






Driving Under the Influence of Cannabis: Impact of Combining Toxicology Testing with Field Sobriety Tests

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BACKGROUND: Cannabis is increasingly used both medically and recreationally. With widespread use, there is growing concern about how to identify cannabis-impaired drivers.

METHODS: A placebo-controlled randomized double-blinded protocol was conducted to study the effects of cannabis on driving performance. One hundred ninety-one participants were randomized to smoke ad libitum a cannabis cigarette containing placebo or delta-9-tetrahydrocannabinol (THC) (5.9% or 13.4%). Blood, oral fluid (OF), and breath samples were collected along with longitudinal driving performance on a simulator (standard deviation of lateral position [SDLP] and car following [coherence]) over a 5-hour period. Law enforcement officers performed field sobriety tests (FSTs) to determine if participants were impaired.

RESULTS: There was no relationship between THC concentrations measured in blood, OF, or breath and SDLP or coherence at any of the timepoints studied ($P > 0.05$). FSTs were significant ($P < 0.05$) for classifying participants into the THC group vs the placebo group up to 188 minutes after smoking. Seventy-one minutes after smoking, FSTs classified 81% of the participants who received active drug as being impaired. However, 49% of participants who smoked placebo (controls) were also deemed impaired at this same timepoint. Combining a 2 ng/mL THC cutoff in OF with positive findings on FSTs reduced the number of controls classified as impaired to zero, 86 minutes after smoking the placebo.

CONCLUSIONS: Requiring a positive toxicology result in addition to the FST observations substantially improved the classification accuracy regarding possible driving

under the influence of THC by decreasing the percentage of controls classified as impaired.

Introduction

The relationship between cannabis use and driving impairment is complex because of the unique pharmacokinetic and pharmacodynamic properties of cannabis's major intoxicant: delta-9-tetrahydrocannabinol (THC) (1). "Impairment" is difficult to define because there is no universally agreed-upon task that can be used to define driving impairment. With ethanol there is a clear relationship between the amount of alcohol consumed, blood alcohol concentrations, and the effects on driving performance (2). With cannabis, these relationships are more complex (3). The relationship between blood THC concentrations and crash risk is not established, but there is a clear understanding that THC impairs driving performance in many, but not necessarily all, individuals (1, 4). The question that remains is how to best identify drivers who are impaired by cannabis.

There are multiple components that influence the relationship between cannabis and impairment. These include factors related to cannabis itself (e.g., % THC content), cannabis use characteristics (e.g., route of administration, frequency, and amount of exposure), characteristics of the individual using cannabis (e.g., experience, prior use), and when impairment is assessed relative to dosing. The psychoactive effects of cannabis inhalation begin within minutes of smoking or vaporization and peak within 3 hours (3), while oral administration causes effects that begin in approximately 1 hour and last up to 8 hours (5). This

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observation is consistent with findings showing driving-related skills recover between 3 and 5 hours after smoking cannabis (4, 6). Unlike alcohol, which is cleared within 24 hours of drinking, THC accumulates with repeated dosing, resulting in some frequent users having baseline blood concentrations >5 ng/mL. Although there may be no measurable impairment, background THC concentrations can exceed the per se driving impairment limits currently employed in some states, which are generally set at 2 or 5 ng/mL of THC in blood (7, 8). The term per se in context of driving under the influence means that when concentrations exceed the specified limit, a person is considered to be under the influence based solely on the toxicology test. After smoking, blood THC concentrations drop about 90% in the first hour (9, 10). Since it can take several hours to collect a blood specimen following a traffic stop (11), it is difficult to estimate circulating blood THC concentrations at the time of driving. In one field study of 602 cases in which drug recognition experts (DREs) determined the driver was impaired due to cannabis only (toxicology confirmed), the median THC concentration was 5.05 ng/mL—meaning that around 50% of the group were below per se limits used by some states (12).

Oral fluid (OF) is an alternative specimen that can be rapidly collected at the roadside to detect recent use of cannabis. OF has several advantages compared with analysis of blood; sample collection is noninvasive, it can be tested on screening devices at the point of contact, and, like blood, preliminary results can be confirmed by robust analytical techniques such as LC-MS/MS (13, 14). Analyzing breath samples for THC content has also been proposed for identifying recent cannabis use (15).

