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The effect of alcohol, THC and their combination on perceived effects, willingness to drive and performance of driving and non-driving tasks

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ABSTRACT

Background: Driving under the influence of drugs (DUID) is one of the main causes of car accidents. Alcohol and marijuana are the most popular drugs among recreational users. Many classify these drugs as "Light" drugs and therefore allow themselves to drive after consuming them.
Objective: The study had two main objectives: 1) to investigate the effect of alcohol (BAC = 0.05%), THC (13 mg) and their combination on driving and non-driving tasks. 2) to investigate the extent to which people are willing to drive based on their subjective sensations and their perceived effects of the drugs.
Method: 7 healthy men and 5 healthy women, ages 24-29, all recreational users of alcohol and marijuana, completed 5 experimental sessions. Sessions included: drinking and smoking placebo, drinking alcohol and smoking placebo, drinking placebo and smoking THC, drinking alcohol and smoking THC, drinking placebo and smoking placebo 24 hours after drinking alcohol and smoking THC. Three types of measures were used: subjective perceptions (with questionnaires), performance parameters of the driving and non-driving tasks (arithmetic task and a secondary target detection task) and physiological changes (heart rate).
Results: Overall, the combination of alcohol and THC had the most intense effect after intake. This effect was reflected in performance impairments observed in the driving and non-driving tasks, in the subjective sensations after intake, and in the physiological measures. Despite significant differences in the size of the effects after the various treatments, there were no differences in the distances subjects were willing to drive while under the influence on each of the treatments.

1. Introduction

Driving under the influence of drugs (DUID) and while intoxicated by alcohol (DWI) are still among the leading causes of car accidents and casualties. According to results of a U.S. national survey on drug use and health Substance Abuse and Mental Health Services Administration (2009) in 2008, 10 million people aged 12 or older reported driving under the influence of illicit drugs during the past year with the highest rate among young adults aged 18 to 25. According to NHTSA's National Center for Statistical and Analysis (2009) 32% of the total fatalities from car crashes in the U.S.A in 2008 were alcohol related. Recent information published by the National Institute On Drug Abuse (NIDA, 2009) on drugged driving indicates that overall, marijuana is the most prevalent illegal drug detected in impaired drivers and motor vehicle crash victims. A large survey conducted in France between 2001 and 2003 on more than 10,000 accidents reports involving over 17,000 drivers revealed that alcohol levels above 0.05% of blood (the legal limit in France) were found in 21% of the drivers, and cannabis was the most frequent drug detected with a prevalence of 6.8% alone and approximately 40% in combination with alcohol (Biecheler et al., 2008). In Australia an investigation of the involvement of drugs in drivers killed in motor vehicle crashes revealed that drivers killed in car crashes who took psychoactive drugs were more likely to be responsible for the crash than those that that did not take psychoactive drugs. This was especially true of cannabis and strong stimulants or alcohol, with the combination of alcohol and drugs increasing the likelihood that drivers caused the crash in which they died (Drummer et al., 2004).

Thus, despite the continuing reduction in DWI (Compton & Berning, 2009) DWI related fatalities are still significant. At the same time DUID seems to be increasing, especially in the case of marijuana (Compton & Berning, 2009; Lacey, et al., 2009b).

Recent studies that examined the effects of alcohol and cannabis on driving concluded to that in order to understand the impair-

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ments and determine ways of dealing with the problem, it is necessary to further investigate the effects themselves (Lenne et al., 2010) as well as understand how users perceive the effects of different drugs and how they deal with these effects in driving situations (MacDonald et al., 2008). These perceptions are likely to affect users' willingness to drive after intake.

The present study tested the effects of the two most popular drugs associated with driving impairment and car accidents - alcohol and THC (the major psychoactive ingredient in cannabis) alone and combined - on (1) the ability of recreational users to perform a driving and a non-driving time-sharing task (arithmetic calculations and a secondary target detection task) while under the influence of either alcohol (BAC = 0.05%), THC (13 mg), their combination, relative to performance not under the effects of drugs, (2) the extent to which they are willing to drive based on their subjective sensations after intake of either drug alone or both.

DWI has long been recognized as a crash risk factor (Moskowitz and Fiorentino, 2000; Compton et al., 2002; Moving et al., 2004). Alcohol alone, mostly dose dependent, impairs performance, particularly cognitive functioning such as information processing, memory, response time, divided attention and spatial perception (Finnigan & Hammersley, 1992; Gengo et al., 1990; Heishman et al., 1988, 1997; Kerr & Hindmarch, 1998). Impairments in driving related tasks have been noted for levels below 0.05% BAC (Moskowitz and Robinson, 1988; Moskowitz and Fiorentino, 2000; Howat et al., 1991) and statistically significant increases in crash risk have been obtained for levels as low as 0.04% (Compton et al., 2002).

Marijuana (mainly dependent on the THC dose used) reduces visual scanning, orientation ability, divided attention and psychomotor performance (Weinstein et al., 2008; Ashton, 2001; Smiley, 1999). Ramaekers et al. (2006) found that the proportion of observations showing impairment of cognition and motor control progressively increased as a function of serum THC in different tasks. Ward and Dye (1999) summarized the literature on the acute psychomotor response following ingestion of cannabis and concluded that cannabis affects mood, memory, and attention, and these in turn may impair temporal processing, (complex) reaction times, and dynamic tracking. Furthermore such effects were observed for doses less than the typical amount consumed by users, with higher doses likely to cause greater impairments.

Few studies compared behavior after alcohol and marijuana. Laberge and Ward (2004) note that alcohol caused drivers to increase their speeds while drivers in simulator and road studies who used cannabis were more aware of their intoxication and tended to compensate by driving slower and adopt a more cautious driving style.

Heishman et al. (1997) showed that a range of alcohol and marijuana doses produced comparable subjective effects and performance impairment in several cognitive tasks and that alcohol, but not marijuana, slightly impaired performance in a number recognition test.

Robbe (1994) in his dissertation investigated the effects of marijuana (100 μg/kg) and alcohol (about 0.04%) on urban city driving and found significant impairments in the handling of the vehicle and action in traffic under alcohol, while marijuana alone did not significantly change mean driving performance. Robbe also found that under both conditions when the reason for driving was described to subjects as "urgent", almost all subjects were willing to drive. In an earlier study Smiley (1999) concluded that both alcohol and marijuana impair performance but the impairment impact after marijuana is mediated because subjects appear to perceive that they are impaired and try to compensate whereas after alcohol they may drive in a more risky manner. In our previous study (Ronen et al., 2008) we found that drivers after alcohol ingestion drove relatively faster than when sober, while after THC intake they drove more slowly (but their lateral control still deteriorated).

The literature on the joint effects of THC and alcohol on driving is sparse and inconclusive. Robbe (1998) found that marijuana alone impairs driving performance mainly under "medium-high" doses, and when combined with alcohol the impairment was greater than with alcohol or marijuana alone. Lenne et al. (2010) tested the effects of cannabis and alcohol on simulated arterial driving and found that their higher level of cannabis (Mean of 12.01 ng/ml) caused greater levels of impairment than lower levels (mean 7.40) while alcohol at the doses used (mean 0.02, 0.05 BAC) had few effects and did not induce synergistic effect when combined with cannabis. Liguori et al. (2002) found no significant additive effects of alcohol and marijuana on brake latency, body sway, and mood. Ramaekers, Robbe and O'hanlon (2000) tested the effects of alcohol (0.04%) and marijuana (100 μg/kg and 200 μg/kg THC) separately and in combination on actual driving performance. Their results indicated that both THC doses and alcohol significantly impaired driving performance with a relative minor deficit observed after alcohol ingestion and moderate after both THC doses with the combination causing a significant increase of impairment.

