7.29* †
DAT: false alarms	7.80 (1.13)	19.00 (4.13)	12.37§	11.40 (2.48)	5.70*	14.40 (3.22)	2.09
DSST: attempted	599.00 (37.43)	580.00 (36.87)	2.24	634.70 (19.19)	18.54*	584.70 (36.03)	0.14 †
DSST: no. correct	582.30 (35.73)	559.60 (34.91)	3.32	610.40 (17.59)	16.62*	561.80 (34.01)	0.03 †
Subjective Effects							
Good Drug Effect	2.90 (1.80)	18.30 (8.71)	0.27	205.40 (41.04)	39.23*	240.90 (38.66)	55.53*
Forgetful	123.40 (58.17)	69.40 (42.14)	4.91§	132.10 (52.61)	6.62*	196.70 (60.33)	27.26* †
Miserable	9.80 (6.20)	70.30 (36.12)	10.05§	11.20 (6.24)	9.57*	20.10 (13.76)	6.80*
Self-Confident	517.10 (56.34)	469.60 (61.17)	5.51§	548.20 (44.44)	14.65*	526.60 (42.47)	7.82*
Stimulated	146.90 (62.55)	190.00 (67.08)	6.11§	219.00 (63.08)	2.77	223.90 (59.69)	3.78*
Tired	70.10 (30.72)	200.70 (65.93)	17.92§	57.30 (25.67)	21.70*	92.70 (37.27)	12.22*
Unmotivated	93.70 (30.58)	209.60 (68.37)	12.38§	94.70 (39.14)	12.17*	176.20 (66.32)	1.03 †

Data are represented as AUC values and data for active marijuana conditions are presented for the night shift only df = 1,40.
Pbo = placebo; DAT = divided attention task; DSST = digit symbol substitution task; Digit = Digit Recall Task; RIT = rapid information task.
§ $p < 0.05$, significant difference between the placebo day and placebo night conditions.
* $p < 0.05$, significant difference from the placebo night condition.
† $p < 0.05$, significant difference from the 1.9% night condition.

effect ratings (e.g., "Unmotivated" and "Talkative") were altered significantly as a function of shift condition.

3.1.3. Sleep

The upper panels of Fig. 3 display how objective and subjective measures of sleep varied between the day and night shifts when participants received placebo. Total sleep time, as measured by the Nightcap, was decreased across all three days that participants worked on the night shift, but this effect was statistically significant only on the first and third day of the night shift ($p < 0.004$). Similarly, subjective estimates of total sleep time and ratings of sleep satisfaction were significantly decreased on the first day of the night shift ($p < 0.006$).

3.1.4. Tobacco cigarette smoking

Tobacco cigarette smoking did not vary as a function of shift condition.

3.2. Effects of marijuana

3.2.1. Cognitive performance

The bottom panels of Fig. 1 show how marijuana affected performance during the night-shift condition. (The night shift data in the upper panels are the same data shown under the placebo condition in the bottom panels.) The 3.56% Δ^9-THC concentration improved performance on the RA task (increased the number trials) and RIT (increased the number of hits) on at least two of the three nights relative to placebo ($p < 0.03$). Both active concentrations increased the number of digits entered during the Digit Recall Task on at least two of the three nights of the night shift ($p < 0.003$). The lower concentration also significantly increased the number of hits on the RIT on the third night ($p < 0.02$). Other significant performance effects produced by marijuana during the night shift are shown in Tables 3 and 4. Fig. 4 illustrates the time course effects of marijuana on RA performance (increased the number trials) one night of the night-shift work period. Immediately after marijuana administration, both Δ^9-THC concentrations produced trends toward disruptive effects. But, the 3.56% Δ^9-THC concentration cigarette significantly improved performance at the 180-min time point, immediately before the lunch period ($p < 0.003$). A similar pattern of effects was observed for other performance tasks.