In the first study to evaluate police officers' performance for detecting drug-related impairment (16), adult male participants were randomized to receive cannabis, diazepam, secobarbital, or d-amphetamine. In this study the officers were trained DREs and were blinded to the participant's study drug. Only one participant was misidentified as under the influence of cannabis, while the individual was actually administered diazepam. The ability of the officers to correctly identify cannabis exposure (sensitivity) was low but dose related, as the officers correctly identified more participants on the high THC dose as compared with the low THC dose.

Heishman et al. (17) performed a placebo-controlled double-blind study examining the ability of DREs to correctly classify participants who had been exposed to placebo, ethanol, cocaine, or THC. These authors showed that when the DRE determined impairment due to drugs other than ethanol (e.g., cocaine or THC), DRE conclusions matched toxicology results in 44% of cases. However, when considering cannabis,

DREs determined that 6/16 of the participants exposed to placebo were impaired (17).

In a follow-up study, Heishman measured maximum THC plasma concentrations of 28 and 61 ng/mL 2 minutes after smoking cannabis in a low- and high-dose group, respectively (18). In this trial, more placebo-exposed participants were considered impaired than the low-dose cannabis group. These authors concluded that DRE determinations of impairment were consistent with toxicology findings in only 32% of the cases (18). The authors point out several reasons for this discrepancy including that, in the field, officers observe other clues including driving behavior, drug paraphernalia, and cannabis odor.

Most of the published research examining the reliability of DRE observations has been conducted under controlled experimental conditions and only included part of the full DRE exam. This is unavoidable in studies where participants are examined more than once because a full DRE exam typically lasts about an hour (16). This has important implications when correlating laboratory studies with field studies, because several important steps of the DRE examination, such as interviewing the arresting officer, searching the participant, examining for physical signs of drug administration, and performing a breath alcohol test, are not possible in a laboratory study conducted over multiple timepoints after smoking cannabis.

In this manuscript we report results from the largest randomized double-blinded-placebo-controlled trial to date that examines the relationship between THC concentrations in various biofluids and performance in a driving simulator. We also report on police officers' assessment of cannabis impairment based solely on field sobriety tests (FSTs) as well as when combined with various biofluid THC concentrations for the classification of persons exposed to active drug or placebo. We report the effect of different cut-points for blood and oral fluid (OF) at different timepoints for classifying participants deemed impaired on FSTs.

Materials and Methods

STUDY PARTICIPANTS

The data presented summarize toxicology findings and FST results from a University of California San Diego Center for Medicinal Cannabis Research study (4). Briefly, 199 participants were randomized and classified as "frequent" or "occasional" users. Participants using cannabis ≥ 4 times/week were termed "frequent" users, while those with intake at least 4 times per month but < 4 times/week were termed "occasional" users. Of these 199 participants, 7 were excluded due to having > 5 ng/mL THC in OF on the day of the experimental visit, and

one participant withdrew, resulting in 191 participants. Participants were randomized to smoke 700 mg of placebo (0.02% THC), 5.9% THC, or 13.4% THC cannabis in a double-blind manner. The characteristics of the dosing material were described previously (8). Participants were required to take at least 4 puffs and could smoke as much as they desired during a 10-minute smoking period. Participants were instructed to “smoke as you would at home to achieve desired highness.” The participants that smoked active drug (5.9% and 13.4% THC) were combined into a single group for all of the analyses in this report because there were no significant differences between how these 2 groups performed on the driving simulator (4) and no correlation was observed between the potential amount of THC smoked (mg based on weight returned following smoking) compared to perceived highness (10). The term “active drug” refers to participants smoking either a 5.9% or 13.4% THC cigarette.

LAW ENFORCEMENT OFFICERS

Officers (N = 11) were members of the California Highway Patrol or other California law enforcement agencies, were certified DRE instructors, and had completed DRE training according to the International Association of Chiefs of Police.

FSTS

The officers performed FSTs consisting of a walk and turn, modified Romberg, lack of convergence, one-leg stand, and finger to nose tests. These tests were described previously (19). Officers did not perform a full DRE exam due to time constraints. Based solely on participants' performance on the FSTs, officers classified them as being impaired or not impaired.

