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ORIGINAL ARTICLE

On the impact of cannabis consumption on traffic safety: a driving simulator study with habitual cannabis consumers

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Abstract

To contribute to the ongoing discussion about threshold limits of Δ9-tetrahydrocannabinol (THC) in road traffic, a driving simulator study with 15 habitually cannabis consuming test persons was conducted. Probands were tested on different routes after consumption of a maximum of three cannabis joints, each containing 300 μg THC/kg body weight (sober testing as well as testing directly, 3 and 6 h after cannabis consumption). Accompanying the drives, medical examinations including a blood sampling were performed. Driving faults and distinctive features in the medical examinations were allocated certain penalty points, which were then summed up and evaluated using the ANOVA model. The results showed that very high CIF values > 30 as well as serum THC concentrations > 15 ng/ml significantly increased the number of penalty points, but no direct correlation to the THC concentrations in serum and/or CIF values was detected. Instead, the point in time after cannabis consumption seems to play an important role concerning driving safety: significantly more driving faults were committed directly after consumption. Three hours after consumption, no significant increase of driving faults was seen. Six hours after consumption (during the so-called subacute phase), an increase of driving faults could be noted although not significant. Considering the limitation of our study (e.g. small test group, no placebo test persons, long lasting test situation with possible tiredness), further studies focusing on the time dependant impact of cannabis consumption on road traffic are required.

Keywords Cannabis · THC · Driving simulator · Road traffic · Safety to drive · Impairment · Subacute phase

Introduction

Cannabis is the most frequently consumed illicit drug with a rising worldwide market [1, 2]. According to the Word Drug Report, about 192 million people have consumed cannabis at least once in 2016 [2]. With recent political changes, cannabis is increasingly being legalized or at least decriminalized for medical and recreational use in many countries. Alongside, the number of people driving (partially legally) under the influence of cannabis increases [2, 3], emphasising the need to find and define adequate guidelines on when cannabis-induced impairments are likely to endanger the road safety and how to deal with drivers proven to be impaired.

Several studies have previously covered the issue of driving under the influence of cannabis and followed epidemiological as well as experimental approaches (e.g. reviews [4–6]). As the study designs vary significantly, the findings are difficult to compare and sometimes seem to contradict each other [3, 6–8].

According to previous experimental and epidemiological studies, a recent intake and/or high blood Δ9-tetrahydrocannabinol (THC) concentrations are associated with relevant effects on cognitive and motor functions likely to cause driving impairments and an increased crash risk (e.g. [5–10]). In this context, the findings of experimental studies have often suggested a higher impact or crash risk than found in epidemiological studies [7, 11], which have often shown no or only slightly increased relative risks of being involved in a severe accident [1, 3, 7]. Besides the different study designs, another

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explanation given for these inconsistencies is the fast elimination of THC from the blood [11], hindering non-experimental studies in which the blood withdrawal usually takes place with relevant delay to the actual driving. The results of experimental studies are often considered to underestimate the risk of driving under the influence of cannabis as well, as drivers are presumed to be aware of their impairment, causing them to adapt their driving habits and therefore (partially) compensate their deficiencies—at least in a test situation [3, 4, 6, 9].

Although detrimental effects seem to be dose-related, they were shown to vary significantly between individuals, especially when compared to the effects of alcohol [3, 6–8, 10, 12, 13]. Heavy regular consumers tend to have detectable THC in their serum, even in an abstinent phase in which no impairments are to be expected [3, 4]. The CIF (cannabis influence factor) has been introduced in order to approach this problem by taking into account not only the THC concentration but also the concentrations of the metabolites THC–OH and THC–COOH [14]. Values > 10 are claimed to indicate an acute or subacute phase of cannabis elimination [12, 14, 15], while values > 30 to indicate a recent intake [12, 16]. When calculating the CIF as a quotient of the concentrations of THC and THC–OH divided by THC–COOH, it should be taken into account that occasional users typically have higher CIF values after smoking cannabis as compared to chronic users (due to higher levels of THC–COOH in their blood caused by accumulation processes). It is believed that the CIF value better describes the observation that after the same THC dose, the effects are more pronounced in occasional consumers than in chronic consumers [14]. Another advantage of the CIF value is that it is almost identical, regardless of the analysis of plasma or blood [16].

So far, no threshold limits for the absolute impairment to drive under the influence of THC could be established. The DRUID study (Driving Under Influence of Drugs, Alcohol and Medicines) suggested a THC concentration of 3.8 ng/ml in serum as this concentration is meta-analytically supposed to be equivalent to a blood alcohol concentration (BAC) of 0.5‰ [1]. Grotenhermen et al. have previously suggested a per se limit of 7–10 ng/ml THC in serum as this concentration would also avoid a possible misclassification of drivers presenting with THC residues from previous cannabis use [17]. However, several other studies have demonstrated that there is no direct correlation between serum THC concentration and driving impairments or any BAC [3, 4, 8, 9, 12, 14].