In contrast to the beneficial effects marijuana produced during night shift work, it had limited effects on performance during the day shift. The 1.9% Δ^9-THC concentration significantly decreased the number of hits on the RIT on all three days of day shift work ($p < 0.04$), increased the number of misses on the RIT on the first two days ($p < 0.05$), and decreased the maximum speed on the DAT on the first and third day ($p < 0.05$).

3.2.2. Subjective-effects ratings

The bottom panels of Fig. 2 display how marijuana affected subjective-effect ratings during the night-shift condition. Both active concentrations significantly increased ratings of "Self-Confident" on all three nights ($p < 0.03$). The 3.56% Δ^9-THC concentration decreased subjective ratings of "Tired" on the first night ($p < 0.05$) and both concentrations significantly decreased these ratings on the third night ($p < 0.002$). In addition, the larger concentration increased ratings of "Stimulated" on all three nights ($p < 0.05$), while both concentrations decreased ratings of "Miserable" on at least two of the three nights ($p < 0.04$). As shown in Tables 2–4, other subjective-effects ratings were also altered significantly during night shift work. Notably, both concentrations significantly increased ratings of "Good drug effect" and "High" on all three nights ($p < 0.0001$) and increased ratings of "Forgetful" on at least two nights of the night shift ($p < 0.05$).

During the day shift condition, both active concentrations of Δ^9-THC significantly increased ratings of "Good drug effect," and "High" on all three days ($p < 0.001$). Both concentrations also significantly increased ratings of "Stimulated" on all three days of the day shift ($p < 0.03$).

3.2.3. Sleep

The bottom panels of Fig. 3 display the effects of marijuana on sleep measures during the night shift condition. The 3.56% Δ^9-THC concentration significantly increased total sleep time on the first night, as measured by the nightcap ($p < 0.03$); this concentration also increased estimations of total sleep time and subjective ratings of sleep