THC MEASUREMENT

THC and related cannabinoids were quantified in blood, OF, and breath on a Waters TQ-S micro LC-MS/MS system. Analytical method details were published previously (14, 20). Precision and accuracy of THC measurements were within $\pm 15\%$ with a lower limit of quantification of 0.5 ng/mL in blood, 0.4 ng/mL in OF, and 80 pg/breath pad. Blood was collected using sodium fluoride as the anticoagulant and analyzed within the time frames described by Desrosiers (21). OF was collected using the Quantisal device (Immunoanalysis), and analyzed within the time frames described by Scheidweiler (22). OF was collected until the blue indicator showed that 1 mL specimen was obtained or for a maximum of 10 minutes. OF results are expressed as ng/mL THC in OF. Breath samples were collected in the SensAbuses drug collection device.

The timelines for biological specimen collections, driving simulations, and FSTs are shown in Fig. 1. The mean (SD) and median (interquartile range) times for sample collection, driving simulation, and FST exams for all subjects are shown in Supplemental Table 1. The mean (SD) and median (interquartile range) times for sample collection, driving simulation, and FST exams for subjects who smoked active drug are shown in Supplemental Table 2.

DRIVING SIMULATOR

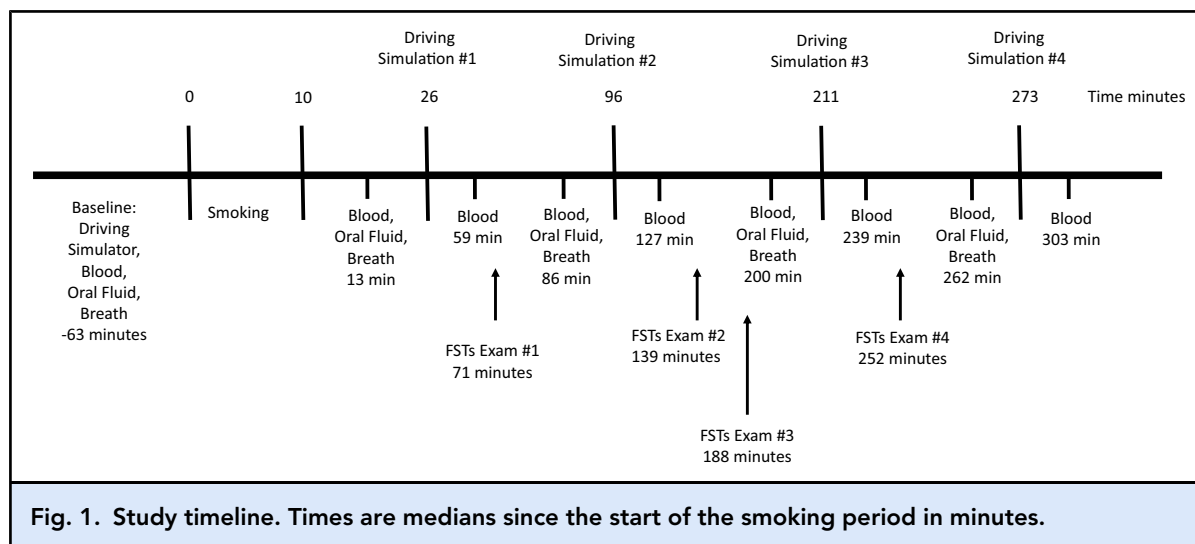
The driving simulator was a STISIM M300WS-Console Driving Simulator System, as described by Marcotte (4). Relationships between 2 measures of driving performance, SDLP, and car following (coherence) and THC concentrations in blood, OF, and breath are reported. SDLP, a measure of weaving in a driving lane, and coherence, a measure of ability to maintain a consistent distance with a leading vehicle, are 2 commonly used indicators of impairment (23–25). An increase in SDLP indicates worse driving performance while a decrease in coherence indicates worse driving performance.

DETERMINATION OF IMPAIRMENT

There is no reference method for identifying impairment following use of cannabis. Real-world driving impairment is the ultimate outcome of interest, but that is difficult to operationally define (crashes, high-risk behaviors, or slowed response to obstacles). Driving simulations, cognitive testing, and FSTs are all surrogates of impairment. Impairment was defined as the officer's interpretation of the participant's performance across all of the FSTs. Any participant with sufficient deficits on the FSTs that a trained police officer deemed them unsafe to drive was defined as being impaired. This definition was selected because, in a traffic stop, an officer's observation of driving performance is the precipitating event, followed by FSTs and possibly a DRE exam. Unlike a traffic stop, in this controlled study officers did not observe participants' driving and made a determination of impairment based only on observations during the FST examination. Results from the FSTs were combined with different cutoff blood or OF THC concentrations to classify participants as impaired, as was done previously (26).