To comply with the objectives of the study, a variety of techniques were used to test actual performance, the perceived effects of the drugs, and the willingness to drive following the administration of the two drugs. Performance was tested after intake on driving and non-driving tasks and a variety of questionnaires were used to gain comprehensive information about the intensity of various sensations people feel after intake of these popular drugs alone and in combination and the implication of these sensations on their willingness to drive.

2. Method

2.1. Participants

Twelve healthy students, 7 males and 5 females, age 24-29 (average age 26.1) with BMI in the accepted normal range of 18.5-25 volunteered to participate in the study. All were recreational users of marijuana and alcohol with "low" to "moderate" use of marijuana (smoking 1–4 times per month). Most reported smoking and drinking mainly on social occasions or during the weekends. All subjects signed a consent form as approved by the institutional review board (Helsinki committee) and tested positive for metabolites of THC in the urine prior to the beginning of experimental sessions.

2.2. Laboratory settings

A STI-SIM fixed-based driving simulator (Systems Technology, Inc.) that was integrated into a passenger car, provided the driver with the look and feel of driving a real car. More details about the vehicle and the simulator are provided in Ronen et al. (2008). The road scenarios, non-driving task, and most of the subjective measures were unique to this study and they are detailed below.

2.3. Road scenarios

For each experimental session, two driving scenarios were used:

1. The "Baseline" scenario. This scenario was used to obtain baseline physiological measures, prior to the planned treatment. It was composed of a mostly straight road with a few curves and low traffic volume. Subjects were instructed to drive for 10 minutes and maintain a speed limit of 55 mph.
2. The "Main" scenario was a 23.4 miles long road consisting of three segments. The order of the three segments was counterbalanced with a different order for the orientation session and

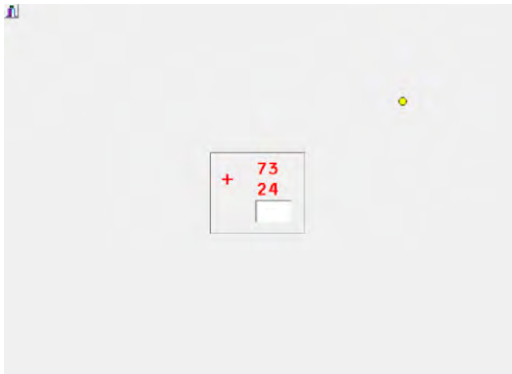

Fig. 1. A picture showing the non-driving tasks.

for each of the five experimental sessions. The order of segments was also counterbalanced across subjects. The segments were:

- 9.2 miles long, monotonic rural road of a flat terrain, mostly straight with a speed limit of 55 mph. The segment contained 5 unexpected events, of which 3 were 4-way intersections with a yield sign. On one of these, the driver had to slow down in order to avoid colliding with an approaching car. The location of the approaching car was counterbalanced across experiments. The other two unexpected events were two pedestrians: one crossing the road and one walking along the road.
- 7.5 miles long road rural road with a few sharp curves and with a speed limit of 45 mph. This segment was designed to simulate driving in foggy conditions and it contained 3 unexpected events. The first and last 2.25 miles sections were foggy and the 1.5 mile section between them was clear. Each foggy section had one unexpected event. A crossing pedestrian and an approaching car that swerved into the driver's lane. The order of events was counterbalanced across sections and experimental sessions for each subject. In the non-foggy segment a road block was placed in the middle of the road.
- 6.7 miles long, mostly downhill rural road with few moderate and few sharp curves with a speed limit of 45 mph. In two different locations, two unexpected events occurred. One was an approaching car that swerved into the driver's lane and the other was a pedestrian crossing the road. The order of events was counterbalanced across experiments for each subject.

2.4. Driving performance measures

The following driving performance measures were collected during each experimental session:

- Root mean square (RMS) of the lane position (in ft)
- RMS of the speed (in miles/h)
- Average speed (in miles/h)
- RMS of the steering wheel deviations (in degrees)
- Number of collisions

2.5. Non driving divided attention task–arithmetic calculations and target detection

For the non-driving task a simple, double-digits, addition or subtraction arithmetic task was used combined with visual target detection. Each exercise was presented at the middle of the screen (as shown in Figure 1) for a maximum of 7 seconds. Two seconds after entering their response or if the 7 seconds of the time given had passed with no response, a new exercise was presented. Subjects were instructed to solve as many exercises possible in the 5 minutes given to the task.

While performing the main arithmetic task, in a secondary reaction time task subjects had to respond as quickly as possible, by pressing a key in the keyboard, whenever they saw a yellow dot on the screen (as shown in Figure 1). This dot, presented in a random location on the computer screen, was 0.12 cm in diameter and increased in size by 0.08 cm every 3 seconds. Immediately after pressing the key, the dot disappeared, and 3-10 seconds later a new dot appeared.

2.6. Performance measures of the non-driving task

The following measures were obtained:

- Total number of exercises completed
- Percentage of success in the arithmetic task (relative to the number of exercises completed)
- Number of exercises with no response
- Average reaction time to the secondary task (sec)
- False recognition of the secondary task (pressing the key when no dot appeared)

2.7. Questionnaires for subjective feelings after intake

A few questionnaires were used to collect information about the overall perceived effect of each treatment (using visual analog scales - VAS) and about specific effects relating to driving (SOFI, Willingness to drive).

- General perceived effects of the drugs was measured using two subjective questionnaires (Wachtel, et al. 2002). A series of visual analog scales (VAS) and a drug effects questionnaire (DEQ) were used. Subjects were asked to respond to each question/statement according to their sensation after intake. The VAS consisted of six scales on which subjects indicated their feeling about an adjective ranging from "not at all" to "extremely". The six adjectives were: "stimulated", "high", "anxious", "sedated", "down" and "hungry". Based on the study of Wachtel et al. (2002) the DEQ consisted of four questions to which subjects responded by marking the VAS. The questions were: To what extent do you feel the drug effects (with the scale ranging from "none at all" to "a lot")? To what extent do you like the effects of the drug (with the scale ranging from "don't like at all" to "like very much")? How high are you (with the scale ranging from "not at all" to "very much")? Would you like to smoke more of what you just smoked (with the scale ranging from "not at all" to "very much")? The questionnaires were given three times in each experimental session.
- To obtain information about willingness to drive after intake, subjects were asked "At this moment after drinking and smoking, what is the maximum distance you would be willing to drive under the following conditions?". For each question they had to circle one of the four distances of 0, 4, 16, and 64 km. Subjects were asked to mark their response about their willingness to drive after intake in three different situations ranging from not urgent to very urgent, according the conditions used by Robbe (1994) for testing willingness to drive after smoking marijuana cigarettes. The statements were: 1) "I would be willing to drive for 0/4/16/64 Km when the reason is unimportant but gratifying, such as driving to a friend or to a party", 2) "I would be willing to drive for 0/4/16/64 Km when the reason is important but there is another option such as when taking a sick friend home when he would otherwise call a taxi", 3) "I would be willing to drive for 0/4/16/64 Km when the reason is urgent like driving a sick baby to an hospital.