Up to now, several important questions regarding the fitness of drivers after cannabis consumption remain open. It has been suggested by other authors that drivers are prone to driving impairments and an elevated risk of traffic accidents not only in the acute phase of THC elimination but also in the so-called subacute phase up to 6 h after the consumption as the own capability to drive is said to be overestimated [14, 18]. Studies explicitly focusing on this time dependent impact of heavy cannabis consumption have not yet been conducted sufficiently. Most study designs approach the question of driving impairments under the influence of cannabis by testing the participants directly after singular or multiple consumption units of cannabis, rather than testing at several points in time without renewed consumption.

We therefore performed a simulator study to assess the impact of cannabis consumption on the driving performance of test subjects that regularly consume cannabis at several points in time after a single consumption period.

Material and methods

Test persons

Fifteen regularly cannabis-consuming test persons were included in the study (12 males, 3 females). The test persons' average age was 25 years (median 24 years). The mean age of the male test persons was 26 years and ranged from 21 to 41 years (median 25). The female test persons were 19, 22, and 22 years old. The regularly consumed amount of cannabis varied between < 1 g and 7 g per week.

Inclusion and exclusion criteria

In order to participate in the study, all test persons had to be at least 18 years old, have signed the consent form and had to be in possession of a valid driver's licence (however, a loss of the driver's licence in the past due to cannabis consumption was not an exclusion criterion). They had to have consumed cannabis at least twice per month within the past 6 months and were asked for 48 h of abstinence prior to the study. Additionally, they had to bring a health certificate stating that the test person does not suffer from any neurological or psychiatric illness, is not on central nervous system-active medication and is neither pregnant nor breast feeding (if appropriate). Another exclusion criterion was the use of other drugs than cannabis.

Not meeting one of the criteria above resulted in an exclusion from the study.

Experimental set-up

Prior to the start of the cannabis consumption, each participant was tested for breath alcohol using a Draeger 6510 Breathalyzer and screened for any drug other than cannabis using a urine analysis (Multi-Drug Integrated E–Z Split Key Cup II; cocaine, amphetamine, methamphetamine, benzodiazepines and opiates). A medical examination including a blood sampling was carried out after each simulated drive. The medical assessment was carried out using the standardized field sobriety test (examination report for suspicion of driving under the influence of alcohol or drugs) which included the

following items: finger-to-finger-test, finger-to-nose-test, sudden turnaround while walking, walking straight ahead, evaluations of consciousness, speech, formal thought process, mood, subjective condition, pupils, pronator drift, standing on one leg and overall impression of the influence of cannabis. During the pronator drift, the test persons were asked to estimate a 30-s time span.

All test persons were asked to get accustomed to the driving simulator until they felt secure in handling it. After the first simulation drive ("sober"), which served as baseline, all participants were handed out a maximum of three cannabis cigarettes (joints) that were to be smoked in a 3-h time window. Shortly after the last joint was smoked, the second simulation drive was performed. The third and fourth simulation drives were performed approximately 3 and 6 h after consumption (Table 1). No further cannabis was consumed during the experiment.

Food and non-alcoholic beverages were provided at any time.

Provided cannabis and way of consumption

For the study, Dutch medical cannabis (Cannabis flos: Bedrocan, 22% dronabinol, < 1.0% cannabidiol; supplier: Dutch Ministry of Health, Welfare and Sport, Office of Medicinal Cannabis, P.O. Box 16114, NL-2500 BC The Hague) was imported with allowance from the German Federal Opium Agency (import authorization no. E 077/2017).

The cannabis was consumed by the participants in a standardized form via cigarettes: Each cigarette contained 300 μg of THC/kg bodyweight and was asked to be inhaled for up to 4 s before holding the breath for about 10 s. A maximum of three joints was provided for each participant.

Driving simulator and courses

The driving simulator used was a modified VW up! with automatic transmission placed in front of a large screen imitating the view through the front window and the rear mirror. The steering wheel and pedals were connected to the simulation shown on the screen. Each test person completed four different routes, each of which was run under similar conditions (sunny weather, daylight, city course) and was considered to be equally difficult according to the developer. Nevertheless, the routes varied especially in length, number of traffic lights and number of unforeseeable obstacles (Table 2). Each course included several unforeseeable obstacles, mainly in the form of pedestrians suddenly crossing the street or other cars ignoring traffic regulation (taking the participants' right of way, suddenly entering the road lane without signalling, running a red light, etc.). The participants' task was to finish driving as quickly as possible while still respecting all general traffic regulations. Prior to the actual test series, each participant practiced on a different route in order to minimize the risk of adjusting to the simulator throughout the study and therefore falsifying the results. Additionally, the participants were not allowed to watch each other's drives in order to eliminate habituation effects. The drives were recorded on videotape for further assessment.

