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Effects of THC on driving performance, physiological state and subjective feelings relative to alcohol

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Abstract

Background: The effects of marijuana or THC on driving has been tested in several studies, but usually not in conjunction with physiological and subjective responses and not in comparison to alcohol effects on all three types of measures.
Objective: To assess the effects of two dosages of THC relative to alcohol on driving performance, physiological strain, and subjective feelings.
Method: We tested the subjective feelings and driving abilities after placebo, smoking two dosages of THC (13 mg and 17 mg), drinking (0.05% BAC) and 24 h after smoking the high dose THC cigarette, while monitoring physiological activity of the drugs by heart rate. Fourteen healthy students, all recreational marijuana users, participated in the study.
Results: Both levels of THC cigarettes significantly affected the subjects in a dose-dependent manner. The moderate dose of alcohol and the low THC dose were equally detrimental to some of the driving abilities, with some differences between the two drugs. THC primarily caused elevation in physical effort and physical discomfort during the drive while alcohol tended to affect sleepiness level. After THC administration, subjects drove significantly slower than in the control condition, while after alcohol ingestion, subjects drove significantly faster than in the control condition. No THC effects were observed after 24 h on any of the measures.

Keywords: Driving performance; Subjective feelings; Marijuana; Alcohol

1. Introduction

It is customary to study the effects of drug abuse on driving by measuring decrements in driving skills. Adding measures of physiological changes and subjective sensations can reveal additional hidden and mediating effects of the drug and can help in understanding the interaction between drug intoxication and road accidents.

Alcohol and drugs – especially marijuana – are often mentioned together in conjunction with driving. However, their effects on driving behavior may differ, and users of alcohol and marijuana may not relate to them and to their affects in the same manner. This issue is especially important among infrequent abusers because their inexperience makes it difficult for them to estimate the deleterious effects of these two drugs when performing complicated tasks like driving. The goal of this study was to determine the differences and similarities between the effects of alcohol and two levels of THC (13 mg and 17 mg) on driving abilities, physiological functioning, and subjective feelings of alcohol and drug impaired drivers.

Alcohol has been long recognized as one of the main causes of driving impairment and car accidents with a very systematic dose–response relationship, with demonstrable impairments at very low blood alcohol concentrations (BAC), beginning with 0.02% BAC (Moskowitz and Fiorentino, 2000), and elevated crash risk at levels of at least 0.04% BAC; increasing exponentially thereafter (Blomberg et al., 2004; Borkenstein et al., 1964; Compton et al., 2002; Moving et al., 2004).

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Alcohol and drug impairments also have an elusive role in the attribution of crash causes. According to Garrison and Reeder (2003) in alcohol related crashes, other factors such as driver distraction and drowsiness are frequently cited as causes, along with other drugs. "These drivers may be just as dangerous as alcohol impaired drivers and, because of drugs, may also be distracted, drowsy, and dangerous" (Garrison and Reeder, 2003).

While alcohol effects on driving have been well established scientifically, because alcohol affects confidence, some people tend to underestimate their level of intoxication after drinking two or three drinks. This problem may or may not be exacerbated with cannabis because its effects are much less known. In this light, the need for studies of the quantitative effects of alcohol and drugs on driving-related skills was aptly stated by Ogden and Moskowitz (2004): "When the layman thinks of impairment, he probably envisages the obvious signs of lack of judgment, poor self-control, and loss of gross motor skills."

Cannabis is one of the most popular recreational drugs that have a long history of suspicion as a source of driver impairment and increased accident risk (Robbe, 1994). The major psychoactive ingredient of Cannabis, delta-9-hydrocannabinol (THC), was isolated, identified and synthesized by Gaoni and Mechoulam (1964). A typical 'joint' of marijuana contains between 0.3 g and 1 g of plant matter and will have 1–15% THC (2.5–15 mg) (Ward and Dye, 1999). Over the years, the potency of cannabis has increased so that according to Leggett (2006), the potency of sinsemilla cannabis, made from the unfertilized buds has doubled. This means that a recreational user today may encounter a stronger and more potent marijuana cigarette containing higher levels of THC than the comparable user of the 'flower/hippie' generation. For this reason, it is also important to test the difference in the impact different levels of THC, and compare each to the corresponding effects of alcohol.

The subjective effects of cannabis include feelings of relaxation and well being, and a sense of sharpened sensory awareness (with sounds and sights seeming more intense). Physiologically THC causes tachycardia and inhibition of nausea and vomiting (Rang and Dale, 1991). There is also some evidence that THC impairs cognition, psychomotor functioning and actual driving in a dose related manner (Ramaekers et al., 2004; Shinar, 2007; Ward and Dye, 1999).