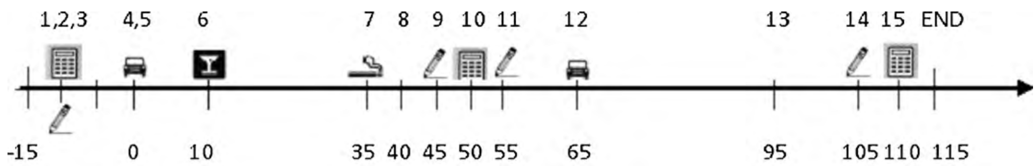

Fig. 2. Stages and timeline of each experimental session as detailed in section 2.6. The time (minutes) shown is calculated according the time from the beginning of the "Baseline" driving.

As in the previous study (see Ronen et al., 2008), to evaluate the fatigue effects we used the Swedish Occupational Fatigue Inventory-20 (SOFI-20) (Ahsberg et al., 2000), that evaluates fatigue in terms of sleepiness, lack of energy, lack of motivation, physical discomfort, and physical exertion.

2.8. Study protocol

Each subject attended the lab for an orientation session before the experimental sessions began. During this session subjects were asked to *sign all the consent* forms, fill out questionnaires, smoke a placebo cigarette, and perform the driving ("Baseline" and "Main") and non-driving tasks. As in the previous study (Ronen et al., 2008), subjects were asked to abstain from drinking more than a glass of an alcoholic beverage a day and to abstain from smoking marijuana for at least a week prior to the experimental sessions, and then continue to refrain from smoking marijuana for the duration of the study. In the experimental sessions, all subjects were tested after a full night sleep and a light breakfast. To avoid variations due to circadian rhythm, all sessions took place between 9:00 am and 14:00 pm, 3–7 days apart.

2.9. Treatments and experimental sessions

The study included five experimental sessions for each subject using five different treatments. Experimental sessions were within subjects, blind and counterbalanced across subjects. Experimental sessions included the following treatments:

1. Alcohol ("Alc"): drinking alcohol mixed with orange juice to reach a level of 0.05% BAC, and smoking placebo cigarette.
2. THC ("THC"): drinking orange juice and smoking a cigarette containing 13 mg THC.
3. THC + Alcohol ("THC + "): drinking alcohol mixed with orange juice to reach a 0.05% BAC and smoking a cigarette containing 13 mg THC.
4. "24" - This treatment was identical to the placebo but was always used twenty-four hours after the combination of THC and alcohol); thus it consisted of drinking orange juice and smoking placebo cigarette.

2.10. Procedure in each experimental session

Each of the experimental sessions consisted of the same stages in the same order as follows:

1. Admission to the lab
2. Filling out the SOFI questionnaire about their state of fatigue at the time of admission
3. Practicing the non-driving task for 5 min.
4. Connecting the driver to the physiological monitoring device.
5. Driving the "Baseline" scenario for 10 min
6. Ingesting an alcoholic or placebo beverage.
7. Verifying that BAC is 0.05% and smoking a THC or placebo cigarette according to smoking protocol.
8. Continuing the physical monitoring for additional 5 min, after smoking.
9. Filling out the VAS, DEQ and Willingness to drive questionnaires (1nd time)
10. Performing the non-driving task for 5 min.
11. Filling out the VAS and DEQ, Willingness to drive questionnaires about perceived effects of the treatments (2nd time).
12. Driving the "Main" scenario for about 30 min, depending on the actual driver speed.
13. Resting for 10 min in the car simulator.
14. Filling out the Willingness to drive, VAS and DEQ and SOFI questionnaires (3rd time).
15. Performing the non-driving task for 5 min.

The sequence of each experimental session and timeline of the activities is illustrated in Figure 2.

2.11. Alcohol and THC cigarettes administration

Alcohol and THC cigarette administration was conducted according to the same protocol used by Ronen et al. (2008)

2.12. Data Analysis

All experimental sessions were designed as a within-subject, blind, counterbalanced sessions. This resulted in very few cases of missing data, mostly due to technical failures.

For each outcome variable (for example in the driving measures four variables were used: RMS speed, RMS lane position, RMS steering deviations, average speed), we performed one-way or two–way ANOVA (depending on the variables tested) with repeated measures within the framework of Linear Mixed Model (LMM) in order calculate overall significance for each variable under the different treatments. After the ANOVA was performed, in cases where the ANOVA was significant, a post-hoc analysis was conducted to identify the source of significance for the different categories (treatments) as detailed in the text of the Results section.

Statistical significance was defined at $\alpha = 0.05$.

Changes in heart rate were calculated relative to the heart rate during the baseline drive (100%). These changes were calculated for four periods during each experimental session: first part of the drive ('Drive 1′), second part of the drive ('Drive 2′), third part of the drive ('Drive 3′) and the recovery period after the drive ('Recovery').

3. Results

3.1. Driving performance measures

3.1.1. Number of collisions

A total of 11 collisions occurred during the 60 experimental sessions (18.3%) as shown in Table 1. Five of the 12 subjects had a collision while under the influence of alcohol combined with THC + , 3 subjects out of 12 had a collision under the influence of THC alone, and 2 subjects out of 12 had a collision under the influence of alcohol alone at the level of 0.05% BAC. None of the subjects had a collision under the placebo treatment even though the driving

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

	Placebo	Alcohol	THC	THC + ALC	24 after
Total number of collisions	0	2	3	5	1
Number of drivers involved	0	2	3	5	1

scenarios consisted of the same segments and elements as all the other experiments.

3.1.2. Vehicle control measures

There were significant main effects of the treatment on two of the vehicle control measures: steering wheel variability (RMS) ($F(4, 3.07)$, $p = 0.026$), and lane position variability (RMS) ($F(4, 2.85)$, $p = 0.035$). Treatment had a borderline significance effect on average speed ($F(4, 2.342)$, $p = 0.07$) and no effect on speed variability (RMS) ($F(4, 1.915)$, $p = .125$).

As shown in Figure 3, post-hoc pair-wise comparisons revealed that on all the vehicle control measures there were no differences between placebo sessions and “24” hours post-treatment sessions (i.e., 24 hours after intake of alcohol combined with THC). Alcohol caused subjects to drive significantly faster compared to sessions with THC alone ($p = 0.015$), and the effect was borderline significant ($p = 0.067$) when the THC was combined with alcohol. In contrast, smoking THC cigarettes caused subjects to drive slower in general and significantly slower than in the “24” hours session ($p = 0.024$).

Both, alcohol alone and in combination with THC caused a decrease in subjects’ ability to keep the steering wheel steady. With both treatments RMS of steering wheel was significantly higher than in the 24 hours post-treatment session, with no difference between alcohol alone and the combination sessions.

Lane position variability increased significantly under the joint effects of alcohol and THC relative to the other treatments which did not differ from each other, as shown in Figure 3.

3.2. Performance on primary and secondary tasks in a non-driving situation

In these tasks, a LMM design with two factors was used to test for treatment and time effects and their interaction (as task performance was measured twice during each experimental session, before the drive and after the drive). None of the interactions for Time and Treatment were significant both for the main non-driving task and for the secondary task.