Safety arrangements on the test area

The driving trials were carried out in a non-public area. The duration of the trials for each participant was approximately 12 h (noon to midnight). Medical care was in place throughout the entire study. After the trials, each test person was driven home and given into the care of another adult person.

Toxicological analyses

In analogy with previous studies [9, 12], fully validated gas chromatography/mass spectrometry (GC/MS) methods were used to carry out the toxicological analyses. Until analysis, the serum was stored in a fridge. For the analysis of cannabis, 20 μl of deuterated standard and 100 μl of isopropanol were transferred into a sample tube. Then, 0.5 ml of serum and 1 ml of acetonitrile were added, vortex mixed for 10 min and centrifuged for 10 min at 14,000×*g* at 10 °C. Next, 1.4 ml of the organic layer was extracted by solid-phase extraction and evaporated to dryness at 50 °C. The residue was reconstituted in 200 μl of isooctane/MSTFA (200/10) and derivatized at 90 °C for 30 min. One microlitre of the derivatized sample was then injected into the GC/MS system using single ion monitoring mode.

Evaluation

In order to objectify the results of the practical trials and the medical examinations, certain features or driving faults were allocated the following penalty points:

a) Medical examination:

- Finger-to-finger-test, finger-to-nose-test, sudden turnaround while walking: secure 0; insecure 1
- Walking straight ahead: secure 0; slowly 1; unsteady 2
- Consciousness: clear 0; dazed 1; confused 2; unconscious 3
- Speech: clear 0; slurred 2
- Formal thought process: without pathologic findings 0; accelerated, decelerated, adhesive, repetitive, erratic 1; confused, distracted 2
- Mood: balanced 0; nervous, distanced, introverted, depressed, excessively cheerful 1; provocative, aggressive, offensive 2

Table 1 Serum concentrations of THC, 11-OH–THC and THC–COOH, CIF values and time after consumption of the participants after each simulation drive: 1 = sober, 2 = directly after cannabis consumption (a.c.), 3 = approx. 3 h a.c. and 4 = approx. 6 h a.c. Penalty points for driving performance and style (weighted) at different points in time (1 = sober, 2 = directly after consumption (a.c.), 3 = approx. 3 h a.c. and 4 = approx. 6 h a.c.)

ID	Drive	Serum concentration (in ng/ml)			CIF	Time (in min)	Penalty points
		THC	11-OH–THC	THC–COOH			
1	1	0.8	0.2	12.0	0	0	1.9
	2	11.7	3.4	45.0	> 30	28	5.9
	3	2.8	1.2	30.0	14	185	12.3
	4	2.3	0.8	23.0	14	340	5
2	1	1.0	< LOD	17.0	0	0	2.9
	2	6.5	1.4	32.0	26	36	3
	3	2.2	0.8	28.0	11	171	0
	4	1.4	0.5	22.0	9	344	5
3	1	3.9	2.2	164.0	4	0	1
	2	41.9	14.3	192.0	> 30	43	6
	3	11.2	6.3	175.0	10	180	0
	4	6.0	3.8	161.0	6	353	1
4	1	0.7	< LOD	12.0	0	0	1
	2	23.5	4.0	80.0	> 30	34	7.9
	3	4.4	1.7	55.0	11	169	1
	4	1.7	0.9	45.0	6	346	4
5	1	0.5	< LOD	2.8	0	0	0
	2	6.8	2.6	12.0	> 30	32	3
	3	1.6	1.0	9.0	> 30	204	0
	4	1.3	0.9	8.9	27	360	0
6	1	1.6	0.4	14.0	15	0	1.9
	2	18.5	4.5	56.0	> 30	29	6.9
	3	4.3	1.9	44.0	15	170	Missing data
	4	2.3	1.3	38.0	10	340	2
7	1	< LOD	< LOD	1.1	0	0	0
	2	3.7	1.7	16.0	> 30	23	3
	3	1.1	0.7	12.0	15	167	0
	4	0.5	0.4	8.8	0	288	4
8	1	< LOD	< LOD	0.8	0	0	0
	2	3.1	0.9	9.4	> 30	49	3
	3	0.4	0.3	6.8	0	210	3
	4	0.2	< LOD	5.8	0	388	1
9	1	2.1	< LOD	28.0	8	0	3.9
	2	19.7	4.1	58.0	> 30	13	6
	3	4.0	1.4	40.0	15	172	0
	4	3.5	1.1	34.0	14	355	9
10	1	< LOD	< LOD	0.0	0	0	10.8
	2	2.6	0.6	7.7	> 30	27	11.3
	3	< LOD	< LOD	5.1	0	197	4
	4	< LOD	< LOD	3.7	0	353	5
11	1	1.6	0.3	29.0	7	0	0
	2	40.9	11.0	101.0	> 30	31	3
	3	5.8	3.0	73.0	13	189	3
	4	3.7	2.1	71.0	8	347	3

Table 1 (continued)