However, a discrepancy between driving impairment observed in controlled laboratory studies and actual involvement of cannabis in car accidents has been observed. Ramaekers et al. (2004) in their review on dose related risk of motor vehicle crashes after cannabis use reported a 4–14% prevalence of THC among drivers who sustained injury or death in traffic accidents. However, attributing the crash cause to THC was complicated because alcohol was also found in 50–80% of the same drivers. Moving et al. (2004) in their culpability analysis of hospitalized injured drivers concluded that cannabis alone does not increase crash risk. One explanation for the difference in the effects of alcohol and THC on car crashes could be the difference in the pharmacokinetics and metabolism of the two drugs. It takes about 30–60 min for BAC to reach its peak after alcohol intake (Wilkinson et al., 1977). In contrast, THC plasma concentration peaks after 5–15 min and decreases rapidly thereafter (Perez-Reyes et al., 1982). Another source of difficulty in interpreting the results of previous studies, is that some of them identified cannabis use by measuring THC–COOH, an inactive carboxy metabolite of THC, that has no psychoactive properties, and that can be detected in blood or urine for days and weeks after intake of marijuana; long after its psychoactive effects have disappeared (Ramaekers et al., 2004).

An issue that has not received much attention – that also distinguishes alcohol impairment from THC impairment is how they affect subjective feelings and how these can affect driving style. While alcohol intoxication tends to increase self-confidence, THC-impaired people are aware of being impaired (Hindrik et al., 1999; Robbe and O'Hanlon, 1993).

In Israel, most alcohol and marijuana users are recreational users, and most of them report smoking marijuana mixed with tobacco that is extracted from cigarettes. Therefore, we induced two levels of THC impairment (13 mg and 17 mg) by having drivers smoke low-tar low-nicotine THC-injected cigarettes. The effects of THC impairments were then compared to alcohol impairments (at 0.05% BAC) on driving-related behavioral physiological and subjective measures.

2. Methods

2.1. Participants

Fourteen Healthy students, 10 males and 4 females, age 26.1 ± 1.3 with BMI of 18.5–24.5 (average of 22.1 ± 1.9) participated in the study. All volunteers were recreational users of marijuana and alcohol with "low" to "moderate" use of marijuana (smoking 1–4 times per month). Most of them reported smoking mainly on social occasions (parties) or during the weekends. All subjects signed a consent form as approved by the institutional review board (Helsinki committee) and were tested positive for metabolites of THC prior to the beginning of experimental sessions.

2.2. Laboratory settings

A STI-SIM fixed-based driving simulator (Systems Technology, Inc.) was integrated into a passenger car, providing the driver with the look feel of driving a real car. The visual display of the road was projected on 3 m × 3 m screen at a distance of 3 m from the driver's eyes, providing a true horizontal field of 40° on a scale of 1:1.

A computer screen placed on the dashboard panel to the right of the steering wheel (usually where the radio system is placed) was used to remind the drivers of the speed limit. Two cameras – placed inside the car – monitored the driver: one directed to the driver face and one located in the back, capturing his or her movements from behind. One more camera was placed at the room used for the interviews and smoking the THC-filled cigarettes.

2.3. Road scenarios

Two scenarios were included in each experimental session:

1. "Baseline" scenario – This scenario was used for baseline physiological measurements prior to treatment administration. Subjects were asked to drive a rural road, with very few curves and low traffic volume at a speed limit of 55 miles per hour (mph), for 10 min.
2. "Main" scenario – This scenario was used after the alcohol/drug intake. The "Main" scenario was a 33.9 miles road composed of four segments. (a) A 10.7 miles two-way two-lane mostly straight rural road, with desert scenery with few trees and with a few curves and low traffic density. Subjects were asked to maintain a speed of 55 mph. (b) A 7.9 miles two-way winding, downhill road, with a speed limit of 45 mph. (c) A 7.2 miles two-lane road in which the drivers were asked to drive behind a lead car, within the speed limit of 55 mph. (d) A 8.1 miles two-lane road with four unexpected events: pedestrian crossing, a road block, a car standing in the middle of the road, and a car coming out of a gas station, with a speed limit of 55 mph. The order of the four segments was counterbalanced across subjects.

2.4. Study protocol

In the week prior to the beginning of the experiment, each subject attended an orientation session. During this session, subjects were asked to smoke a placebo cigarette according to the smoking protocol and drive the "Baseline" and one of the "Main" scenarios constructed of all four segments as mentioned above. Subjects were asked to abstain from drinking more than a glass of an alcoholic beverage a day and to abstain from smoking marijuana at least a week prior to the experimental sessions, and then continue to refrain from smoking marijuana for the duration of the experiment.

All subjects were tested after a full night sleep and ate a light breakfast (as they were used to) prior to the beginning of the experiment, and refrained from further food intake before the session started. To avoid variations due to circadian rhythm, all sessions took place between 9:00 am and 14:00 pm, 3–7 days apart.

2.5. Experimental sessions

The study included six within-subject experimental sessions, double blind with the order of sessions counterbalanced across subjects. The six sessions, included:

1. Control ("Control"): drinking orange juice without smoking.
2. Placebo ("Con +"): drinking orange juice and smoking a placebo cigarette.
3. Alcohol ("Alc"): drinking alcohol mixed with orange juice to reach a level of 0.05% BAC and smoking a placebo cigarette.
4. THC low dose ("THC L"): smoking a cigarette containing 13 mg THC and drinking juice.
5. THC high dose ("THC H"): smoking a cigarette containing 13 mg THC and drinking juice.
6. Twenty-four hours after smoking the maximum THC dose ("After"): a session 24 h after smoking the high dose THC cigarette, and drinking orange juice without smoking.