3.2.1. Non driving main task–Arithmetic task

There were main effects of treatment and time on most of the dependent measures, as shown in Figure 4. The number of exercises completed during each experimental session is a reflection of the reaction time to each exercise during the time the arithmetic task was performed. In general, the quicker the subject responded the more exercises he or she completed in the 5 minutes allocated to this task. Treatment ($F(4, 4.087)$, $p = 0.04$) and Time ($F(1, 23.001)$, $p = 0.00$) both significantly affected the number of exercises completed. Post-hoc pair-wise comparisons revealed that these results were mostly caused by the effects of alcohol alone and in combination with THC, primarily during the first time the task was performed; with the effect of the combination of THC and alcohol also persisting during the second time the task was performed.

Percentage of success in the arithmetic task was significantly affected by treatment ($F(4, 4.975)$, $p = 0.001$) and time ($F(1, 8.250)$, $p = 0.005$) with no significant interaction effect. THC alone and the combination of THC and alcohol reduced the percentage of success in the arithmetic exercises as revealed by post hoc pair wise comparisons; mainly during the first time the task was performed. The same pattern of effects persisted during the second time the task was performed but the treatment affects were smaller.

As detailed earlier (section 2.5), if a subject did not respond to an exercise after 7 seconds, another exercise was presented. Figure 4 shows the number of exercises with no response after each treatment. Treatment effect ($F(4, 4.241)$, $p = 0.03$) was significant and Time was borderline significant ($F(1, 7.873)$, $p = 0.06$) with their interaction not significant. In general the combination of alcohol and THC increased the number of exercises with no response throughout the experiment, as shown in Figure 4.

3.2.2. Non-driving secondary task performance

The combination of THC and alcohol, and alcohol and THC alone all caused a slight increase in reaction time to the secondary task, mainly in the period before the drive; resulting in a significant

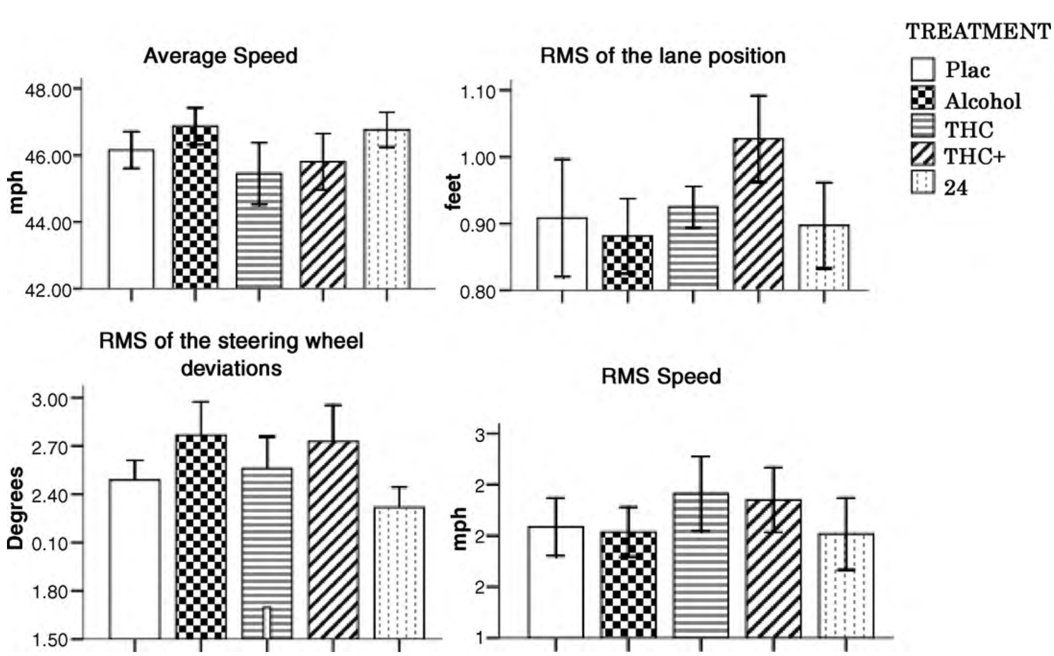

Fig. 3. Treatments effects on driving performance variables (mean ± S.E., $n = 12$).

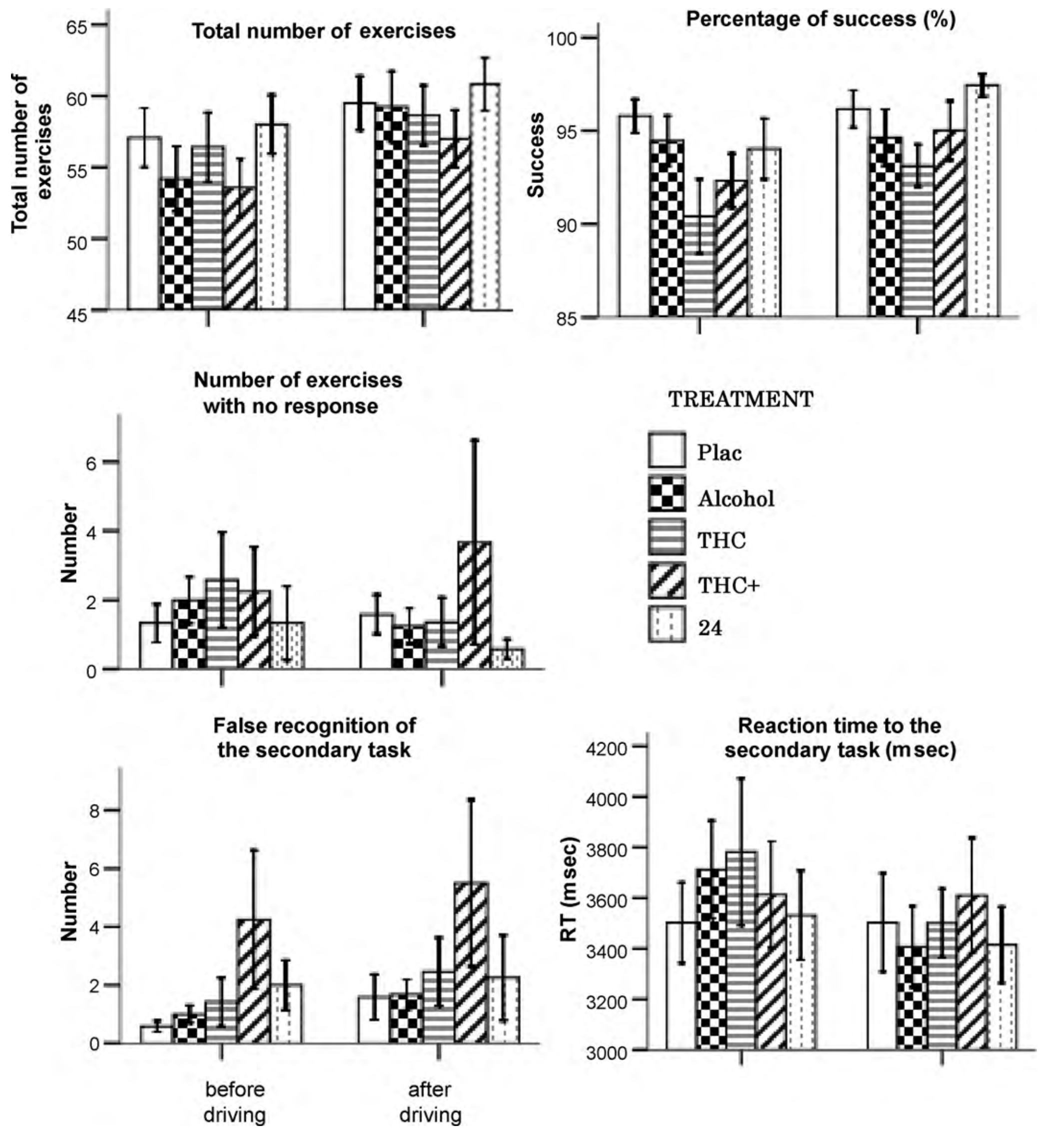

Fig. 4. Treatments effects on performance results of the non-driving (arithmetic task) and secondary task (mean ± S.E., *n* = 12).

time effect ($F(1,6.371)$, $p = 0.013$) but with no treatment ($F(4,0.783)$, $p = .539$) or interaction effect, as shown in Figure 4.