ID	Drive	Serum concentration (in ng/ml)			CIF	Time (in min)	Penalty points
		THC	11-OH–THC	THC–COOH			
12	1	0.6	0.2	14.0	0	0	1
	2	31.4	4.6	69.0	> 30	34	6.
	3	5.7	1.8	60.0	13	193	Missing data
	4	2.8	1.0	34.0	11	363	2
13	1	3.7	1.4	40.0	13	0	3.8
	2	42.9	11.1	92.0	> 30	23	1.3
	3	7.0	3.7	74.0	15	186	0
	4	5.4	2.7	72.0	12	342	5
14	1	> LOD	> LOD	2.5	0	0	1
	2	27.5	11.9	61.0	> 30	36	5.9
	3	3.9	3.2	40.0	19	197	9.1
	4	1.5	1.8	28.0	12	367	1
15	1	> LOD	> LOD	1.5	0	0	9.8
	2	2.4	0.9	9.7	> 30	20	10.9
	3	0.6	0.4	6.5	0	191	6.1
	4	0.4	0.3	5.3	0	340	4

The third drive of the test persons no. 6 and no. 12 was interrupted due to technical errors, and therefore, the penalty points were not evaluated

- Subjective condition: normal 0; sensation of heat, freezing, headache, aching limbs, tiredness, thirst 1; nausea, vertigo 2
- Pupils: without pathological findings 0; narrow or wide without reaction to light 2
- Pronator drift (eyes closed): secure 0; insecure, falling 2
- Standing on one leg: secure 0, insecure 1, falling 2
- Overall the influence of cannabis was …: not noticeable 0, slightly noticeable 1, clearly noticeable 2, extremely noticeable 3

b) Driving performance:

- Accidents: each accident 3
- Roadway deviation: slightly and without further pathological findings 0; numerous correcting motions, leaving the lane with the tires of one side of the car, touching the pavement 1; driving on the oncoming lane, leaving the lane (detected by the programme) 2

Table 2 Main characteristics of the four routes (a.c. = after cannabis consumption)

Drive	Length (in km)	Traffic lights	Unforeseeable obstacles
1 (sober)	2.19	2	2
2 (a.c.)	1.42	3	4
3 (+ 3 h a.c.)	1.36	4	4
4 (+ 6 h a.c.)	4.21	4	4

- Traffic lights: running a green light 0, running a yellow light 1, running a red light 3

c) Driving style:

- Save 0; careful, tentative, single insecurities 1; clear insecurities, risky 2

The category "driving style" combines aspects of speed (driving too fast or too slowly) and the driver's behaviour, especially at traffic lights (approaching exceedingly slow, speeding up) and in potentially critical situations (appropriate decelerating or acceleration of the car).

Statistical analyses

The statistical analyses were performed for the two aspects "medical examination report" and "driving performance and style" separately, the latter requiring the addition of the previously collected penalty points for driving performance and driving style. As the test courses varied in length, amount of traffic lights and unforeseeable obstacles (Table 2), the penalty points for roadway deviations were weighted before addition in order to compensate possible effects caused by a variation of course. Two participants were unable to finish their third drive due to technical errors. These data were therefore excluded from further statistical evaluation regarding driving performance and style.

The amount of penalty points were evaluated in four different groups based on:

- THC concentration (< 1, 1–5, > 5–15, > 15 ng/ml)
- CIF value (< 1, 1–9, 10–30, > 30)
- The time after consumption (sober, directly after consumption, 3 h and 6 h after consumption).

The CIF value was calculated according to Daldrup and Meininger [14]:

$$\mathrm{CIF} = \frac{\mathrm{THC{-}conc.[ng/ml]}/314.5 + 11{-}\mathrm{OH{-}THC{-}conc.[ng/mg]}/330.5}{\mathrm{THC{-}COOH{-}conc.[ng/ml]} \times 0.01/344.5}$$

Since each participant is measured multiple times, a one-way repeated-measures ANOVA (analysis of variance) was performed, in which a THC concentration < 1 ng/ml, a CIF < 1 or the sober drive was considered the baseline for the subsequent groups.

P values were calculated for these groups using one-way analysis of variance with repeated measures (mixed model), in which a THC concentration < 1 ng/ml, a CIF < 1 and the sober drive were primarily compared with a hypothetical amount of 0 penalty points, therefore forming the intercept for the subsequent groups. *P* values were significant when < 0.05.

Results

Drug screening and testing for breath alcohol

Both the initial urine screening and the follow-up blood examinations revealed no intake of medication with effect to the central nervous system or drugs other than cannabis. Breath alcohol was not detected in any of the participants, either.

Serum concentrations of THC and relevant metabolites

Table 1 gives an overview over the concentrations of THC and its relevant metabolites during the trial. A direct correlation between these concentrations and impairments, both in the medical examination and driving performance and style, was not detected. Two participants (ID no. 6 and no. 13 in Table 1) arrived at the day of the study with an initial CIF > 10 which indicates an acute or subacute influence of cannabis (Table 1) [15].