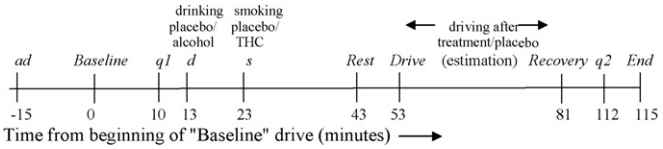

Fig. 1. General design of an experimental session. *ad*, admission in the lab; *Baseline*, driving the "baseline" scenario; *q1*, questioner before treatment; *d*, drinking (placebo or alcohol); *s*, smoking (placebo or THC cigarettes, except in the "control" and "After" sessions); *Rest*, rest before the drive; *Drive*, driving the "main" scenario, *Recovery*, rest after the drive; *q2*, questioner after treatment and drive.

2.6. Experimental session design

Each experimental session consisted of the following stages:

1. Admission in the lab and connection to the physiological monitoring device.
2. Entering the simulator car and driving the "Baseline" scenario for 10 min.
3. Filling out a questionnaire about their physical state before treatment.
4. Ingesting an alcoholic beverage or placebo, waiting for 10 min and then smoking a cigarette that contained either no THC, or 13 mg THC, or 17 mg THC (after alcohol only placebo cigarettes were used). In the "Control" and "After" sessions, the subjects did not smoke.
5. Waiting for 20 min and then entering the simulator car and resting for 10 min.
6. Driving the "Main" scenario for about 28 min (depending on the driver's speed).
7. Resting for 10 min more in the car in order to monitor their recovery.
8. Completing a post-driving questionnaire concerning their physical state during the last part of the drive.

This sequence of events is schematically illustrated in Fig. 1.

2.7. Alcohol and THC cigarettes administration

2.7.1. Alcohol and placebo administration

In the "Alc" sessions, each subject consumed alcohol in the amount of 0.5 g/kg body weight of Alcohol (40% 'vodka'). Alcohol was diluted with an orange drink to give a total volume of 400 ml. During all other sessions, a placebo drink was administered containing only 400 ml of the orange drink. Subjects were given 3 min for intake.

2.7.2. Alcohol monitoring

Blood alcohol concentration was tested prior to driving the "Main" scenario using a Lion Alcolmeter Model S-3 breathalyzer.

2.7.3. THC cigarettes administration

THC and placebo cigarettes preparation: THC (13 mg or 17 mg) dissolved in ethanol was injected with an even distribution into a 0.5 g commercial brand cigarettes containing 1 mg

tar and 0.1 mg nicotine. After injection, the ethanol was evaporated using nitrogen gas. All cigarettes were injected, either with THC or only with ethanol. Subjects were unable to distinguish between placebo or THC cigarettes. Prior to injection, the filters were removed from the cigarettes.

Smoking protocol: After receiving a sign from the experiment administrator, the subject exhaled as much as possible, then inhaled into the lungs from the cigarette for 2 s and retained the smoke in the lungs for 10 s as instructed by the experiment administrator. After exhaling, the subject rested for 40 s. This process was repeated until the cigarette was finished.

3. Outcome measurements

Three types of measures were used:

3.1. Performance measures including

- Root mean square (RMS) of the lane position (in ft)
- RMS of the longitudinal speed (in miles/h)
- Average speed (in miles/h)
- RMS of the steering wheel deviations (in degrees)
- Number of collisions
- Reaction time to a secondary task (in s). The task consisted of responding to a light in an array of three lights with corresponding three buttons, placed on the dashboard above the screen to the right of the steering wheel. Occasionally, during the drive one of the lights was randomly lit and driver's task was to press the corresponding button as quickly as possible.

3.2. Subjective questionnaire

The Swedish Occupational Fatigue Inventory-20 (SOFI-20) (Äahsberg et al., 2000) was used to measure subjective feelings related to the driving task. The questionnaire was administered on each session, before the treatment and at the end of the drive after the treatment. The SOFI consists of 20 questions related to feelings on five dimensions: Physical discomfort, Physical exertion, Lack of energy, Lack of motivation, and Sleepiness. For each question, the subjects had to rate their feelings on a scale for "0" – does not feel at all to "6" – feel extremely. The first time subjects filled the questionnaire they were instructed to rate their physical state at the time they entered the lab, and the second time they filled the questionnaire they had to rate how they felt during the last part of the drive main drive.

3.3. Physiological monitoring

ECG signals were recorded from two skin surface electrodes at a sampling rate of 500 Hz using an 'Atlas Researches LTD.' polygraph connected to a PC computer by an optic fiber.

Heart rate R waves were detected by conventional signal analysis techniques and R to R intervals calculated. Heart rate (HR) and heart rate variability values were calculated.