Treatment effect was also manifest in the target detection task in a significant increase in false reactions and pressing the computer key in the absence of a dot ($F(4, 3.720)$, $p = 0.007$). The effects of the Time ($F(1,1.985)$, $p = 0.162$) and the interaction were not significant. The combination of alcohol and THC was the most prominent in both periods before and after the drive.

3.3. *Subjective effects*

3.3.1. *Visual Analog Scales (VAS) results*

Out of the six adjectives (“stimulated”, “high”, “anxious”, “sedated”, “down” “hungry”) four were significantly affected by the Treatment: “high” ($F(4, 62.57)$, $p < .001$), “anxious” ($F(4, 4.91)$, $p = 0.01$), “sedated” ($F(4, 59.24)$, $p < 0.001$), and “hungry” ($F(4, 5.60)$, $p < 0.001$). Three had significant Time effect: “high” ($F(2, 3.37)$, $p = 0.037$), “sedated” ($F(2,3.08)$, $p = 0.049$) and “hungry”($F(2, 22.629)$, $p < 0.001$), and none had significant interaction effects, as can be seen in Figure 5.

The combination of alcohol and THC caused a significantly greater sensation of “sedation” in comparison to all other treatments. The combination of THC and alcohol followed by THC alone yielded a relatively high sensation of “high” and “hungry” (mainly after the drive) with no difference between them. Alcohol also caused a sensation of “high” and “sedation” but less than THC and THC combined with alcohol, as shown in Figure 5. Although the main treatment effect of “anxious” sensation was significant after intake of THC combined with alcohol and THC alone, the magnitude of this effect was relatively small level with an average scores ranging from 1 to 2 on a scale of 10.

3.3.2. *Perceived drug effects based on the DEQ*

Analysis of the four questions (“To what extent do you feel the drug effects?” (drug effect), “To what extent do you like the effects of the drug given to you?” (like the effect), “How high are you?” (high), “Would you like to smoke more of what you consumed?” (smoke more) revealed that intake of THC and alcohol and to a lesser extent THC alone and alcohol alone caused a relatively high sensation of the drugs that diminished throughout the course of the experimental sessions, as shown in Figure 6. There was a significant main effect of treatment ($F(4,104.4)$, $p < 0.001$) and time ($F(2,4.02)$, $p = 0.02$) on the magnitude of the sensation (feeling) of the drugs. It was significantly higher after intake of the combination of alco-

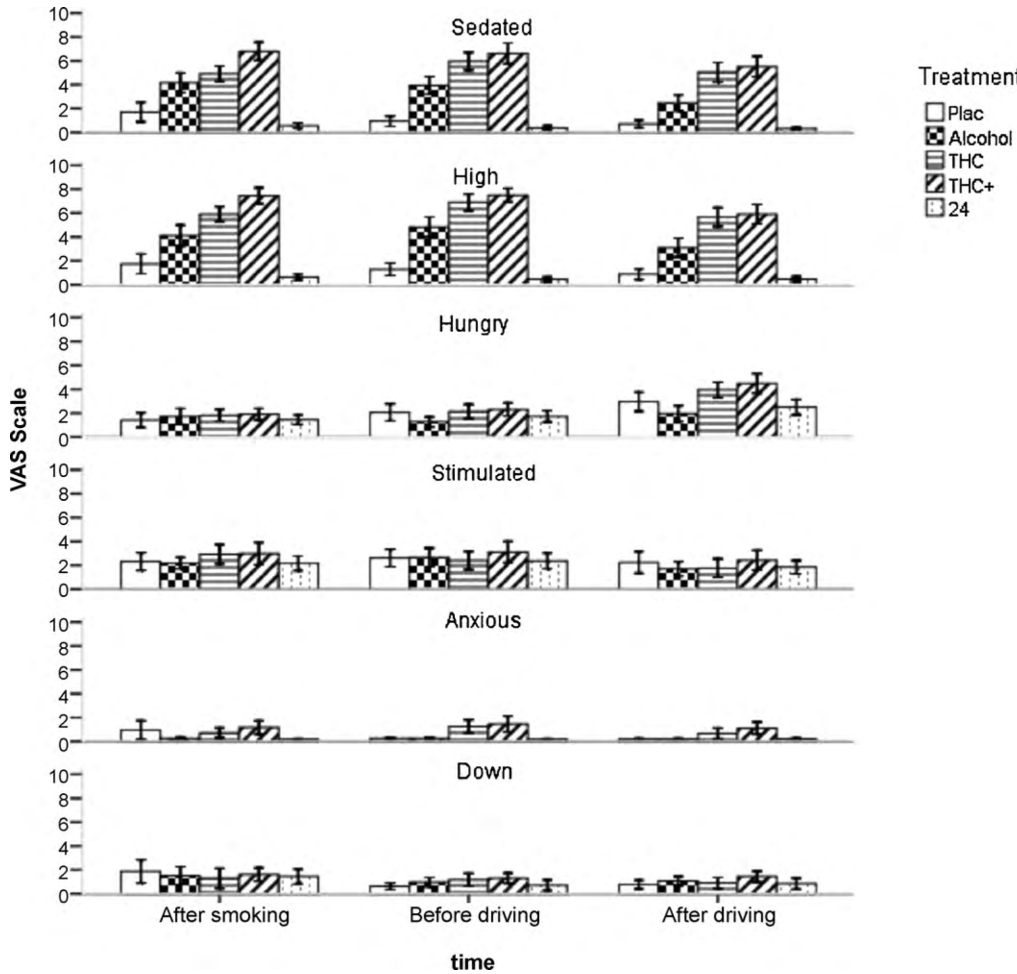

Fig. 5. Treatments effects on the subjective visual analog scale (VAS) questionnaire (mean ± S.E., $n = 12$).

hol and THC than after the other treatments. A significant main effect was also found on the extent of “High” sensation (F(4,70.04), p < 0.001) and on the extent that subjects liked the drug given to them (F(4,34.81), p < 0.001). Neither Treatment nor Time had significant effects on the desire of subjects to smoke more after the first intake.

