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Robert L Fitzgerald, Anya Umlauf, Jacqueline A Hubbard, Melissa A Hoffman, Philip M Sobolesky, Shannon E Ellis, David J Grelotti, Raymond T Suhandynata, Marilyn A Huestis, Igor Grant, and Thomas D Marcotte. Driving Under the Influence of Cannabis: Impact of Combining Toxicology Testing with Field Sobriety Tests Clin Chem 2023; 69(7): 724–33. <u>https://doi.org/10.1093/clinchem/hvad054</u>

Guests: Dr. Rob Fitzgerald is the Director of the University of California San Diego Center for Medical Cannabis Research bioanalytical laboratory and Dr. Tom Marcotte is Professor in the Department of Psychiatry at UCSD, and Co-Director of the Center for Medical Cannabis Research.

Bob Barrett: This is a podcast from *Clinical Chemistry*, a production of the American Association for Clinical Chemistry. I'm Bob Barrett. With increasing use of cannabis for both medical and recreational purposes, there is a need to accurately identify impaired drivers. Unlike alcohol, in which the relationship between amount ingested, blood concentration, and functional impairment is well defined, predicting impairment from a given blood THC concentration is far from straightforward.

Many factors complicate the assessment of driving impairment following cannabis use including percent THC content and frequency of use. In practice, this makes it difficult to establish a single blood concentration associated with impairment that works for all individuals. Some may show signs of impairment below the one-size-fits-all threshold while others may remain unimpaired at concentrations well above that threshold.

Field sobriety tests can be used as a functional assessment, but these have been shown to falsely identify impairment in a large number of study participants who did not use cannabis. A new research article appearing in the July 2023 issue of *Clinical Chemistry* addresses this problem by combining field sobriety tests with toxicology testing to accurately identify driving impairment following cannabis use. In this podcast, we're excited to talk with the article's lead and senior authors. Dr. Rob Fitzgerald is the director of the University of California, San Diego Center for Medical Cannabis Research bioanalytical laboratory and is a boardcertified clinical toxicologist.

Dr. Tom Marcotte is a neuropsychologist, Professor in the Department of Psychiatry UCSD, and co-director of the Center for Medical Cannabis Research. Both have an active research interest in the relationship between measured drug concentrations and their biological effects and both have conducted research for this study at the Center for Medical Cannabis Research at UCSD. So, Dr. Fitzgerald, let's start with you. Can you briefly describe this current study?

Rob Fitzgerald: Sure. Thanks for asking. We all know that cannabis is widely used, but we don't have really good objective data saying how to identify those who are impaired by cannabis for driving. And so, a primary question that we wanted to answer in this study was how to identify those who are or are not impaired due to cannabis and it's the largest randomized, placebocontrolled trial looking at the effect on THC that's been done to date. It's also the first time that we use relatively modern cannabis. So, the cannabis that we use had either 5.9% or 13.4% THC. All of the previous studies use 2% or 6%. So, we were at least getting closer to what's currently available in cannabis dispensaries.

> We had them smoke the cannabis. We instructed them to smoke as they would at home to reach their desired effect, and then we put them through a series of driving simulators followed by trained law enforcement doing field sobriety tests. We also collected toxicology samples in blood, oral fluid, and breath. So really, what we are reporting in this manuscript is the impact of toxicology testing in relation to driving performance and how it may improve the classification accuracy of field sobriety tests.

- Bob Barrett: Well, thank you doctor. Now, Dr. Marcotte, you used a driving simulator as one of the outcomes of interest. Can you tell us about that?
- Tom Marcotte: Of course. So, for this study, we use a fully interactive driving simulator that includes steering wheel, breaks, accelerator, pedals, a three-monitor wide field of view system, and I developed five 25-minute driving simulations that were really designed to emulate real world and regular driving. So, people will go through residential, city, and country environments. They need to make left-hand turns across oncoming traffic, merge onto a highway, pass through yellow lights, et cetera.

Importantly, I decided not to make this gamelike. I did not want people to be hyper attentive, always looking for something that will jump out in front of them. So, there are only a limited number of crash avoidance situations. And then importantly for this manuscript, nestled within these 25minute simulations, we had two structured driving scenarios. One was a divided attention task in which participants had to respond to an iPad off to the side of the monitors. And while they performed this, we looked at their standard deviation of lateral position or how much they swerved while they were doing the task. And then the second task was a car following tasks where the automobile in front of you speeds up or slows down and the participant is to adjust his or her speed to match the changes seen in the lead car.

