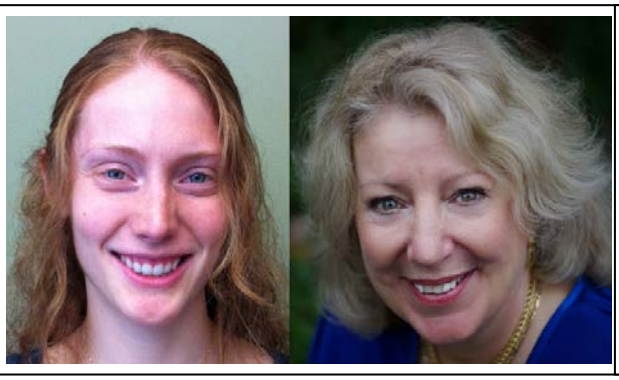
Clinical Chemistry

Cannabis Effects on Driving Skills



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Guest:
Dr. Marilyn Huestis is the Chief of the Chemistry and Drug Metabolism branch of the National Institute on Drug Abuse. Rebecca Hartman is a doctoral candidate at the University of Maryland.

Bob Barrett: This is the podcast from *Clinical Chemistry*. I am Bob Barrett.

Cannabis is the most prevalent illicit drug identified in impaired drivers. The effects cannabis has on driving continue to be debated, making legislation and prosecution difficult.

In an article in the March 2013 issue of *Clinical Chemistry,* Rebecca Hartman, a doctoral candidate at the University of Maryland and Dr. Marilyn Huestis of the Chemistry and Drug Metabolism branch of the National Institute on Drug Abuse at NIH reviewed the effects of cannabis on driving skills. They're our guests in this podcast and Dr. Huestis, we will start with you. Why is driving under the influence of cannabis still such a contested issue?

Dr. Marilyn Huestis: There are many reasons. One of the biggest issues is the fact that many of the designs of the older studies that were done on this topic, the epidemiological studies, they either did not include biological markers of recency of cannabis use or they included an inactive metabolite like carboxy-THC and this has no relationship to impairment. So the detection of carboxy-THC is much longer than the period of impairment generally. So that was one of the big problems.

Second of all our analytical techniques have improved over time and also many times, especially if there is trauma included in an accident, there can be a long delay between the timing of the accident and the specimen collection which certainly is problematic, because we know that the primary active component in cannabis which is THC, delta-9 tetrahydrocannabinol, disappears from the blood very rapidly. So in many of these cases, even though the person may have been on cannabis at time of the accident, they didn't draw the blood quick enough to be able to find it.

Also the other major contributor is the fact that in our society people use more than one drug, so it takes a very

long time to get enough cases that included, for instance cannabis itself, without the presence of alcohol or other drugs that enabled us to prove statistically that there was an increased ratio for accidents and fatalities after cannabis.

Another issue contributing is because in this country we've had many ups and downs with the legality of marijuana or cannabis, and currently 17 states I believe have medical marijuana laws that make it legal. It's not legal from a point of view of driving in any of those states, but it makes a public debate on it quite important.

And it's only recently that we have the important information from the 2007 National Roadside survey that NHTSA, National Highway Traffic Safety Administration administered, that showed that we actually had a higher prevalence of drugs in drivers than alcohol, and this was a big surprise.

We had seen it in many ways in the laboratory. We have seen it on the road studies and we had begun to see it through large studies like Drummer's study of 2004 showing that we had an increased odds ratio, but now in the United States with this survey we began to see that this is a major public health problem and needs to be addressed.

Bob Barrett: And Rebecca, we will go to you, just what are the main effects of cannabis on driving?

Rebecca Hartman: Well the important thing to remember with driving is that it's a very complex task. It requires focused detention on a lot of different things simultaneously. You have to be paying attention to what's going on in front of you as well as your environment, your surroundings. Is that pedestrian who appears to be crossing the street, going to stop and wait for you? Is he going to keep moving?

So the ability to focus on a whole bunch of factors simultaneously is crucial to the task of driving, and cannabis impairs divided attention. And that can lead to its worst effects on your ability to drive.

It also increases your lane weave rather like alcohol, you know, how much you are swerving back and forth in the lane, and your decision-making ability. Again, should I go through this yellow light or should I stop? Do I have enough time to get through the light or is it safer for me to stop here?, things of that nature. Cannabis affects your decision-making processes and so it can therefore have an impact on your driving.

It also causes sleepiness and sort of a drowsiness effect and on long stretches of mountainous driving you can sort of

lose focus and attention and so all of the sudden if you need to react to something, you may not have the ability to process it rapidly enough to prevent yourself from getting into an accident.