STATISTICS

Correlation between driving performance (SDLP and coherence) and THC concentrations in blood, OF, and breath were determined using Spearman rho. *P* values were adjusted (p_{adj}) for multiple testing using the false discovery rate method. *P* values are from χ^2 tests for comparing proportions of impaired (or, equivalently, proportions of nonimpaired) between the THC



and placebo groups. P values < 0.05 were considered significant.

Results

The relationship between THC concentrations in blood, OF, and breath obtained immediately after smoking active drug (i.e., peak measured concentration, median of 13 minutes post-smoking) vs driving performance at the first post-smoking driving simulation (median 26 minutes post-smoking) are shown in Fig. 2. No correlation was observed between blood THC concentration and SDLP (Fig. 2, A; $\rho = -0.02$, $p_{\text{adj}} = 0.89$) or coherence (Fig. 2, B; $r = -0.102$, $P = 0.46$). These same parameters (SDLP and coherence) compared to THC concentrations measured immediately after the driving simulator (60 minutes post-smoking) also showed no relationship. The same results were observed for all other time points, as well as for analyses comparing THC concentrations and changes in simulator performance between the pre-smoking and post-smoking simulations (data not shown). We also analyzed the OF and breath data in a similar manner (Fig. 2, C–F) and demonstrated no relationship between biofluid concentrations and driving performance. The data in Table 1 shows the Spearman correlation (P values) between biofluids and driving performance and are similar to the data shown in Fig. 2 but include all of the time points in the study, vs Fig. 2, which only shows data for the first driving simulation. The data in Table 1 are important because drivers could potentially be stopped at various times after smoking cannabis. Table 1 shows that biofluid results from immediately preceding the simulator had no correlation

(all P values > 0.05) with driving performance at any time during the study for the active drug group. Table 2 is included because, in the field, driving performance is observed prior to collection of biofluid specimens, which are often obtained several hours after the traffic stop. Here we show that the initial driving performance (26 minutes) did not correlate with blood, OF, or breath at any collection period (13, 86, 200, or 262 minutes after smoking) for the active drug group. Both tables show no relationship between biofluid concentrations and driving performance at any time point.

In addition to THC, we also measured cannabidiol, 11-hydroxy-THC, 11-nor-9-carboxy-delta-9-THC, 11-nor-9-carboxy-delta-9-THC-9-carboxylic acid glucuronide, cannabigerol, delta-9-THC glucuronide, delta-9-tetrahydrocannabinolic acid, and tetrahydrocannabinol (14, 20). None of the 10 cannabinoids in our analysis correlated with the simulator driving performance (SDLP or coherence) at any time point.

Table 3 shows results of FST determinations of impairment for participants who smoked placebo or active drug. Only participants who had FSTs examined at all time points (63 placebo and 121 active drug) were included. At FST exam #1, performed a median of 71 minutes from the start of smoking, 98/121 participants (81.0%) who received active drug were classified as impaired. At the same time point, 31/63 participants who smoked placebo were classified as impaired (49.2%). There was a significant difference between participants who smoked active drug that were classified as impaired by the FSTs vs placebo for the first 3 FST examinations. By 252 minutes post start of smoking, there was no significant difference between those who received active drug vs placebo for FST classification of impairment. As the study day progressed, lower percentages of both