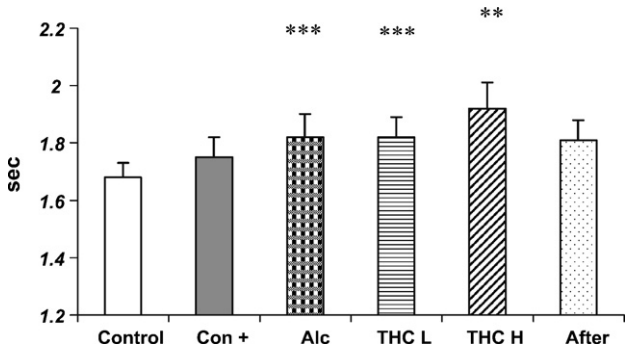

Fig. 2. Reaction time to the secondary task (mean ± S.E., $n = 14$).**, Significantly different from "Control" and "Con +" sessions ($p \leq 0.05$). ***, Significantly different from "Control" sessions ($p \leq 0.05$).

3.4. Data analysis

Statistical significance was defined at $\alpha = 0.05$. Each driving performance measure and each dimension in the subjective questionnaire was analyzed using one-way ANOVA for repeated measures followed by post hoc Fisher LSD pair-wise comparisons to identify the source of the significant effects. For each dimension in the subjective questionnaire, the difference score between the level reported after the drive and the level reported before the drive was first calculated. Heart rates were calculated for five periods in each session: "Baseline" drive, "Rest" before the drive, the first half of the drive ("Drive 1"), the second half of the drive ("Drive 2"), and "Recovery" in the car after driving. Heart rates were normalized for each session separately according to the "Baseline" drive that was given a score of 100%. The normalized scores were analyzed using two-way ANOVA for repeated measures (Period × Treatment) followed by Post hoc Fisher LSD pair-wise comparisons to interpret significance among treatments and periods.

4. Results

4.1. Performance results

4.1.1. Reaction time

There was a main effect of treatment on the on reaction time to the secondary task ($F(5,2.722)$, $p = 0.027$). Post hoc tests showed that after smoking the higher dose of THC (17 mg), response time was significantly higher than in the "Control" (Drinking orange juice only) and "Con +"(drinking orange juice and smoking placebo cigarette) conditions. Alcohol and the lower level of THC (13 mg) also increased reaction time significantly compared to the "Control" but the magnitude of the effect was smaller than the effects of the higher level of THC as shown in Fig. 2.

No significant difference was found among "Control", "Con +" and "After" (24 h after smoking the 17 mg THC cigarettes and drinking orange juice only) session, showing that there was no placebo effect and no residual THC effect on reaction time.

4.1.2. Driving performance

There were significant treatments main effects on average speed ($F(5, 9.057)$, $p = 0.000$), lane position variability (RMS) ($F(5,3.881)$, $p = 0.004$)) and steering wheel variability ($F(5,2.45)$, $p = 0.042$). Only speed variability was not significantly affected by the treatment ($F(5,1.096)$, $p = 0.371$).

Average speed was the most sensitive driving performance variable affected by both THC and alcohol but with an opposite effect. Smoking THC cigarettes caused drivers to drive slower in a dose-dependent manner, while alcohol caused drivers to drive significantly faster than in the "Control" conditions as illustrated in Fig. 3. Lane position variability increased significantly – relative to the two control conditions and the '24 h after condition – with both dosages of THC in a similar manner, impairing the driver's ability to maintain lane position, as illustrated in Fig. 3. After alcohol intake, lane position variability also increased but was not significantly different from the control sessions. In addition to driving faster, alcohol also decreased the driver's ability to keep the steering wheel steady, as reflected by an increase in steering wheel variability. Post hoc Fisher LSD pair-wise comparisons revealed that this effect was also found after smoking the lower level of THC ($p \leq 0.05$), but not after smoking the higher dose of THC. The high dose of THC also increased speed variability, relative to the variability in the "Con +" session. ($p \leq 0.05$). There were no significant differences among the three conditions – "Control", "Con +" and "After" – in any of the driving measures, as shown in Fig. 3.