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Bob Barrett: Well, you mentioned alcohol, how does this differ from the effects that alcohol has on driving?

Dr. Marilyn Huestis: One of the important differences is that alcohol obviously works in different mechanisms on affecting the brain. And we know that there are differences between the two, but what's really important is that when you have alcohol in combination with cannabis, that you really increase the detrimental effects on driving performance.

So one example is alcohol tends to lower inhibitions and there is a strong increase in risk taking and tendency to drive faster. However, cannabis, we have seen that many individuals are aware that they are impaired and they think that they can slow down, that they can overcome this impairment that they have.

However, it's been shown over and over again that they are not able to. And one very, very interesting aspect of this is that for instance in a study where they gave cannabis users cannabis to smoke, and then they tested them in neurocognitive tests, they showed that they could both get the same answers.

And of course people then assume that cannabis has not affected the ability to perform well on that test, but when they did this in conjunction with brain imaging, they showed that the individual had to recruit much more of the brain in order to be able to produce that same score. And this is what we find with cannabis especially, divided attention. And divided attention means that you have to be able to take in the information from multiple sensory sources, you have to be able to understand that data and make a good choice and selection on how to respond.

And this is one of the main areas that we find with cannabis that it really affects divided attention and this is -- if you look at the types of accidents that occur after cannabis, you will frequently find something like the person is smoking, they are going down the road, they are watching and thinking that they are in control and suddenly a child will come out on a bicycle right in front of them. And they are just not able to take in that information, to process it, to make a decision on the appropriate course of action and to implement that action.

So this is one of the differences that we see, divided attention being very important for cannabis. Then you have to think about what about the challenges for studying cannabis in driving and so Rebecca why don't you talk about some of those issues that we have had to consider in our cannabis in driving research.

Rebecca Hartman: Well because of these differences, you can't just assume that a study that worked in detecting alcohol impairment is going to detect that cannabis impairment as well. You have to take into account that alcohol doesn't produce the same effect so we had redesign some old simulator studies in order to have more decision making and processing tasks than you might find in an alcohol study.

Bob Barrett: Dr. Huestis, how many states have driving under the influence of cannabis laws established like we do now for alcohol?

Dr. Marilyn Huestis: So 17 states either have a zero tolerance, meaning any detectable level of drug, or a specified limit in blood for the concentration of THC. And many others are in the process of trying to establish such a law. And there is very large movement from policy makers to try to get a model drug law, drug per se law that will cover the complex issues involved and that would be uniform or standardized across states and we are in the process of that issue right now.

To be honest, some of the laws are not written very well. For instance some laws actually include urine and say that the presence of the inactive metabolite in urine is illegal and this person should not be able to drive. There is a lot of controversy over that type of the law because the presence of carboxy-THC in urine is not in any way correlated with impairment.

So we are trying to develop good laws and they are necessary because it's very difficult to assign a particular concentration of a drug with impairment, and that's really no different than with alcohol.

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It doesn't mean that everyone--and across the states we have per se law for alcohol of 0.08%--it doesn't mean that everyone is impaired at 0.08 and that no one is impaired at 0.07. It's a spectrum of impairment across that range and so based on, I think you have to look at this from a public health and safety standpoint, there is been great strives in this country over the last 30 years in reducing drunk driving with alcohol based a lot on the efforts of MAD and other organizations to reduce that. But at the same time we have

had an increase in the incidence of drugged driving, and I mentioned one thing: until the 2007 national roadside survey, we didn't have any prevalence data that was as extensive as that to tell us what a problem it is.

The other main issue is that, for financial reasons, if someone is in a car accident where there is extensive morbidity or mortality, they will measure the alcohol concentration, and if it's above the upper limit then they will not go forward and do other drugs that are present in blood in many, many states in this country.

So we haven't even had a good signal on how serious an issue it is. And now we have that information and the Office of National Drug Control Policy, ONDCP, which is the primary organization in this country that sets drug policy, they have made it one of the top three strategies in the national drug strategy program for reducing drug use, and that's one of the top three strategies now.

So we have more information, and we have a will to do it and there are legislatures all over this country that are trying to enact these laws, but there is a tremendous controversy about it. In Colorado this bill has been introduced for multiple years and has not yet been able to pass.

So, one of the problems is the long detection window of THC in blood in chronic daily cannabis smokers. So if an individual is smoking cannabis on a less than daily basis, the THC is only going to be detectable in blood for a short period of time, similar to the window of driving impairments.