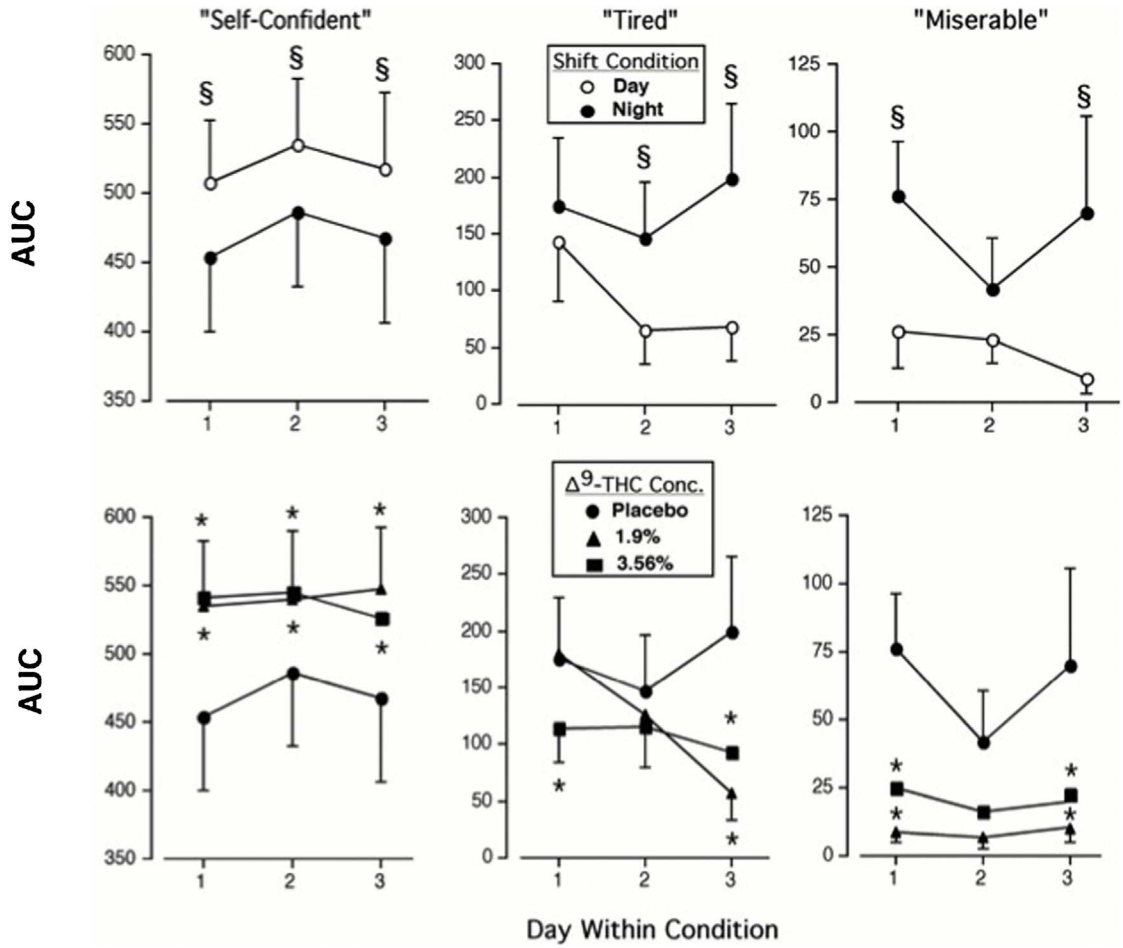

Fig. 2. Upper panel: AUC values for visual analog scale ratings of 'Self-Confident,' 'Tired,' and 'Miserable' as a function of shift condition and day within condition. §Significant difference between the day and night shift conditions for that day following placebo administration ($p < 0.05$). Bottom panel: AUC values for visual analog scale ratings of 'Self-Confident,' 'Tired,' and 'Miserable' as a function of Δ^9-THC concentration and day of the night shift condition. *Significant difference between placebo and Δ^9-THC concentration for that day ($p < 0.05$). Error bars represent one SEM. Overlapping error bars were omitted for clarity.

satisfaction on the first night ($p < 0.05$).

During the day shift condition, there were no significant effects of Δ^9-THC on objective or subjective measures of total sleep time or sleep satisfaction.

3.2.4. *Tobacco cigarette smoking*

Relative to the placebo condition, the larger Δ^9-THC concentration cigarette significantly reduced the number of tobacco cigarettes smoked by participants during the night shift across all three nights ($p < 0.04$). On average, participants smoked two fewer tobacco cigarettes after receiving the 3.56% Δ^9-THC concentration cigarette. The 1.9% Δ^9-THC concentration condition also reduced tobacco smoking compared with the placebo condition, but this effect was significantly only on night one. Participants smoked two fewer tobacco cigarettes ($p < 0.02$).

4. Discussion

Psychomotor performance and subjective-effect ratings were altered during the night shift compared to the day shift: performance and a few subjective ratings were decreased (e.g., "Self-Confident"), whereas other ratings were increased (e.g., "Tired"). These results are consistent with data from previous investigations on the effects of rotating work schedules on human performance and mood under controlled laboratory conditions (e.g., Reid and Dawson, 2001; Sharkey et al., 2001; Hart et al., 2003a, b). Contrary to our prediction, smoked marijuana did not exacerbate night shift-related disruptions. Instead, the drug mainly attenuated night shift-related disruptions in frequent marijuana smokers.

As expected, when participants worked on the night shift and received placebo, their performance was disrupted in several domains. The most pronounced alterations were noted on tasks that measured attention and vigilance. Specifically, participants performed significantly worse on the DAT (measures of speed and hit latency) and the RIT (measures of hits and misses) on all 3 nights of the night shift. In addition, inhibitory control disruptions, as measured by two separate tasks (i.e., DAT: false alarms and RIT: false alarms), were observed on 2 of the 3 nights. These findings replicate data collected under similar conditions (Reid and Dawson, 2001; Sharkey et al., 2001; Hart et al., 2003a, b, 2005, 2006) and confirm that individuals who are required to make abrupt work shift schedule changes are prone to performance decrements. The study design used here is similar to irregular or rapidly rotating shift schedules in the natural ecology (Sallinen and Kecklund, 2010), and the current data are also congruent with recent findings from a study conducted in a more naturalistic setting. Chang et al. (2011) compared the performance of nurses working 2, 3, or 4 consecutive nights and found more perceptual and motor ability disruptions among nurses who worked two consecutive nights compared with those who worked four consecutive nights. The results indicate that performance disruptions are more pronounced during the first few days of the night shift. Taken together, the data suggest that an acclimation period greater than 24 h might be necessary in order to offset shift schedule change-related disruptions.