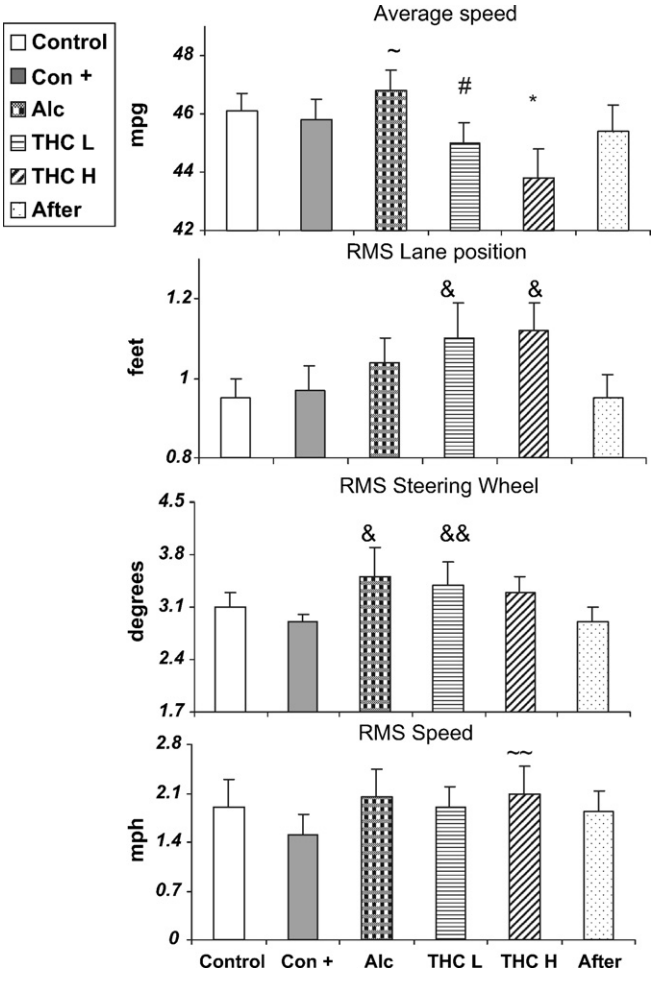

Fig. 3. Treatments effects on driving performance variables (mean ± S.E., $n = 14$). *, Significantly different from all other conditions ($p \leq 0.05$); #, significantly different from "Control and "Alc" conditions ($p \leq 0.05$); ∼, significantly different from all sessions except "Control" conditions ($p \leq 0.05$); ∼∼, significantly different from "Con +" and "After" conditions ($p \leq 0.05$); &, significantly different from "Control", "Con +" and "After" conditions ($p \leq 0.05$); &&, significantly different from "Con +" and "After" conditions ($p \leq 0.05$).

Table 1
Total number of collisions and number of subjects involved during the different experimental sessions

	Control	Control+	Alcohol	THC low	THC high	After
Total number of collisions	2	2	4	3	6	3
Number of drivers involved	2	2	3	3	6	3

4.1.3. Number of collisions

A total number of 20 collisions occurred during 84 experimental sessions. This number was too low for statistical analysis. However, a dose-related pattern could still be discerned. Six different subjects had one collision each after smoking the higher dose of THC compared to three subjects that collided once after smoking the lower THC dose and three drivers that had a total of four collisions after alcohol intake. The distribution of collisions across the six conditions is given in Table 1. The number of collisions occurring after the lower level of THC and after alcohol was not significantly different from the number of collisions occurring during the control sessions and 24 h after smoking the high dose of THC.

4.1.4. Subjective results

Statistical analysis of treatments effects on each individual dimension of the SOFI questionnaire, yielded three significant main effects (out of the five); Physical discomfort (F (5,4.96, $p = 0.001$), Lack of energy (F (5,3.18), $p = 0.013$) and Physical effort (F (5,7.97), $p < .000$). Post hoc tests revealed that the most significant effects were felt after smoking the higher dose of THC (17 mg), as shown on Fig. 4 The physical effort and physical discomfort felt by subjects were significantly higher after smoking the higher dose of THC than after the "Control" (drinking orange juice only), "Con +" (drinking orange juice and smoking placebo cigarette), "After" (24 h after smoking the 17 mg THC cigarettes and drinking orange juice only) and "Alc" (drinking alcohol 0.05% and smoking placebo cigarette) conditions. A similar, but weaker pattern was seen after smoking the lower dose of THC (13 mg), yielding significant greater levels of physical discomfort and physical effort felt by subjects after smoking, compared to the "Control", "Con +" and "After" conditions.

Subjects also felt lack of energy after smoking the higher dose of THC, at the same level they felt after alcohol intake, and were both significantly higher than after "Control", "Con +" and "After" sessions.

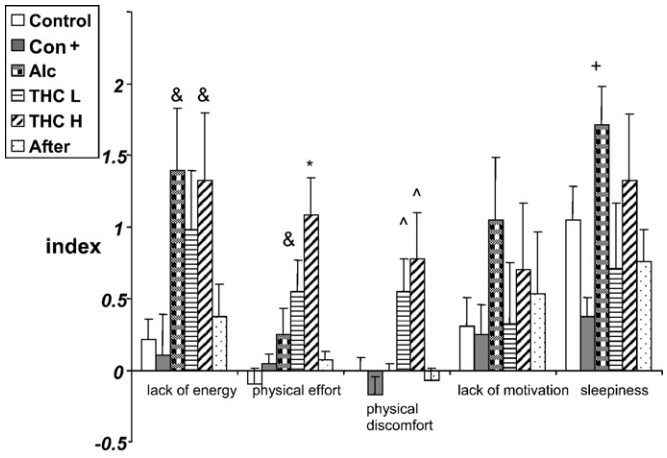

Fig. 4. Differences in the subjective feelings between the end and beginning of each session on the five SOFI dimensions (mean ± S.E., $n = 14$). *, Significantly different from all other sessions ($p \leq 0.05$); &, significantly different from con, con+ and 24 after sessions ($p \leq 0.05$); ^, significantly different from con, con+, Alc and 24 after sessions ($p \leq 0.05$); +, significantly different from "Con +" sessions ($p \leq 0.05$).