The THC concentrations (in serum) of the first blood samples, taken before the consumption of cannabis varied between < LOD and 3.9 ng/ml. The initial THC–COOH concentrations ranged from < LOD to 164 ng/ml. The THC concentrations in the second blood samples, taken right after the joints had been smoked, ranged from 2.4 to 42.9 ng/ml and the THC–COOH concentrations from 7.7 to 192 ng/ml. Directly after smoking the cannabis cigarettes the CIF rose above 30 in every case except one (ID no. 2 in Table 1).

Medical examination reports

Most participants showed little distinctive effects in the medical examinations. The average amount of penalty points was significantly elevated after the second (maximum influence, $p < 0.01$) and third drive (3 h after cannabis consumption resp. a.c., $p = 0.02$; Fig. 1) and with high THC concentrations > 15 ng/ml ($p < 0.01$; Fig. 2) or CIF values > 30 ($p < 0.01$; Fig. 3).

The estimation of the 30 s period was mostly accurate within a range of ± 5 s. Most deviations were seen in the sober drive (four persons counted less than 25 s, two counted more than 35 s). In the following examinations, no more than two persons deviated more than 5 s. Only twice deviations of ten or more seconds were noted (no. 7, first drive, 42 s; no. 1, fourth drive, 20 s).

Driving performance and style

The median (black line) of the penalty points is elevated in the second (directly a.c.) and fourth (6 h a.c.) simulation drive as shown in Fig. 4. Only directly after consumption, this elevation was significant in comparison to the sober simulation drive, though (second drive $p < 0.01$; fourth drive $p = 0.43$). Three hours after cannabis consumption (third drive), no significant elevation of penalty points could be noted when considering the median of all test persons. Four participants did show an elevated amount of penalty points in this drive (nos. 1, 8, 11 and 14; Table 1), and six persons showed a decrease of penalty points (nos. 2, 3, 9, 10, 13, 15; Table 1). However, the average amount of penalty points (red diamonds in Fig. 4) is roughly comparable in simulation drives 1, 3 and 4.

Comparing the amount of allocated penalty points of the fourth drive to the second drive, four participants exhibited an increase (nos. 2, 7, 9, 13; Table 1) and ten a decrease (nos. 1, 3, 4, 5, 6, 8, 10, 12, 14, 15; Table 1). When comparing the fourth drive to the third drive, seven participants exhibited an increase (nos. 2, 3, 4, 7, 9, 10, 13; Table 1) and four a decrease (nos. 1, 8, 14, 15; Table 1) of penalty points. One participant exhibited the same amount of penalty points in the second, third and fourth drives (no. 11; Table 1).

A significant elevation of penalty points can be seen at high THC concentrations > 15 ng/ml ($p < 0.01$; Fig. 5) and high CIF values > 30 ($p < 0.01$; Fig. 6). For lower THC concentrations and CIF values the median of penalty points did not differ from the baseline.

The test persons with the IDs 6 and 13 did not show significantly different results than the other test persons, although presenting a much higher CIF value at the beginning of the trial and therefore during the sober drive.

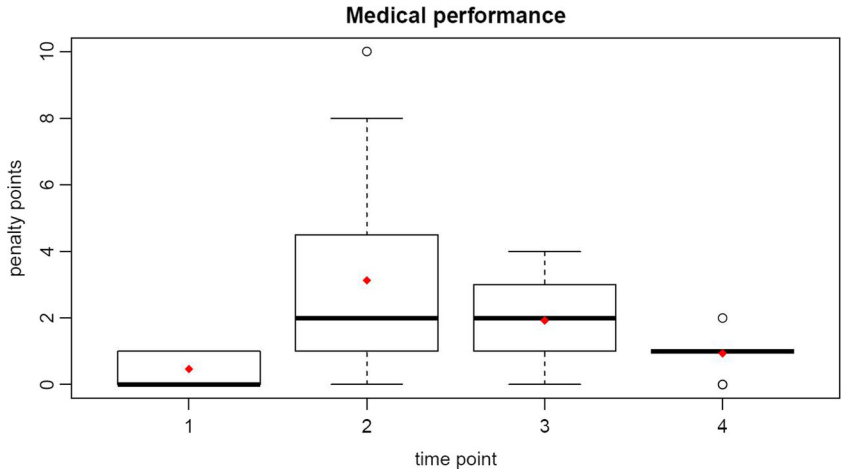

Fig. 1 Box plot diagrams illustrating the penalty points in the medical examination at different points in time (1 = sober, 2 = directly after consumption (a.c.), 3 = approx. 3 h a.c., 4 = approx. 6 h after consumption). The boxes contain the middle 50% of the values, the thick black lines indicate the median and the whiskers, i.e. the small horizontal lines, connected by dashed lines to the boxes mark the minimum and the maximum of the values except when there are outliners, which are specifically indicated by circles. Diamonds indicate the mean of the values

Discussion

All findings have to be seen in the light of the general limitations of the study. The study design did not include placebo test persons. All test persons were well informed about the test situation. The test group was small and consisted mainly of young males. Gender and age, however, can be considered representative to the group of people generally found driving under the influence of cannabis [1]. The driving simulator used did not provide side mirrors or indicators which is problematic when evaluating the behaviour in situations in which these are generally used, e.g. turning left or right or overtaking. As a result, these slightly more complex driving situations were avoided in the courses, making the courses easier.