3.3.3. Willingness to drive after intake

Treatment had a significant effect on the willingness to drive as shown in Figure 7. “when the reason is unimportant though gratifying”, under the influence of alcohol alone, THC alone and the combination of THC and alcohol. Subjects were willing to drive an average distance ranging of 5.85 - 7.08 km with no significant difference between treatments, compared to the “placebo” and the “24” sessions (F(4, 11.3), p < 0.00) with no significant time or interaction effects.,

“When the reason is important but there is another option” under the influence of alcohol alone, THC alone and the combination of THC and alcohol, subject were willing to drive an average distance of 7.54K - 10.362 km, compared to the “placebo” and the “24” sessions (F(4,21.5), p < 0.00), with no significant differences between treatments.

“When the reason is urgent like driving a sick baby to an hospital” under the influence of alcohol alone, THC alone and the combination of THC and alcohol, subject were willing to drive an average distance of 19.4 - 25.05 km, compared to the “placebo” and the “24” sessions (F(4,15.604), p < 0.00) with no significant difference between treatments.

3.3.4. Effects on the Swedish Occupational Fatigue Inventory (SOFI)

The combination of THC and alcohol had significant and intense effects on most of the SOFI dimensions as shown in Figure 8. This was true for “Lack of energy” (F(4,4.46), p = 0.004), “Physical exertion” (F(4,4.230), p = 0.006) and “Lack of motivation” (F(4,2.6), p = 0.049). The effect of the alcohol + THC combination on “Sleepiness” was borderline significant (F(4,2.51), p = 0.055). The only dimension that was unaffected by the treatments was “Physical discomfort” (F(4,1.03), p = 0.403). Post hoc analysis revealed that alcohol alone caused a significant greater “Lack of motivation” compared to “24” sessions (p = 0.032), and that THC alone had a significant effect on “Physical exertion” compared to “24” sessions (p = 0.042).

3.4. Physiological reactions - heart rate

Treatment (F(4,127.289), p < .001), Time (F(3,17.862), p < .001) and the interaction between them F(12,3.345), p < .001) all had significant effects on heart rate. Pair-wise comparisons revealed that at the beginning of the drive (drive 1) relative heart rate was significantly higher after THC alone and with its combination of alcohol than in all other treatment, with no differences between them. During the course of the drive the difference in heart rate between THC alone and THC combined with alcohol increased until it became significant in the last part of the drive and in the recovery (rest) period where the combination of THC and alcohol yielded a higher heart rate than THC alone. During the rest period, heart rate was

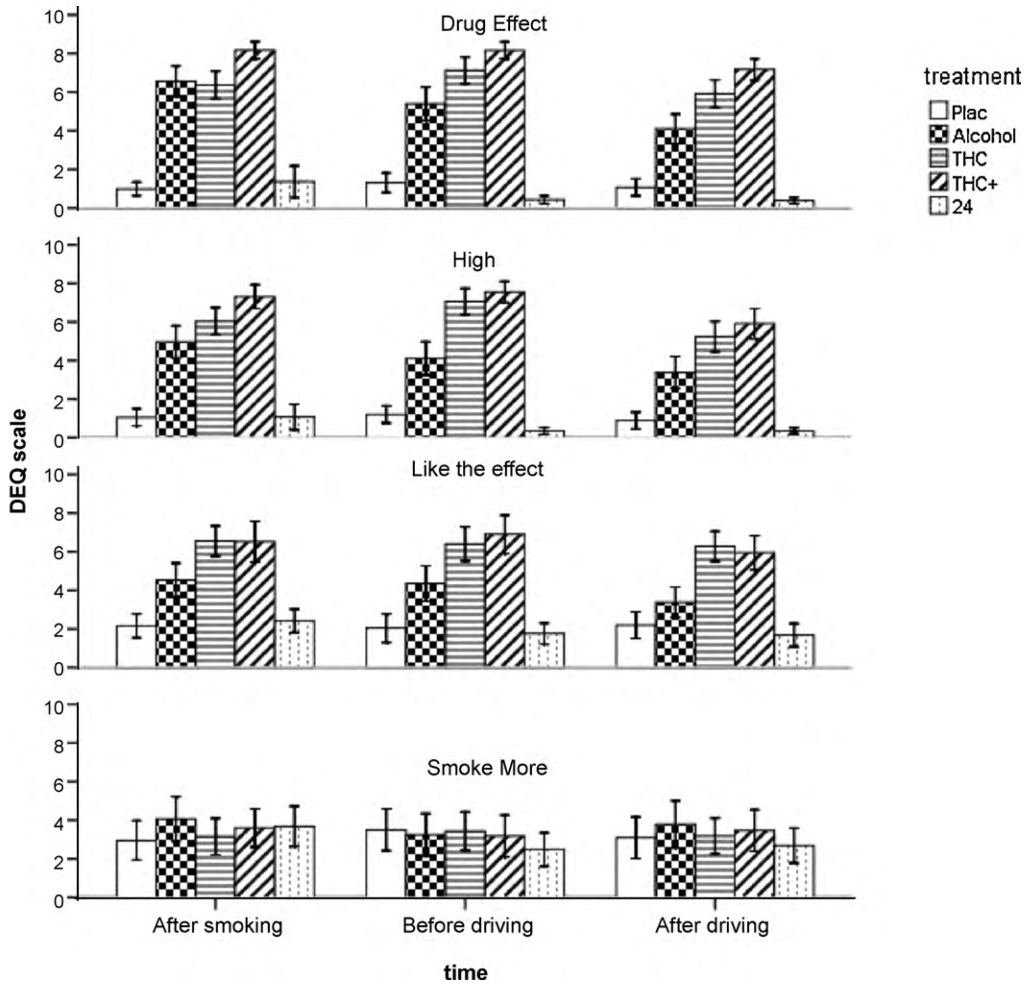

Fig. 6. Treatments effects on the subjective drug effects questionnaire (DEQ) (mean ± S.E., $n = 12$).

also higher at the end of alcohol alone sessions than at the end of the placebo sessions. The significant Time effect was primarily due to the decrease of heart rate during THC sessions (alone and with alcohol) as shown in Figure 9.

4. Discussion

This comprehensive study adds essential empirical data to one of the most problematic issues related to driving under the influence of alcohol and marijuana using variety of subjective, physiological and performance measures. Overall results of the subjective questionnaires indicated that subjects felt that the combination of THC and alcohol was the most potent treatment and seemed to have an additive effect on some of the subjective sensations relative to the effects of the two drugs alone. In questions with visual analog scales (VAS), the combination of alcohol and THC caused a significantly greater sensation of "sedation" in comparison to all other treatments. The combination of THC and alcohol followed by THC alone yielded a relatively high sensation of "high" and "hungry" (mainly after the drive) with no difference between them. The drug effects questionnaire (DEQ) also showed similar sensitivity to the treatments: the combination of the two drugs yielded a relatively high sensation of "drug effect", significantly higher than in all other treatments. The effects on other dimensions of the questionnaire like feeling "high" and liking the effect of the drug were significantly greater after THC (alone and when combined with alcohol) than after the placebo, "24", and alcohol alone. Overall, there were no differences between placebo and the "24" session that followed the THC combined with alcohol session. Curran et al. (2002) tested the acute effects of oral intakes of 7.5 mg and 15 mg THC and found a significant dose effect of the drug, with an increase in liking the drug, feeling "stoned" and feeling the effect of the drug.