The sensation of sleepiness was greatest after alcohol intake, but was significantly different only from "Con +" condition, due to large variability among subjects. No significant differences among any of the conditions were found for lack of motivation.

The three conditions of "Control", Con +" and "After" did not differ from each other on any of the five SOFI dimensions. Finally, although the experiment was double blind by design, within minutes of finishing smoking all subjects were able to distinguish between the placebo cigarettes and the THC-injected cigarettes. This information was typically volunteered in positive comments about the quality of the drug, such as "this is good stuff".

4.1.5. Factor analysis of performance and subjective data

A varimax normalized factor analysis was used in one initial run for eight measures; the five SOFI dimensions and three performance measures (average speed, RMS of the lane position, and reaction time to the secondary task). The final factor solution for the analysis met the following criteria: (a) eigenvalue > 1.0; (b) item–dimension correlation of ≥0.55. Two factors emerged as shown in Table 2. The first factor was associated exclusively with the subjective measures of fatigue. The second factor was associated with the feelings of physical effort and discomfort and the performance measures of speed and reaction time.

To determine the effect of experimental sessions (1–6) on each factor we conducted a one-way ANOVA on each factor. For Factor 1, there was no main effect, $F(5, 78) = 1.61$, $p = .167$, For Factor 2, there was a main effect $F(5, 78) = 3.47$, $p = .007$. A post hoc analysis showed that the two THC conditions were significantly different from the two control sessions. Alcohol and After sessions were significantly different from the THC H session.

Table 2
Factor Loadings (Varimax normalized) extraction: principal components (marked loadings are >0.55)

	Factor 1	Factor 2
Lack of energy (sf)	0.914731	0.163857
Physical effort (sf)	0.562567	0.551923
Physical discomfort (sf)	0.439414	0.594122
Lack of motivation (sf)	0.788862	0.056503
Sleepiness (sf)	0.887561	0.047593
Speed (pr)	−0.065367	0.689367
RMS lane position (pr)	0.379706	0.298379
Reaction time (pr)	0.107678	0.681909
Explained variance	2.916412	1.719162
Proportion of total variance	0.364551	0.214895

sf , subjective feeling variable; pr, performance variable.

4.1.6. Physiological results (heart rate)

Two-way ANOVA (Treatment × Period) on relative heart rate (difference between the session heart rate and the "baseline" measured during the drive just prior to the treatment on that session) revealed significant effects of treatment (F (5,135.7), $p = 0.00$), time period (F (3,3.6), $p = 0.019$) and the interaction between them (F (15,2.5), $p = 0.002$), as shown in Fig. 5. The difference score was measured relative to the average HR during the rest period before the drive ("Rest" in Fig. 5), the first half of the drive (Drive 1), the second half of the drive (Drive 2), and the period immediately after the drive (Recovery). THC affected relative HR in a dose-related manner. The greatest change was observed after smoking the THC cigarettes during the "Rest" before driving as shown in Table 2. The higher level of THC (17 mg) caused a 53.2% increase in HR compared to the HR prior

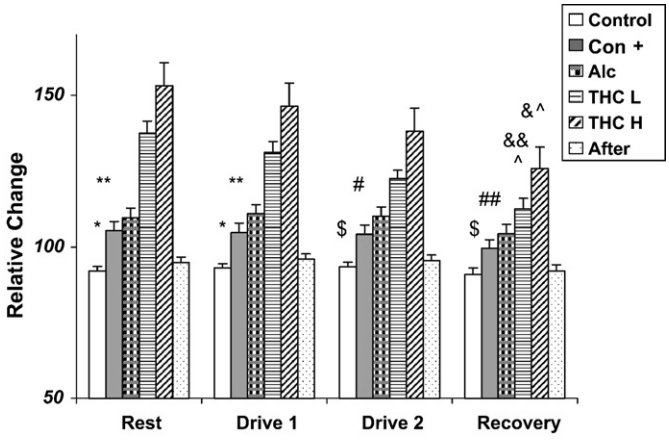

Fig. 5. Relative changes (%) in heart rates (mean ± S.E., $n = 14$) compared to the "Baseline" drive at each individual experimental session prior to treatment. "Rest" is the period before driving. "Drive 1" is the first half of the drive. "Drive 2" is the second half of the drive. "Recovery" is the rest period after driving. *, "Control sessions were significantly different from all other sessions except "After" sessions ($p \leq 0.05$); **, "Con +" sessions were significantly different from all other sessions except "Alc" sessions ($p \leq 0.05$); #, "Con +" sessions were significantly different from all other sessions except "Alc" and "After" sessions ($p \leq 0.05$); ##, "Con +" sessions were significantly different from "THC L" and "THC H" session ($p \leq 0.05$); &, "THC H" sessions were significantly different from all other sessions; &&, "THC L" sessions were significantly different from "Control", "Con +" and "After" sessions; ^, "Recovery" period was significantly different than the "Rest" period.

to treatment (average HR was 108.3 beats per minute (bpm), while HR after the lower level of THC (13 mg) caused a relative increase of 37.5% (average HR was 102.9 bpm). This pattern remained relatively constant during the whole experimental session though the relative HR decreased significantly over time as illustrated in Fig. 5. Average HR was 25% higher after 17 mg THC during the recovery phase after driving, and 12% higher after 13 mg THC compared to HR during "Baseline" of each separate experimental session. Relative HR during rest period in the control session was 92% of the "Baseline" HR (average HR was 67.8 bpm).