Independent of the point in time after consumption, a very high CIF value > 30 as well as a serum THC concentration > 15 ng/ml significantly increased the number of penalty points, which corroborates the assumption that an acute intoxication leads to driving impairment.

Consistent with previous studies, a direct correlation between the individual fitness to drive (amount of penalty points) and the THC concentrations and/or CIF values was not found [3, 4, 8, 9, 12, 14]. Therefore, determining a threshold limit for legal purposes based on these values alone seems to be arbitrary.

Significant driving impairments were noted directly after the cannabis consumption—in the acute phase of cannabis influence.

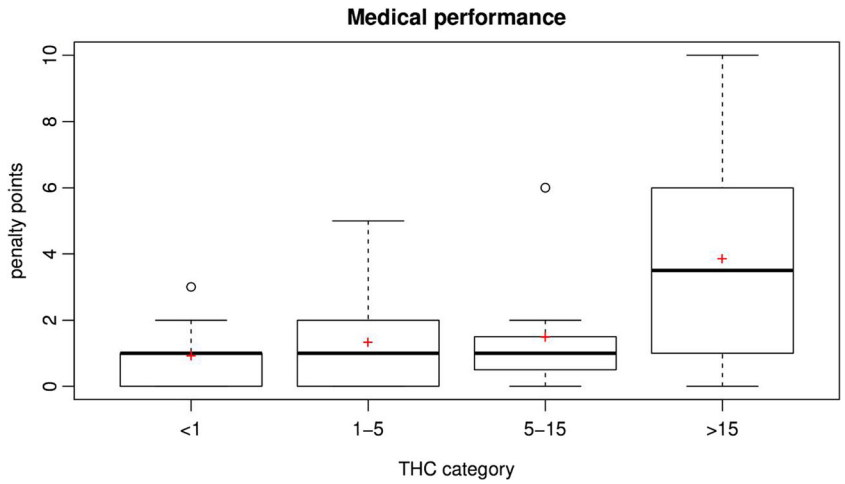

Fig. 2 Box plot diagrams illustrating the penalty points in the medical examinations in relation to the THC concentrations in serum. The THC concentrations were summed up in four groups (< 1, 1–5, 5–15, > 15 ng/ml). The boxes contain the middle 50% of the values, the thick black lines indicate the median and the whiskers, i.e. the small horizontal lines, connected by dashed lines to the boxes mark the minimum and the maximum of the values except when there are outliners, which are specifically indicated by circles. Crosses indicate the mean of the values

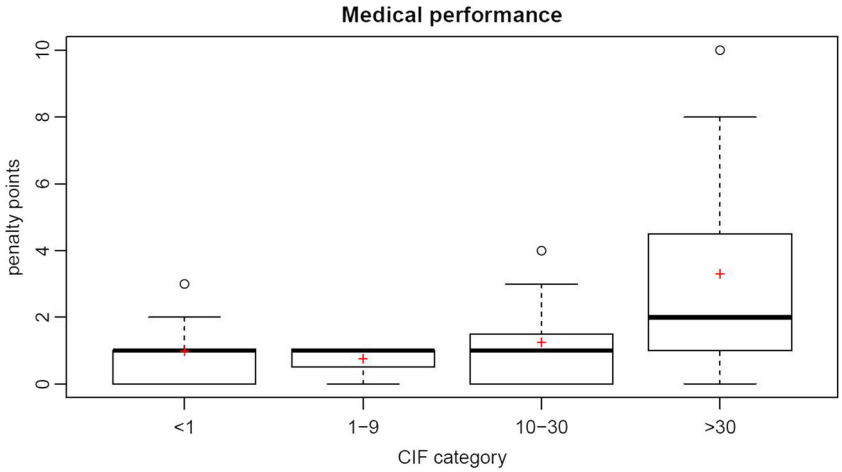

Fig. 3 Box plot diagrams illustrating the penalty points in the medical examination in relation to the CIF value. The CIF values were summed up in four groups (< 1, 1–9, 10–30, > 30). The boxes contain the middle 50% of the values, the thick black lines indicate the median and the whiskers, i.e. the small horizontal lines, connected by dashed lines to the boxes mark the minimum and the maximum of the values except when there are outliners, which are specifically indicated by circles. Crosses indicate the mean of the values

Around 3 h after the consumption, only a few test persons showed an increased amount of penalty points, but overall, driving performance and style no longer differ significantly from the sober drive. It might be that the participants' awareness of possibly existing impairments enables them to compensate for them, at least in a test situation [3, 4, 6, 9].