In the present study alcohol alone also affected the various sensations related to drug effects (compared to the placebo and "24" sessions) but to a lesser extent than the THC (with or without alcohol). These findings are similar to those of Ramaekers et al. (2000), who also found that subjects reported stronger feelings of intoxication after alcohol or THC intake compared to placebo, and higher sensations of intoxication after combining alcohol with low and high THC. They also found that at the end of their tests the mean ratings of intoxication were at about half the initial level. In the present study, a significant decrease in the sensation of the drugs was also observed during the course of sessions as can be expected, mainly due to the relatively fast decay of the THC effects. The combination of THC and alcohol caused similar significant effects as alcohol on other dimensions of the SOFI, such as sleepiness, physical exertion, and lack of motivation. These results corroborate our previous findings (Ronen et al., 2008) that showed stronger feelings of sleepiness, physical effort, and lack of energy following smoking THC. Robbe (1998) findings that the perceived effort to accomplish a driving task increased significantly after smoking marijuana but not after drinking alcohol are consistent with our results. Our results also showed that the subjective sensations mirrored the physiological changes. Usually, smoked THC has a relatively fast effect on mood with quick elevation of plasma concentration after smoking and a

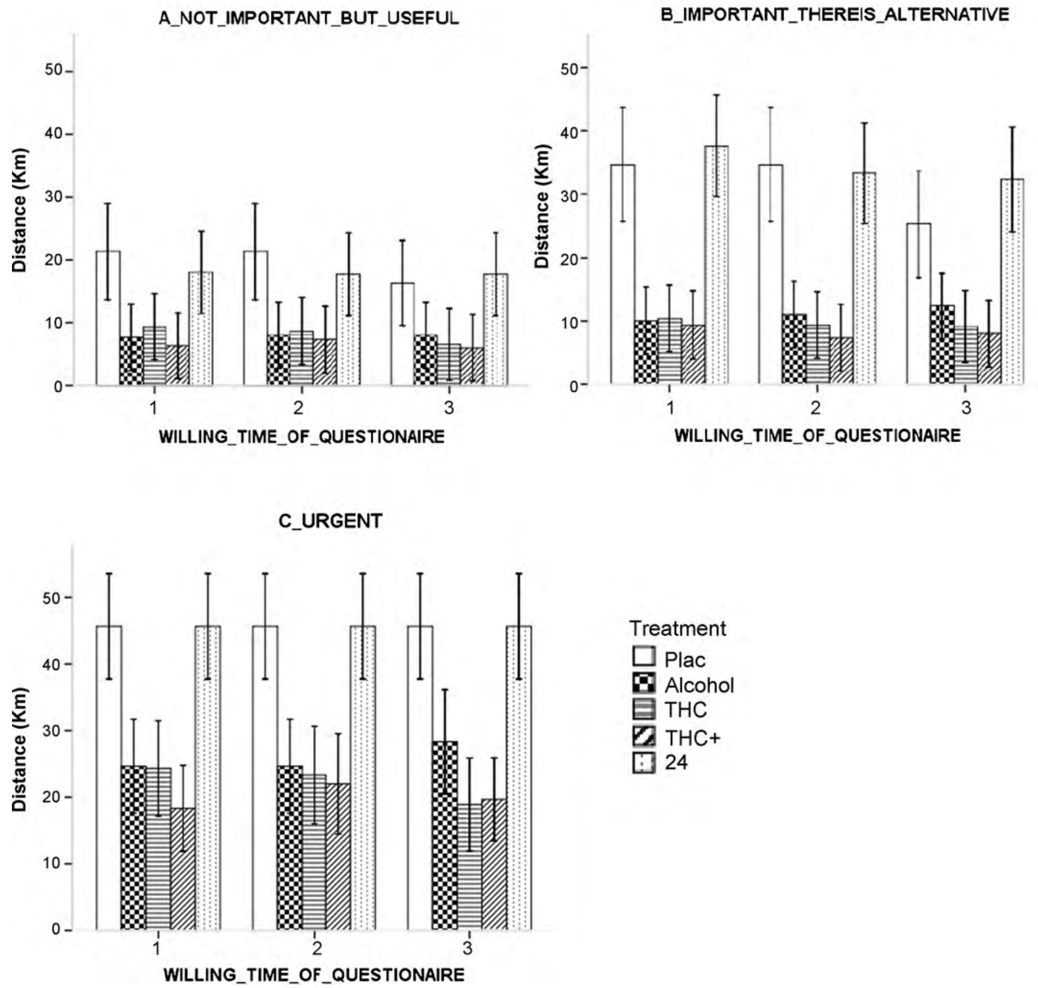

Fig. 7. Treatments effects on the average distance subjects were willing to drive after intake (mean ± S.E., $n = 12$).

relatively fast decline over time (Perez-Reyes et al., 1982). This time and intensity effect of THC alone and in combination with alcohol was clearly reflected in our physiological recordings. Heart rate acceleration, which can be used as an indicator for THC absorption (Kanakis et al., 1976; Schaefer et al., 1975; Perez-Reyes et al., 1982; Ronen et al., 2008) was significantly greater after ingestion of the THC than after ingesting the placebo or alcohol. The decline over time from the initial high heart rate at the beginning of the drive was more apparent during THC alone sessions than in the sessions when THC was combined with alcohol, leading to a significant difference between the two treatments by the end of the drive when heart rate remained higher after administration of the combination than after the THC alone. This difference was probably due to the relatively longer-lasting physiological effect of alcohol compared

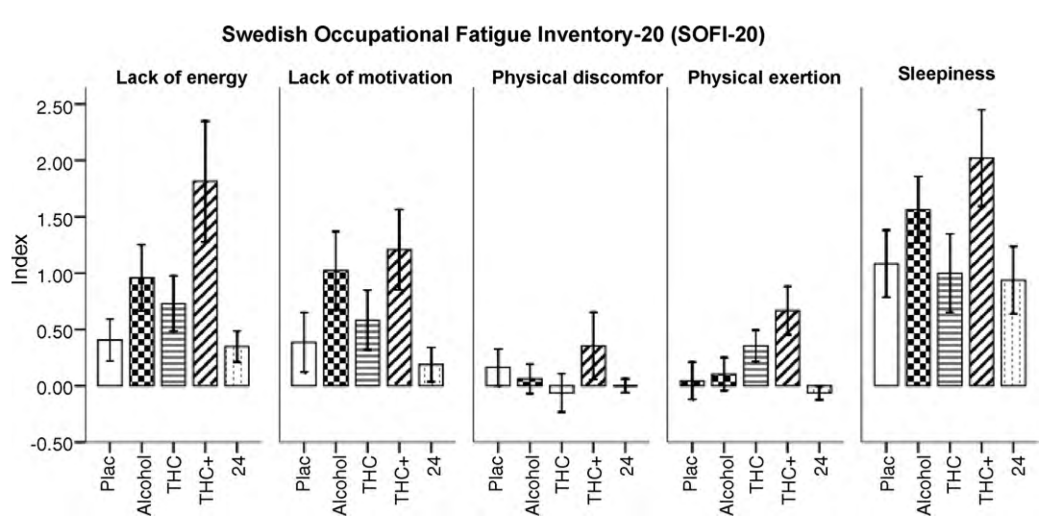

Fig. 8. Differences in the subjective feelings between the end and beginning of each session on the five SOFI dimensions (mean ± S.E., $n = 12$).