Alcohol intake also significantly increased HR compared to "Control" sessions but less than both levels of THC (HR during "Rest" after treatment was 9% higher than HR during the baseline). Alcohol effects on HR remained constant during the whole experimental session. HR also increased after smoking the placebo cigarette compared to the "Control" sessions where subjects did not smoke at all. However effect of the placebo cigarette decreased over time and HR during the "Recovery" period after smoking the placebo cigarettes was similar to HR during the "Baseline" prior to smoking. There were no differences between "Control" and "After" sessions (Table 3).

5. Discussion

Before discussing the subjective and driving performance results, it was important to establish that the THC and the alcohol were physiologically active while driving. Heart rate acceleration or speeding is a commonly found physiological effect of marijuana intake, with a consistent dose–response relationship (Kanakis et al., 1976; Perez-Reyes et al., 1982; Robbe, 1994; Schaefer et al., 1975). HR can also be used as an indicator for alcohol dose intake, but not at low doses (Moravi et al., 1988). Relative to this measure, the results showed that the two doses of THC were physiologically more potent than 005% BAC, and that heart rate acceleration distinguished between the two doses of THC. During the rest period before the drive, heart rate increased by 53% after intake of the higher dose THC, by 37% after intake of the lower THC dose, and by 9% after the alcohol intake, compared to baseline measurements prior to each treatment. In contrast to THC, after alcohol, HR maintained relatively constant throughout the experimental session, while THC effects deteriorated during the session. This difference between THC and alcohol in temporal nature of the effect could have implications for driving, 60–90 min after low–moderate marijuana intake – to the extent that subjective sensations of impairment are related to the heart rate – drivers may feel that the drug effects have dissipated because most of the THC effects on HR seem to have vanished (depending on dosage smoked). In contrast, alcohol effects, even after moderate doses, may persist for longer durations and impair judgment and driving abilities for longer durations as well.

Placebo cigarettes containing only low levels of nicotine also elevated HR significantly compared to "Control" sessions, in which the subjects did not smoke. This is because HR is known to be affected by nicotine. Nicotine causes sympathetic stimulation with hemodynamic effects that include an increase of heart rate (Joseph and Fu, 2003); though to a lesser extent than from alcohol or THC.

Subjective feelings and driving performance were affected by both levels of THC cigarettes (13 mg and 17 mg) in a dose-dependent manner. Although a moderate dose of alcohol (0.05% BAC) appeared to impair subjects' ability to drive at a similar level as that observed after smoking the lower level of THC, some of the alcohol effects were opposite of those observed after smoking THC, as discussed below.

Usually, a battery of questionnaires including visual analog scales and specific questions about mood changes are used to investigate the subjective effects of drugs (e.g., Heishman et al., 1997; Wachtel et al., 2002). Heishman et al. (1997) found that the high doses of alcohol (BAC – 90 ml/dl) and marijuana (THC 188 ng/ml) produced identical subjective rating of perceived impairment and similar degrees of actual impairment on a digit symbol substitution test and a word recall test. In the present study, we used a five-dimensional ordinally-scaled questionnaire (Äahsberg et al., 2000) to describe feelings while driving under the influence of the drugs. This questionnaire focuses mainly on fatigue and physical load and effort, thus enabling to test these aspects that are usually not present in drug questionnaires even though they may have a large impact on driving and the decision to drive after intake. This measure was quite sensitive to the drug and alcohol effects. Both doses of THC increased physical discomfort and physical effort, with greater effects reported after the higher level of THC. Relative to the pleasure involved, subjects reported that the lower dose of THC was more enjoyable, while after driving under the influence of the high level of THC

Table 3
Relative changes (%) in heart rates (mean ± S.E., $n = 14$) compared to the "Baseline" drive of each individual prior to treatment

	Period	Treatment	Mean (%)	Standard error	n
1	Rest	Control	92.0378	1.5	14
2	Rest	Con +	105.3832	2.8	14
3	Rest	Alc	109.3977	3.3	14
4	Rest	THC L	137.5094	3.9	14
5	Rest	THC H	153.2487	7.6	14
6	Rest	After	94.9010	1.84	14
7	Drive 1	Control	93.0820	1.4	14
8	Drive 1	Con +	104.7717	2.9	14
9	Drive 1	Alc	110.8925	2.9	14
10	Drive 1	THC L	131.0904	3.6	14
11	Drive 1	THC H	146.3940	7.7	14
12	Drive 1	After	96.0392	1.7	14
13	Drive 2	Control	93.4359	1.6	14
14	Drive 2	Con +	104.2447	2.9	14
15	Drive 2	Alc	109.9299	3.1	14
16	Drive 2	THC L	122.4469	2.9	14
17	Drive 2	THC H	138.1266	7.6	14
18	Drive 2	After	95.5253	1.9	14
19	Recovery	Control	90.9762	2.2	14
20	Recovery	Con +	99.6230	2.8	14
21	Recovery	Alc	104.3894	3	14
22	Recovery	THC L	112.4366	3.5	14
23	Recovery	THC H	125.7020	7.2	14
24	Recovery	After	91.9636	2.2	14