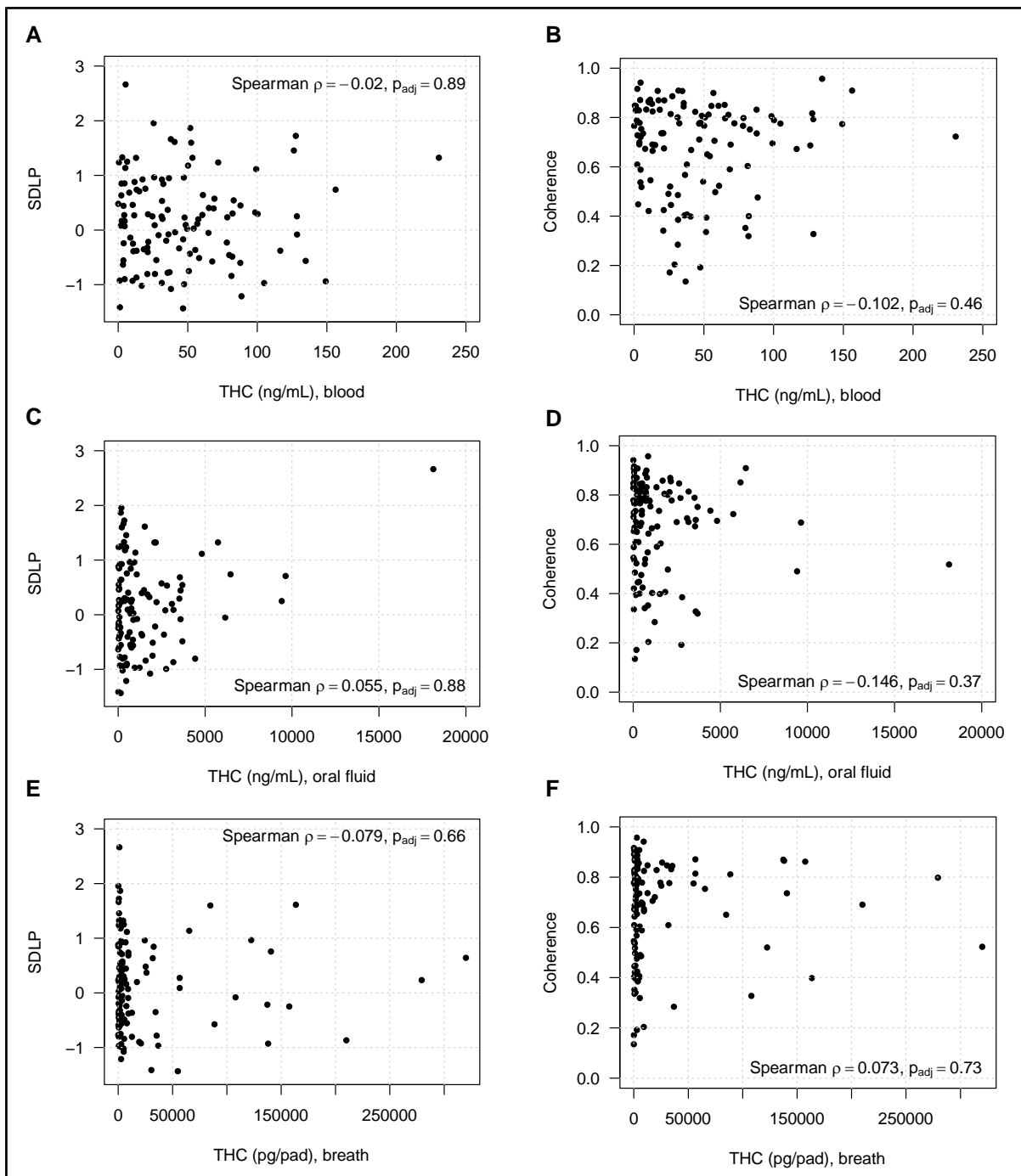


Fig. 2. Relationship of peak THC concentration in blood, oral fluid, and breath obtained a median of 13 minutes post-smoking active drug vs performance in driving simulation at 26 minutes. None of the relationships depicted were significant. (A), Correlation between blood THC concentrations and SDLP, an indication of swerving; (B), Correlation between blood THC concentrations and car following (coherence); (C), Correlation between oral fluid THC concentrations and SDLP; (D), Correlation between oral fluid THC concentrations and coherence; (E), Correlation between breath THC and SDLP; (F), Correlation between breath THC and coherence.

Table 1. Spearman correlations (*P* value) between THC concentrations in various biofluids and driving simulation outcomes among participants in the active drug group. For these analyses, THC biospecimen concentrations collected just prior to the driving simulation are evaluated against SDLP and coherence (car following). *P* values were adjusted for multiple testing using the false discovery rate method.