During the fourth simulation drive of the trial—around 6 h after cannabis consumption—the median of the number of allocated penalty points rose again, although this elevation was not significant and the average amount of allocated penalty points remained roughly comparable to the sober simulation drive. An explanation for a possible increase of median penalty points when entering the so-called subacute phase of cannabis consumption could be that participants are likely to feel sobered up, therefore no longer paying extra attention to their driving, allowing the existing impairments to manifest themselves. Another explanation that has to be considered regarding the subacute phase of cannabis consumption is the fact that the participants had been in a study situation for almost 12 h and regularly stated to feel tired and that they normally would no longer drive a car. Mistakes made during the fourth drive—which took place around or just before midnight—therefore cannot be clearly distinguished from mistakes made due to tiredness.

Overall, driving during nighttime and in the subacute phase of THC elimination does depict a realistic situation [3] in which additive effects of natural and cannabis-induced tiredness are likely to occur, if a person decides to drive, nevertheless. In order to eliminate the effect of natural tiredness during the subacute phase of cannabis consumption to a minimum, the trial as well as the accompanying cannabis consumption would have to start in the (early) morning, which does not seem to reflect the consuming habits of most leisure consumers.

The most common driving mistakes in our study were leaving the road lane, followed by accidents due to unforeseeable events or running a yellow/red light. Other authors also

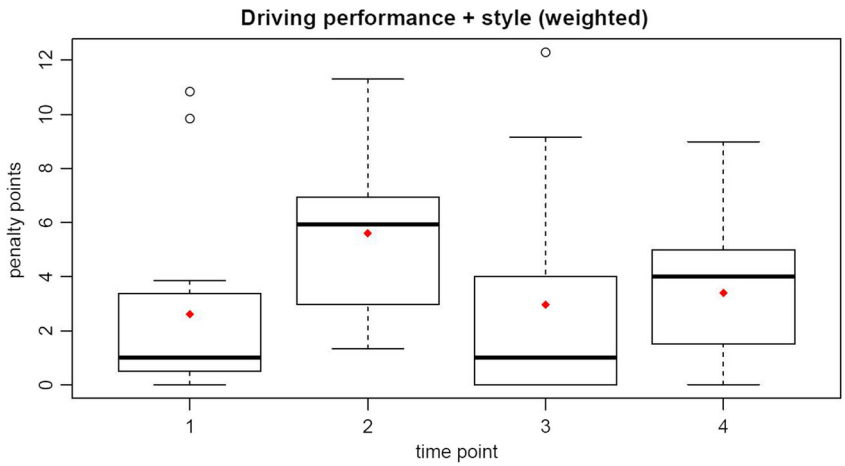

Fig. 4 Box plot diagrams illustrating the penalty points for driving performance and style in relation to the time (1 = sober, 2 = directly after consumption (a.c.), 3 = approx. 3 h a.c., 4 = approx. 6 h after consumption). The boxes contain the middle 50% of the values, the thick black lines indicate the median and the whiskers, i.e. the small horizontal lines, connected by dashed lines to the boxes mark the minimum and the maximum of the values except when there are outliners, which are specifically indicated by circles. Diamonds indicate the mean of the values

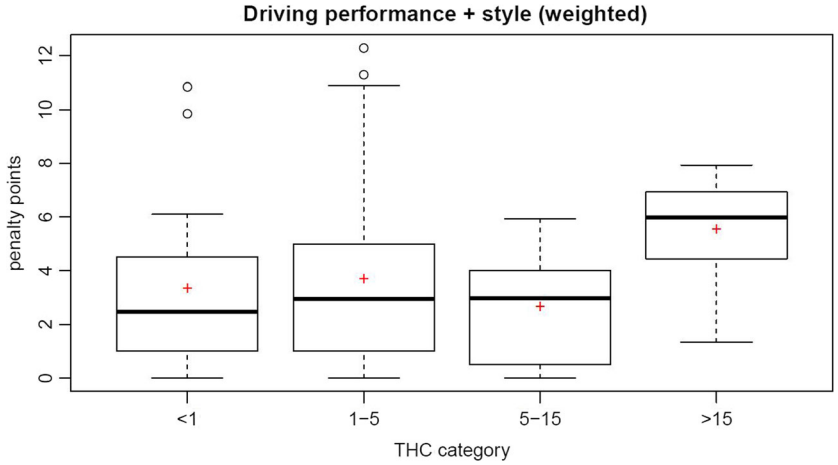

Fig. 5 Box plot diagrams illustrating the penalty points for driving performance and style in relation to the THC concentrations in serum. The THC concentrations were summed up in four groups (< 1, 1–5, 5–15, > 15 ng/ml). The boxes contain the middle 50% of the values, the thick black lines indicate the median and the whiskers, i.e. the small horizontal lines, connected by dashed lines to the boxes mark the minimum and the maximum of the values except when there are outliners, which are specifically indicated by circles. Crosses indicate the mean of the values

reported leaving the road lane as a leading driving impairment after cannabis use (in driving simulators), as especially highly automated behaviour was repeatedly stated to be vulnerable to cannabis intake (e.g. [1, 3, 6, 7, 10, 11]).