One possible explanation for the performance decrements observed during the night shift is that the abrupt change in work schedule produced sleep disruptions that affected next-day performance. Indeed,

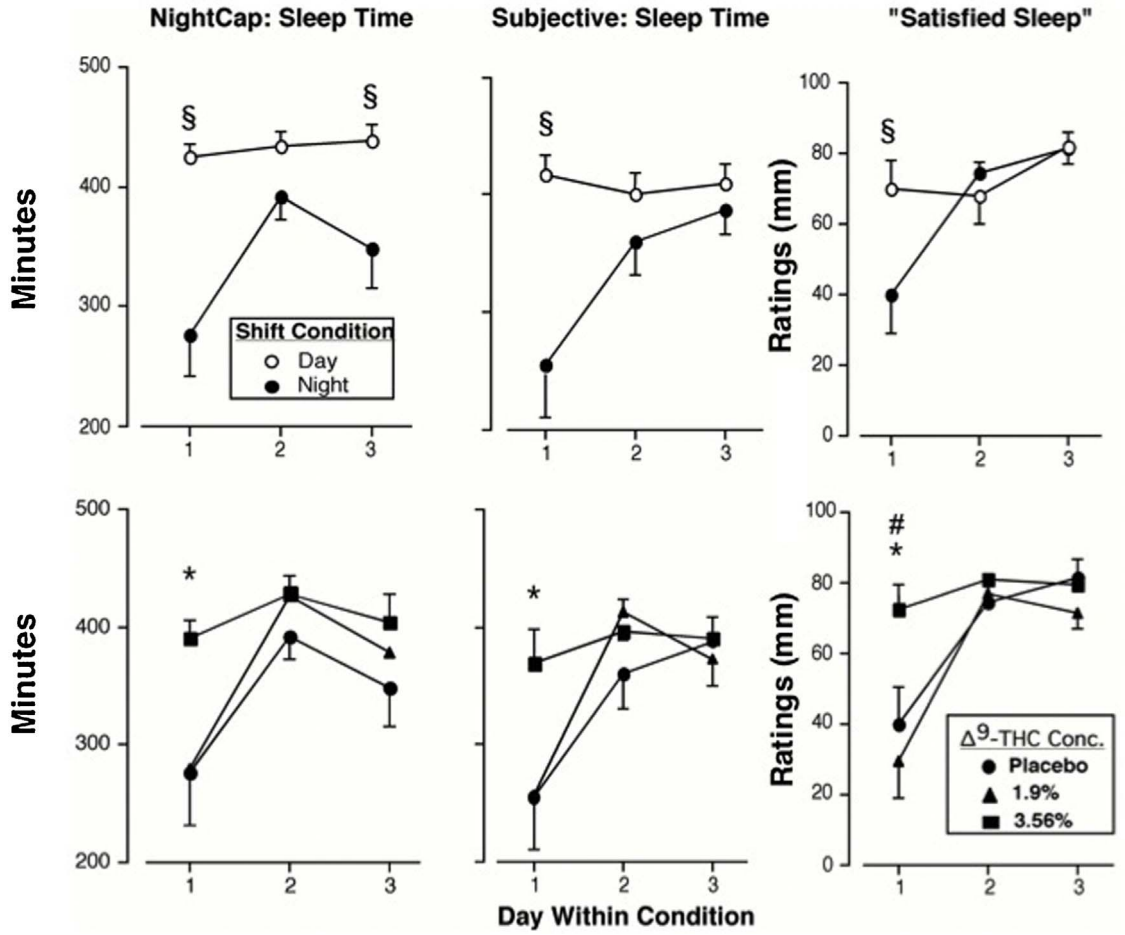

Fig. 3. Upper panel: Total sleep time from the previous evening as measured by the Nightcap and selected mean subjective effects from the sleep questionnaire as a function of shift condition and day within condition. §Significant difference between the day- and night shift conditions for that day following placebo administration ($p < 0.05$). Bottom panel: Total sleep time from the previous evening as measured by the Nightcap and selected mean subjective effects from the sleep questionnaire as a function of Δ^9-THC concentration and day of the night shift condition. *Significant difference between placebo and Δ^9-THC concentration for that day ($p < 0.05$). #Significant difference between 1.9 and 3.56% Δ^9-THC for that day ($p < 0.05$). Error bars represent 1 SEM. Overlapping error bars were omitted for clarity.

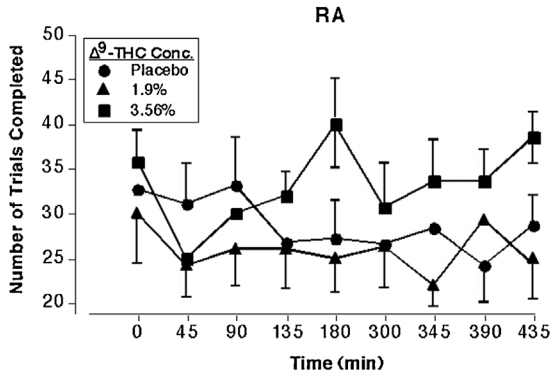

Fig. 4. The number of trials completed on the Repeated Acquisition Task (RA) as a function of Δ^9-THC concentration and time on one night of the night-shift work period. Marijuana was administered at time point 0. Error bars represent 1 SEM. Overlapping error bars were omitted for clarity.

objective and subjective sleep measures lend partial support for this view. Data from the Nightcap® showed that total sleep time was reduced by 2.5 h on the first night of the night shift. These data replicate previous findings indicating that night shift work is associated with 2–4 h of reduced sleep (Torsvall et al., 1989; Åkerstedt, 1995; Niu et al., 2011). Furthermore, participants reported reduced sleep quality on the first night of the night shift: e.g., their estimates of total sleep time and ratings of sleep satisfaction were significantly lower. Mood was also disrupted during the night shift. Participants reported feeling less "Self-Confident" on all three nights they worked on the night shift and endorsed items indicating that they were tired, miserable, and unmotivated on at least two nights. These data are consistent with previous findings when participants were abruptly placed on a night shift work schedule (Hart et al., 2003a, b).