Simulation timepoint	Blood THC correlation (<i>P</i> value)	Oral fluid THC correlation (<i>P</i> value)	Breath THC correlation (<i>P</i> value)
SDLP			
Baseline	−0.013 (0.887)	−0.055 (0.882)	−0.057 (0.680)
Simulation 1	−0.020 (0.887)	0.055 (0.882)	−0.079 (0.663)
Simulation 2	−0.062 (0.874)	−0.046 (0.882)	0.036 (0.700)
Simulation 3	−0.221 (0.134)	−0.014 (0.882)	0.080 (0.663)
Simulation 4	−0.160 (0.286)	0.023 (0.882)	−0.089 (0.663)
Coherence			
Baseline	−0.079 (0.495)	0.044 (0.719)	−0.048 (0.764)
Simulation 1	−0.102 (0.460)	−0.146 (0.368)	0.073 (0.728)
Simulation 2	−0.122 (0.460)	0.033 (0.719)	0.078 (0.728)
Simulation 3	−0.112 (0.460)	−0.136 (0.368)	0.018 (0.845)
Simulation 4	0.039 (0.699)	0.078 (0.673)	−0.153 (0.510)

Table 2. Spearman correlations (*P* value) between THC concentrations and driving simulation outcomes among participants in the active drug group. For this analysis, SDLP and coherence results from the first post-smoking simulated driving session (26 minutes) are evaluated against all biofluid samples. *P* values were adjusted for multiple testing using the false discovery rate method.

Timepoint (min) (fluid collection)	Blood THC correlation (<i>P</i> value)	Oral fluid THC correlation (<i>P</i> value)	Breath THC correlation (<i>P</i> value)
SDLP			
13	−0.020 (0.835)	0.055 (0.576)	−0.079 (0.531)
86	−0.074 (0.596)	0.052 (0.576)	0.051 (0.585)
200	−0.092 (0.596)	0.088 (0.576)	−0.096 (0.531)
262	−0.107 (0.596)	0.057 (0.576)	−0.200 (0.121)
Coherence			
13	−0.102 (0.528)	−0.146 (0.114)	0.073 (0.683)
86	−0.062 (0.528)	−0.188 (0.074)	−0.038 (0.683)
200	0.073 (0.528)	−0.178 (0.074)	−0.096 (0.683)
262	0.102 (0.528)	−0.219 (0.068)	−0.041 (0.683)

active drug and placebo participants were considered impaired. Detailed analyses and discussion regarding the FSTs, overall driving performance, and characterization of the placebo group are addressed in Marcotte et al. (27).

Figure 3 shows how adding a requirement for a positive toxicology test in addition to the FST results changes the classification of impairment. For this figure we evaluate FST results alone (top line in graph) along

with 3 different THC cutoff concentrations (>0.5 ng/mL, 2 ng/mL, and 5 ng/mL). For this analysis we applied the FST assessment from 2 different time points. We chose FST exam #1 (shaded area, 71 minutes post-smoking) and FST exam #3 (188 minutes post-smoking) because the first represents the FST examination at the highest THC concentration and the latter is about 3 hours after smoking when effects should be starting to wear off (6). Figure 3, A shows

Table 3. FST determination of impairment for active drug (THC) or placebo, shown as a percentage. P values were adjusted for multiple testing using the false discovery rate method.			
FSTs exam #	THC	Placebo	P
Exam 1			<0.001
Impaired (%)	81.0	49.2	
Not impaired (%)	19.0	50.8	
Exam 2			<0.001
Impaired (%)	62.5	28.6	
Not impaired (%)	37.5	71.4	
Exam 3			0.032
Impaired (%)	36.4	19.0	
Not impaired (%)	63.6	81.0	
Exam 4			0.160
Impaired (%)	22.5	12.7	
Not impaired (%)	77.5	87.3	