- Bob Barrett: Well, Dr. Fitzgerald, let's follow up now. What was the relationship between THC and metabolite concentrations and driving performance?
- Rob Fitzgerald: Yeah, so the two tasks that Tom talked about that we measured, one was the standard deviation of lateral position, how much they swerved. We were interested to see if blood concentrations had any correlation with that, like were they predictive? And we found that they were not. So, blood concentrations surprisingly had no correlation with driving performance. We also looked at oral fluid and breath results and same thing; it was zero correlation between blood concentrations in any of the driving tasks, as well as oral fluid and breath. So, really what this points to is very strong evidence against a per se, but with alcohol there's a reasonable relationship between alcohol concentrations in blood and effects, but that's not true with cannabis and THC.
- Bob Barrett: Now, I understand that there have been other studies that have evaluated field sobriety tests and cannabis. Dr. Marcotte, what makes this study unique?
- Tom Marcotte: Well, a number of the previous studies have had some limitations. So, quite often, the field sobriety tests were conducted by research staff. They may have received some training from law enforcement officers, but obviously do not have the dozens, if not hundreds, of hours of training that law enforcement goes through, nor the real-world experience that officers have. Many of the previous studies would expose participants to the field sobriety tests before they receive the THC or placebo. So, they now had experience with the measures. And most of the studies were small sample sizes, usually 20 to 40 participants.

In contrast, for our study, through an incredible collaboration from the California Drug Recognition Expert Program, we had DREs, who are the highest level of training for officers who detect impaired drivers, do the evaluations. We had the first field sobriety test occur after drug exposure as would occur in the real world, and we had a sample size of 184 participants.

In using this design, we showed that the field sobriety tests significantly discriminated between those receiving THC or placebo and about 81% of the participants who smoked active drug were classified as being impaired at the first time point after smoking. However, we also found that 49% of the placebo participants were categorized as FST impaired by the officers. Now, we have an upcoming paper examining the details of the FSTs, simulator performance, and officer

estimates regarding treatment assignment, but as Dr. Fitzgerald noted, the goal for this project in this manuscript was really to determine the impact of including toxicology findings, as might be done in the real world.

- Bob Barrett: Dr. Fitzgerald, what was the effect of combining toxicology with field sobriety testing?
- Rob Fitzgerald: So, we looked at the effect of combining specific toxicology cut points, say a 2 nanogram per mil THC concentration in blood, with the field sobriety test. So, essentially what we were looking at is reclassification of both those who smoked active drug as well as reclassification of those who smoked placebo. And so for blood, adding a toxicology cut point in addition to the field sobriety test did decrease the number of subjects who were positive on both. And that's of some concern, but what we were really interested in was what was the effect of adding a toxicology cut point to the placebo group where 50% of them were classified as being impaired on the field sobriety test.

And what we showed was is that by adding a requirement for a positive toxicology, with the field sobriety test, dramatically reduced the number of, you might call them false positive subjects who got placebo but also were classified as being impaired from the field sobriety test. We also showed that oral fluid was a little bit better in that it had less effect on the active drug group, but a bigger effect on the placebo group. So, oral fluid tended to be a little bit better in our experience.

We should point out that even though the toxicology testing does decrease the number of placebos who are described as being field sobriety impaired, it doesn't really prove that they actually had impairments. So those are still things that need to be worked out.

- Bob Barrett: Well, finally then, Dr. Marcotte, what future studies still need to be performed.
- Tom Marcotte: As you can imagine, there are a number of really interesting questions still to be addressed.

One is an expiration of how toxicology from different matrices, whether it's blood, oral fluid, or breath, including possibly new approaches that have yet to be developed can provide critical information about things such as time since exposure. I know people are looking into developing breathalyzers and I will just say for every one of these different instruments, from breathalyzers to oral fluid, it's really important to make sure that there is robust validation data from controlled studies. I will also say that really understanding the relationship between FSTs and toxicology in real-world products, including high THC concentrates such as one might see when a person is dabbing or vaping THC, is a very important area to examine. In our study, we had people smoke as they would to get high at home. We did not necessarily have people who were extremely high, such as who law enforcement might come across on the freeway. So, it's really important to be able to do that research. I will say that we remain hindered by the Scheduled I status of cannabis. So, we cannot access those products that the public is using from dispensaries. We can only use cannabis from DEA approved manufacturers, who at least up to this point have not really been able to mimic and provide products that perform similarly to those that you would find in a dispensary.

And then lastly, I'll say that our study only looked at the field sobriety tests. The DRE program has a much more comprehensive evaluation in determining drugs that might be impairing. And so, I think it would be important to do additional work in terms of validating those protocols with relationship to cannabis use.

Bob Barrett: That was Dr. Tom Marcotte and Dr. Rob Fitzgerald from the University of California, San Diego. They published a new research study on the detection of driving impairment using a combination of toxicology and field sobriety testing in the July 2023 issue of *Clinical Chemistry* and they've been our guests in this podcast on that topic. I'm Bob Barrett. Thanks for listening.