It is noteworthy that performance disruptions persisted throughout the three nights that participants worked on the night shift, while measures of daytime sleep improved by the second day. One potential reason for these data is short-term circadian misalignment. Working on the night shift forces the body to function during the circadian trough of alertness, potentially compounding problems caused by sleep deprivation. Thus, the enduring performance disruptions may reflect a slow adjustment of the circadian rhythm and/or an accumulation of sleep debt that prevents optimal performance. Indeed, previous research has indicated that the speed of circadian adjustment is approximately 1 h per day, meaning that it would require at least 1 week for a diurnal cycle to switch to a nocturnal circadian cycle (Wever, 1980; Hastings, 1998). While we did not assess circadian phase, the current data show that daytime sleep improved over the course of three nights of night-shift work. Therefore, we speculate that a longer acclimation period to night shift conditions would also improve performance.

We predicted that smoking marijuana would exacerbate performance disruptions during the night shift. This hypothesis was not supported. The drug produced limited effects on performance on the first night of the night shift but attenuated decrements on subsequent

nights. On the second night, marijuana lessened performance disruptions on four measures. Both active Δ^9-THC concentrations reduced disruptions in inhibitory control (e.g., RIT: false alarms) and recall (e.g., Digit task: total entered) and only the larger concentration lessened disruptions in sustained attention (e.g., RIT: hits and misses). On the third night, marijuana also attenuated shift-related performance decrements: both Δ^9-THC concentrations lessened disruptions in domains measuring reaction time (e.g., DAT: hit latency), vigilance/sustained attention (e.g., DAT: misses and maximum speed; RIT: hits), and recall (e.g., Digit: total entered).