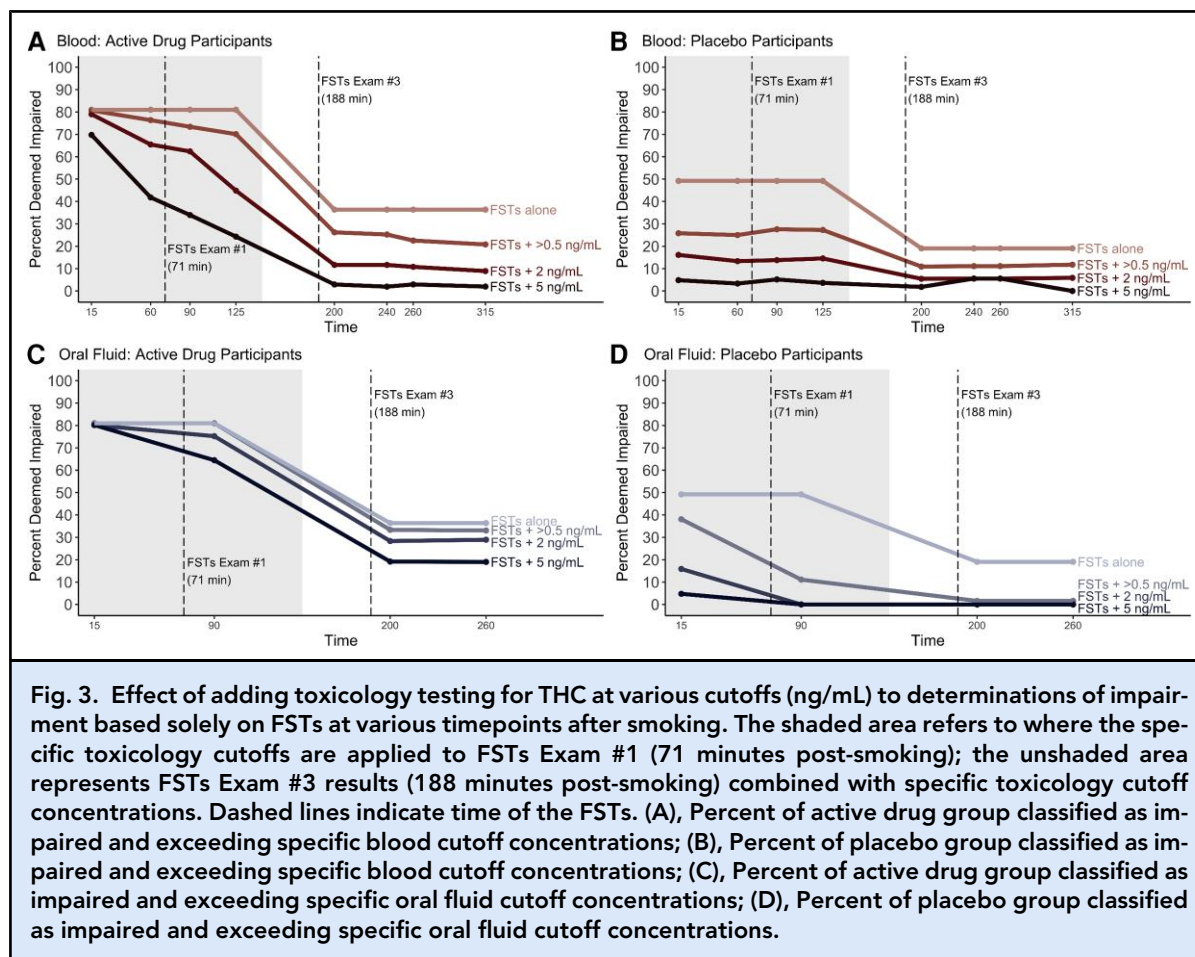
that at 90 minutes after smoking, when a 2 ng/mL blood THC cutoff is required in addition to the FST results, 62.4% of subjects who received active drug met both criteria, compared to 81.0% when just the FSTs were employed. Figure 3, B shows that, for the placebo group, requiring a 2 ng/mL blood cutoff decreased the percent of the placebo cohort classified as impaired to 13.8% at 90 minutes post-smoking compared to 49.2% when just the FSTs were used. The placebo group exceeding the toxicology thresholds reflect their baseline THC concentrations, as might be encountered in the field for drivers who use cannabis, even though it was not recent (i.e., greater than 48 hours before the collection) (7). Figure 3, C shows that at 90 minutes after smoking, when a 2 ng/mL OF THC cutoff is required in addition to the FST results, 75.2% of active drug subjects met both criteria vs 81.0% when just the FSTs were used. Figure 3, D shows that requiring a 2 ng/mL OF cutoff decreased the number of the placebo cohort who were classified as impaired to 0% at 90 minutes post-smoking vs 49.2% when just the FSTs were used. Supplemental Table 3 shows the effect of combining different toxicology concentration cutoffs (OF and blood) and FST results for classifying the active drug and placebo cohorts for all time points. We did not include the effect of adding breath samples to FST examinations because our previously published results (10, 11) showed that, using the breath collection device we employed, THC rapidly dissipates and by the second post-smoking time point was undetectable in most participants.