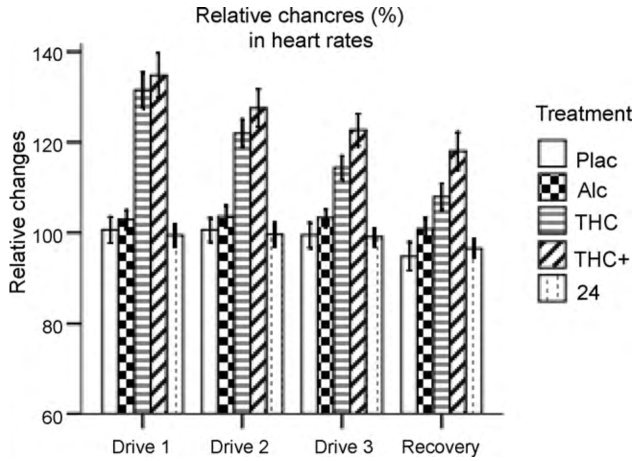

Fig. 9. Relative changes (%) in heart rates (mean ± S.E., $n = 12$) compared to the "Baseline" drive at each individual experimental session prior to treatment.

to THC. Alcohol is also known to elevate heart rate (Moravi et al., 1988) and may lead to sensations of fatigue and sleepiness over time. These effects were reflected in the results of the SOFI (2000) questionnaire that revealed greater levels of lack of energy after the drive during sessions in which the combination of alcohol and THC were administered, compared to all other sessions.

Although subjective and physiological results indicated a difference between the treatments, we did not find any difference between them in terms of the distance drivers were willing to drive. The only effect we observed was a general increase in the driving distance subjects were willing to drive as the urgency of the drive increased. Robbe (1994) found that after alcohol or marijuana, significantly more subjects were willing to drive when the reason was urgent compared to when the reason was described as unimportant. Since the present experiment was conducted in the lab under supervision, it is likely that in real life, where there is no supervision and the motivation to drive may be higher, the percentage of drivers who would risk driving under the influence of alcohol or THC might be higher. Our results also imply that although our subjects clearly felt the effects of the drugs, they assumed that they can adjust their driving according to their condition and perform well enough to complete the drive safely. Robbe (1994) concluded that drivers under the influence of alcohol tend to underestimate the adverse effects of alcohol on driving and do not invest compensatory effort. In contrast, while under the effects of marijuana drivers tend to overestimate the effect of the drug and compensate whenever they can.

In general, the effects on performance were consistent with the effects observed on the physiological and subjective measures. Subjects were generally impaired under the influence of the drugs with the highest impairment observed after intake of the combined alcohol and THC. In terms of vehicular control, five out of the twelve subjects that participated in the study had a collision while under the influence of the combination of alcohol and THC, three had collisions after smoking THC alone, and 2 had collisions after drinking alcohol alone. None had collisions during the placebo or "24" sessions. In addition, our results on vehicle control showed that the combination of alcohol and THC had the most significant effect, elevating lane deviations relative to placebo, alcohol, and "24" sessions. We also found that the combination of THC and alcohol caused an increase in steering wheel deviations to the same extent as alcohol alone, but THC alone did not cause such impairments. Ramaekers et al. (2000) also found that the effects of the combination of THC and alcohol were more severe than the effects of the two drugs alone. As in our previous study (Ronen et al., 2008), when THC alone was administered, subjects drove significantly slower than when they were under the influence of alcohol, which actually made them drive faster. This is consistent with Robbe (1998), which according to his findings noted that they support the belief that drivers become overconfident after drinking alcohol but may become more cautious and self critical after consuming small amounts of marijuana. Lenne et al. (2010) also found that performance following inhalation of cannabis was associated with increase of headway and decrease in mean speed while alcohol at the low levels studied in their experiment (0.02 and 0.05 BAC) had fewer effects including a slight increase in mean speed. Overall the sensitivity of the different driving variables to THC (when taken alone) was less than in our previous study. This may be due to the fact that in the present study we used a more demanding driving environment consisting of more unexpected events and more difficult road conditions like fog and intersections. These conclusions are supported by the results of previous studies that showed that relatively complex driving tasks that required conscious–higher level - control are less affected by THC than automated behaviors (Ramaekers et al., 2004). Kerr & Hindmarch (1998) in their review of the effects of alcohol alone or in combination with other drugs on information processing concluded that the more complex the task, the more likely it will be affected by small doses of alcohol.

As might be expected from the separate effects, under the combination of THC and alcohol speed was not significantly different than in the placebo sessions; probably because the two drugs counteracted each other. Sewell et al. (2009) noted that marijuana smokers tend to compensate effectively by utilizing variety of behavioral strategies but combining marijuana with alcohol eliminates the ability to use such strategies effectively and performance is then impaired.

Performance on the non-driving primary and secondary tasks generally also correlated with the physiological and subjective perceptions of the drug effects; with the combination of alcohol and THC causing the greatest overall impairment which decreased over time. In the primary arithmetic task, under the influence of the two drugs combined, subjects completed fewer exercises with significantly lower percentage of success. In the secondary detection task the THC and alcohol resulted in an increase of false alarms, mostly towards the last part of the session. THC and alcohol separately also impaired performance, as alcohol–with and without THC - caused subjects to solve fewer exercises under the time limitation. THC alone caused significantly lower percentage of success in solving the arithmetic exercises. Similarly, Heishman et al. (1997) found that alcohol (10–90 mg/dl) and marijuana (63–188 ng/ml) produced comparable impairment in digit-symbol substitution and word recall tasks but the drugs did not affect time perception and reaction time.

Generally there were no residual effects of THC and alcohol after 24 hours. Previous studies (Curran et al., 2002; Ronen et al., 2008) also did not indicate any residual effects observed 24 hours after intake of THC.

In conclusion, the results indicated that the overall effect of the combination of THC and alcohol had greater effects and caused more impairments than the two drugs separately. Despite the fact that the subjects could clearly feel the effects of alcohol (0.05% BAC) or marijuana (THC in this study, 13 mg) - despite the blind design–they were still willing to drive under the influence. It seems that the only consideration that affects the drivers' risk taking is not the drug effects but the urgency of the drive This is also despite the fact that the drugs impaired both driving and non-driving performance. Thus, despite real and perceived impairment, it is likely that even in real life people under the influence would be willing to expose themselves to hazardous situations in driving.

Study limitations:

Although the protocol of this study was carefully kept, few limitations should be mentioned:

- We asked subjects to abstain from drinking or smoking for at least a week prior to the beginning of the experimental sessions and between the experimental sessions. Subjects were reminded of that throughout the experiment and were asked to sign a consent form stating that they will behave accordingly. As detailed in the method section, during each session a physiological and performance baseline was used in which we did not find any trace of the drugs or any other abnormalities that could be attributed to recent drug use. Thus, we have a good reason to believe that although the subjects were not under constant monitoring the protocol was adhered to. In any case, in our within subjects design, each subject served as his/her own control for all baseline measurements.
- In studies investigating the effects of an alcohol drink compared to a placebo it is customary to try different ways to disguise the placebo. However, there is not an agreed upon placebo to alcohol drinks that totally fools subjects. This is true, especially when the alcohol drink contains a significant amount of a strong beverage like vodka. Regardless, this issue should have no effect on our findings because in our within-subject design the main goal was to compare the effects of alcohol combined with THC to the effects of each drug alone, and the drug administration protocol was the same during all sessions.

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