The medical examination test showed distinctive features when the drivers were acutely under the influence of cannabis as well around 3 h later (second and third drives) and had very high THC concentrations and/or CIF values. At the time of the fourth drive, the findings were no longer remarkable. Regarding the medical examinations, an important compromising factor of our study was the fact that the examining doctor knew when and how much cannabis the participants had consumed.

As another finding of this study, the rise of THC concentrations after smoking three cannabis cigarettes containing a bodyweight-adapted amount of THC exhibited great interindividual differences, implicating a considerable variation in the bioavailability. No reliable correlation between consumed cannabis and THC concentrations was detectable.

The results of the study indicate that the time passed since the last cannabis consumption, as well as very high CIF values and THC concentrations seem to be the most significant predictors for driving impairments in regular cannabis consumers. A threshold for an absolute impairment to drive cannot be presented, however.

In reality, the exact time passed after the last cannabis consumption is difficult to determine, as it depends on truthful information of the driver and neither THC and/or THC metabolite concentrations nor CIF values are currently reliable predictors. The medical examination in the current form can detect impairments in the acute phase but seems to be insufficient in the subacute phase. As the medical examination, along with the taking of the blood sample(s), is usually performed with some delay to stopping the driver, the examination performed by the police right after the stoppage is all the more important for further evaluation of the driver's fitness to drive. This meets the DRUID studies' demand for proper trainings of

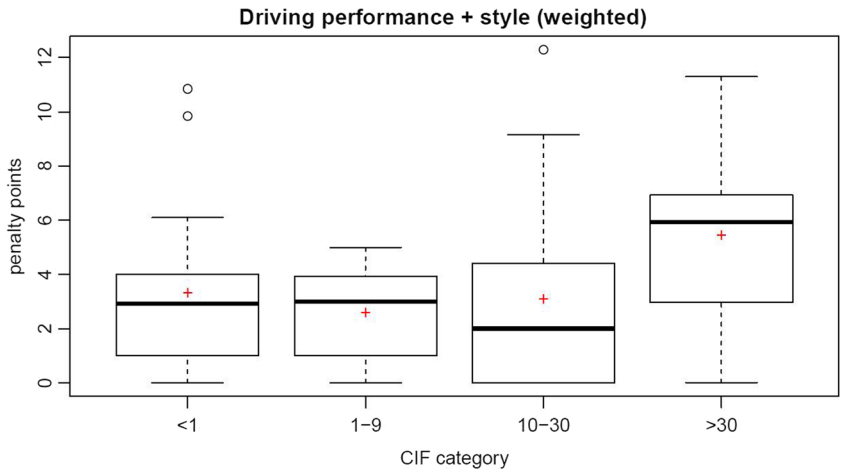

Fig. 6 Box plot diagrams illustrating the penalty points for driving performance and style in relation to the CIF values. The CIF values were summed up in four groups (< 1, 1–9, 10–30, > 30). The boxes contain the middle 50% of the values, the thick black lines indicate the median and the whiskers, i.e. the small horizontal lines, connected by dashed lines to the boxes mark the minimum and the maximum of the values except when there are outliners, which are specifically indicated by circles. Crosses indicate the mean of the values

police officers in order to improve the detection of drug abuse close to the event [1].

In accordance with previous assumptions [14, 18] the risk for driving mistakes might increase again in the subacute phase of cannabis elimination, which would be in contrast to the lack of distinctive features during the medical examination in this phase.

Following the results of the study, both driving immediately after the cannabis consumption and driving in the subacute phase of THC elimination may pose a problem for traffic safety. For a valid conclusion, a much larger trial with more test persons in a more sophisticated driving simulator is needed. Using a driving simulator is recommended, as it can directly test the driving behaviour without putting the participants at risk [8, 10, 19]. Preferably, the driving experience can be designed in a more realistic way using courses that are slightly more complex and a driving simulator exhibiting all the necessary features to drive, including side and rear windows and mirrors, indicators and potentially gear changes. In addition, we suggest longer drives on different routes of approximately the same length and with similar amounts of potentially dangerous situations.

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Compliance with ethical standards

Ethical standards The experiments of this study comply with the current German laws. The study protocol was pre-approved by the ethics committee of the University Hospital Düsseldorf.

Conflict of interest The authors declare that they have no competing interest.

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