Discussion

Biofluid THC concentrations, as well as other cannabinoid concentrations, did not correlate with SDLP or coherence at any time point. The lack of correlation between THC and driving performance on a simulator was reported previously in studies up to about 3.5 hours after inhaling THC (4, 26). Previously we reported that the composite driving score, a combined measure of impairment, did not correlate to blood THC concentrations (4). Since SDLP and coherence are 2 of the most commonly reported simulator results sensitive to cannabis (25, 28), details of these findings in relation to blood, OF, and breath THC concentrations are reported. The complete lack of a relationship between the concentration of the centrally active component of cannabis in blood, OF, and breath is strong evidence against the use of per se laws for cannabis. Our results are consistent with a recent meta-analysis that concentrations of THC are “relatively poor indicators of cannabis-induced impairment” (29). Unlike ethanol (30, 31), there is no established relationship between blood THC concentrations and simulator driving performance measures (4, 26). In the largest randomized double-blinded placebo-controlled trial to date, our data confirm that THC concentrations (and/or metabolites/related cannabinoids) in blood, OF, or breath cannot be used as a sole indicator of impairment.

Previously we reported that participants smoking active cannabis produced a significant ($P < 0.05$) decrement in driving performance that lasted for about 3.5 hours (4). Thus, when evaluating the ability of FSTs to detect impairment, it is expected that they classify more participants exposed to active drug as being impaired early following cannabis inhalation as opposed to later time points. Table 3 shows that FSTs classified 81.0% of the active drug participants as impaired at the first FSTs exam while only 22.5% were classified as being impaired at the last time point (251 minutes post-smoking). As evidenced by driving performance in the simulator (4), and results from the FSTs exam, not all participants who smoked active drug were impaired at the time of the FSTs. The relationships between simulator driving performance and individual FST results are reported in a separate publication (27).

Of note, in isolation (e.g., without driving observations or a full DRE exam or toxicology testing), the FSTs classified 49.2% of the placebo group as impaired. This is consistent with previous reports from smaller studies examining the ability of FSTs to identify impairment following cannabis use (17, 18). Practice effects were limited in this study compared to previous studies that exposed participants to FSTs prior to administering study drug. In our study, participants were first exposed to FSTs after the smoking session. This likely increased the sensitivity of the FSTs to active drug but also could



have contributed to the high number of placebo participants who were categorized as impaired.

Adding a requirement for a positive toxicology test to the FST exam results slightly decreased the percentage of participants who smoked active drug that were classified as being impaired but dramatically decreased the percentage of placebo group subjects that were classified as impaired. When the same cutoff concentration was used, OF showed less of an impact than blood for reclassifying the active drug cohort while reclassifying a higher percentage of the placebo group as not impaired. While adding toxicology results may be helpful in increasing the level of suspicion that cannabis was involved in driving impairment, they do not demonstrate causality. Therefore, the results of this study do not translate into supporting per se approaches.

LIMITATIONS

When interpreting these results, several factors need to be considered. First, when relating THC biofluid concentrations to driving performance, our participants' driving skills were evaluated using a driving simulator in a

controlled environment that does not reflect all of the variables that confound actual driving. Second, our participants were instructed not to use cannabis for at least 2 days prior to the study and were excluded from the study if their OF contained ≥ 5 ng/mL THC at baseline. This likely complicates the application of our results to real-world data where participants frequently smoke more than one cannabis cigarette, with chronic users smoking multiple cannabis cigarettes on a daily basis. Third, the same officer examined each participant at multiple time points, which could influence the interpretation of impairment at later time points. In addition, officers also knew the participants would be under the influence of cannabis alone or placebo. Finally, a full DRE exam was not performed, and impairment was determined based solely on the FSTs results.

Conclusions

In the largest trial to date involving experienced users smoking cannabis, there was no correlation between

THC (and related metabolites/cannabinoids) in blood, OF, or breath and driving performance. Our data support the current practice in many areas of the United States that requires officer observations of impairment along with toxicology testing before prosecuting drivers for being under the influence. We provide some evidence for the use of OF as opposed to blood as being more useful in reducing the likelihood of false accusations of driving under the influence of cannabis. The selection of an optimal cutoff is an important determinant of road safety that deserves further study. A better understanding of how a full DRE exam compares with FSTs is also warranted.

Supplemental Material

Supplemental material is available at Clinical Chemistry online.

Nonstandard Abbreviations: THC, delta-9-tetrahydrocannabinol; OF, oral fluid; SDLP, standard deviation of lateral position; FST, field sobriety test; DRE, drug recognition expert; coherence, car following.

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