The above effects were observed, despite the fact that both Δ^9-THC concentrations markedly increased ratings of forgetfulness on two nights of the night shift; ratings of inability to concentrate were also increased on one night. It might be that these subjective ratings would have had to be dramatically altered in order to observe deleterious performance effects because the current participants were tolerant to many marijuana-related cognitive impairing effects. Indeed, they reported smoking marijuana on a regular basis, on average 3.5 days per week.

To our knowledge, the current study is the first investigation of marijuana-related effects during simulated shift work, making it difficult to compare our results to earlier research in this area. Previously, we reported that stimulant medications such as methamphetamine and modafinil attenuated many night shift-related performance decrements (Hart et al., 2003b, 2006). It is tempting to speculate that the stimulant-like properties of marijuana played a role in decreasing night shift-related performance decrements observed in the current study. When participants smoked cigarettes containing the larger Δ^9-THC concentration, they reported feeling markedly more stimulated and less tired on the majority of nights (Fig. 2 and Tables 2–4). But, marijuana-related effects were comparatively small (methamphetamine and modafinil attenuated virtually all night-shift-related performance disruptions), and immediately after marijuana administration (i.e., up to 90 min) there was a trend towards disruptive performance effects, followed by marijuana-associated improvements that persisted over the course of the remaining work period. Thus, the mechanism through which marijuana attenuated night-shift-related performance decrements remains unclear.

A possible explanation for the current results is that marijuana aided in overall sleep recovery during the night shift. The larger concentration increased both objective and subjective measures of total sleep time, and improved sleep quality as measured by ratings of “Satisfied Sleep.” In general, marijuana-related effects on sleep are smaller than, but congruent with, the sleep medication zolpidem (Hart et al., 2003a, 2005). Together, these observations suggest that marijuana cigarettes containing low to moderate Δ^9-THC concentrations offset some disruptions caused by work shift schedule changes, but further research is needed to elucidate the mechanism(s) mediating these effects.

The present findings should be considered in the context of several important caveats. The current study did not assess a broad range of Δ^9-THC concentrations. It is likely that increasing Δ^9-THC concentrations or the number of joints smoked would have exacerbated night shift-related disruptions. Similarly, the current study participants were experienced marijuana users who smoked multiple times each week (i.e., more than three times per week). It is well documented that frequent marijuana users show fewer behavioral signs of disruption during intoxication than infrequent users. Thus, the generality of the present findings might be limited, as a different pattern of results might have been obtained if infrequent users were studied. Relatedly, it is possible that because study participants were frequent marijuana smokers, they may have experienced marijuana withdrawal symptoms during placebo conditions and such symptoms could have influenced study findings. This seems less likely because withdrawal symptoms are typically observed only in heavy marijuana smokers, or individuals who smoke multiple marijuana cigarettes on a daily (or near daily) basis (Haney, 2005). Heavy marijuana smokers were excluded from this study in order to avoid this potential confound. Finally, the current study participants were subjected to abrupt work schedule changes with little time to acclimate, whereas some individuals working night shifts do so for extended periods of time. Therefore, the findings may be relevant only to individuals who undergo abrupt changes in work schedules without an acclimation period.

In conclusion, these data demonstrate that performance, sleep, and mood are disrupted during night shift work when participants are subjected to abrupt shift changes. The data further show that marijuana cigarettes containing low to moderate Δ^9-THC concentrations can decrease some night shift-related performance and mood disruptions. Because these are the first data describing these effects, future studies are needed before broad conclusions are drawn.

Author disclosures

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Conflict of interest

We declare no competing interests.

Contributors

D.R. Keith analyzed the data and wrote the first draft of the paper. C.L. Hart and R.W. Foltin designed the study. C.L. Hart supervised data collection. C.L. Hart, M. Haney, and E.W. Gunderson interviewed potential participants. All of the co-authors approved the final draft of the paper.

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