"Rest" – period before driving, "Drive 1" – first period of driving, "Drive 2" – second period of driving, "Recovery" – rest after driving.

many of them complained about discomfort. The questionnaire results also showed that higher levels of THC are much more extended than the lower dose of THC and caused a similar elevation in sleepiness and lack of energy as reported after alcohol intake. These results extend the knowledge about the subjective effects of THC as described by Robbe (1994). Robbe compared the effects of three doses of THC 100 μg/kg, 200 μg/kg and 300 μg/kg to placebo on the subjective ratings on several dimensions related to the effort and quality after intake and following the drive. He found dose-dependent effects in the perceived effort and perceived driving quality. Robbe (1994) also asked his subjects about their willingness to drive after THC consumption and found that the lower the administered THC dose and the more urgent the reason for driving, the more subjects declared that they would be willing to drive. Two more highly relevant questions are whether subjects would have stopped driving if they had the chance to do so, and whether their willingness to drive after a bad experience of driving under the influence of marijuana would change if they needed to drive again on a different day. These questions should be addressed regarding the two drugs separately and in combination.

Alcohol mainly caused increase in sleepiness and lack of energy. These effects are expected from depressants, and demonstrate the difference in the effects of the two drugs. No subjective differences were found between control sessions and 24 h after intake of the high dose of THC. These results correspond to those of other studies, such as by Curran et al. (2002) who found no subjective and cognitive effects after 24 h or 48 h following 7.5 mg and 15 mg oral intake of THC.

Driving performance measures and reaction time to the secondary task corresponded with the physiological effects and the results from the subjective questionnaires. The higher THC dose significantly impaired performance with a much more extended and less specific effects than the lower dose and alcohol, except steering wheel variability. The impairment observed after the lower level of THC resembled the impairment after alcohol consumption. In general, THC in doses between 40 μg/kg and 300 μg/kg causes a dose-dependent reduction in performance on laboratory tasks measuring memory, divided and sustained attention, reaction time, tracking and motor function (Ramaekers et al., 2006). Although previous studies have found performance impairments after doses up to 300 μg/kg THC that were equivalent to the impairing effects of alcohol with doses that produce BAC of ≥0.05 g/dl (Ramaekers et al., 2006), differences between the two drugs were also observed. For example, Liguori et al. (2002) found that alcohol increased brake latency without affecting body sway while THC increased body sway but did not affect brake latency. The present study reveals that although some similarities in the degree of impairment could be observed – mainly with the lower level of THC (13 mg) and alcohol, where both increased reaction time and RMS of the steering wheel – some discrepancies also appeared between the effects of the two drugs. In particular, subjects seemed to be aware of their impairment after THC intake and tried to compensate by driving slower, alcohol seemed to make them overly confident and caused them drive faster than in the control sessions. Another difference between the effects of THC and alcohol was revealed in the responses to the subjective questionnaire. THC mainly increased the perceived effort and discomfort while alcohol mainly affected alertness (although sleepiness and lack of energy were also affected by the higher level of THC).

Ward and Dye (1999) in their review of cannabis effects on driving found that cannabis (1) increases variability of longitudinal speed and lateral control, (2) increases decision times, and (3) reduces speed making driving appear more "cautious". Our results show that although subjects drive slower after smoking THC, this does not mean that they are more cautious. THC caused increased reaction time and lane position variability while alcohol caused subjects to drive faster but also impaired reaction time and increased steering wheel variability. These results reinforce Ward and Dye's (1999) conclusion that "the form of impairment from alcohol consumption appears to be qualitatively different than for cannabis. Notably, alcohol seems to result in a 'riskier' driving style (e.g., faster speeds) rather one that is more cautious". The findings of our study also show that although impairment was observed after smoking 13 mg THC cigarettes, an addition of 4 mg THC to a single cigarette (17 mg), may significantly increase the affects of THC in recreational marijuana users, increasing perceived fatigue and driving impairment compared to the lower dose

In conclusion, based on our results, smoking the active ingredient in marijuana, THC, at dosages of 13 mg and 17 mg, may impair driving ability in recreational users of marijuana and can lead to produce unsafe driving. These effects are dose dependent and are reflected in all three types of measurement techniques used: performance, subjective sensations, and physiological. The higher dose of THC (17 mg) was found to be more potent than the lower dose (13 mg) causing higher increase in heart rate and a greater feeling of discomfort and physical effort while driving after smoking. In terms of performance, the effects of 0.05% BAC seem to be similar to those of the low-level (13 mg) THC cigarettes although subjects drove faster after alcohol compared to driving sessions after THC smoking. No THC-related effects were measurable 24 h after smoking the high (17 mg) level of THC.

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