But if they are chronic daily cannabis user, they are going to have an extensive long detection period which means they may no longer be under the influence or impaired, and so one of the most important issues is whether these low concentrations that we find in blood of these chronic daily cannabis smokers, whether that indicates that there is impairment.

Bob Barrett: Do people develop tolerance to cannabis impairment? I ask that to you, Rebecca.

Rebecca Hartman: Well it's been found that they develop a tolerance to some of -- the most obvious aspects of cannabis impairments that one might observe in more recreational or occasional smokers. However, studies show that they are still impaired in critical tracking, so again the ability to stay in a lane or keep a cursor sort of focused on a specific point and the divided attention.

And although it appears that divided attention tasks were not affected at some points during the window of peak effects which starts around half an hour and goes to a couple of hours after smoking, even the chronic daily cannabis smokers are impaired on critical tracking and those crucial divided attention tasks.

Dr. Marilyn Huestis: The big question when we published our data showing that in chronic daily cannabis smokers, THC could be detected out for as long as three weeks or more, this became a big issue as to whether or not these low levels that were present in the body and therefore also we know present in the brain and other tissues, whether or not this represented a mechanism for the impairment. And so we have done two recent research results that have really impacted this.

The first was, we looked at the number of CB1 receptors in the brain in these chronic daily cannabis smokers and we did PET imaging, Positron Emission Tomography imaging, and we showed a significant decrease in these receptors in the brain and the CB1 receptors are critically important for a multitude of functions in the human.

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And we showed that these were significantly down regulated. There was neuroadaptation to reduce the number of these receptors that were available with chronic smoking, and we showed that over a three-week to four-week period that we had significant up regulation in these receptors in the specific areas of the brain that are known to be involved with cannabinoid function. So that was a very important piece of information, telling us that in these chronic daily cannabis smokers there was residual impairment that accompanied the residual drug concentration.

And then the second piece of information is can you show it in a task that is validated to reflect impaired driving? And so we recently have completed a study in these same individuals where we had the down regulated CB1 receptors. We had tested them in critical tracking and divided attention, two of the tasks that Rebecca just spoke about, and we showed impaired performance in both of these tasks, at baseline, when individuals had been smoking on a daily basis. And we showed some improvement towards normal function over a three-week period, but over that period they were still significantly impaired in critical tracking and divided attention. These are really surprising data and they really support the long-term residual effects of chronic daily cannabis smoking.

Bob Barrett: Now in the real world, recreational use frequently involves both alcohol and cannabis simultaneously. How much worse does that combination impair driving?

Dr. Marilyn Huestis: Well it has been shown to have a substantial effect. There was unique on road study that was performed to test the effect of the combination and that study utilized low doses of cannabis by today's standards.

A hundred and two hundred micrograms, kind of two levels per kilogram, which is again low quantities of THC by today's typical recreational user's standards were combined with blood alcohol content of 0.04 and it was found that their impairment imitated the impairment that you would find with the blood alcohol content of 0.09% for the lower dose and 0.014% for the higher dose of cannabis when they were combined with this low dose of alcohol. So that was the pretty substantial increase and that was relative to just THC by itself, alcohol by itself, and placebo.

Bob Barrett: Well, we'll come out of the laboratory and just start talking about what can be done. What can be done to help prevent driving under the influence of cannabis?

Dr. Marilyn Huestis: I think the most important thing for this moment is having the data, reliable data, that can inform this important public health question. And so having adequate research is really key and from this data then we hope to be able to educate the public. However, in a whole series of surveys, individuals have said that they think they understand they are impaired, that they can adjust for their impairment, and that they can continue to drive without risking and they, in asking these individuals how often they had driven under the influence of cannabis, they indicated that if there was a reason for them to need to drive, that they felt they could.

So education is important, but it's probably not enough, and as has been shown in Australia and in the European Union they have a number of important initiatives to reduce drugged driving in general and cannabis also specifically. They have seen that the deterrent affect of monitoring roadside driving is really an important issue.

So in other countries they have random stops which reduce drug use and driving tremendously, and in the passage of a model drugged driving law, we think that that would be very helpful for deterring driving under the influence of cannabis or other drugs.

So I think it's going to be a combination. We need research to determine the facts and to understand the effects of the drug. I think we need prevention to educate the public about the affects of drugged driving and I think we need a

deterrent with roadside drug testing all of which we will hopefully reduce the incidents in the US.

Bob Barrett: Well finally let's look ahead, how can we improve or understanding of the effects of cannabis on driving in the future, to better inform policy makers and the public?

Dr. Marilyn Huestis: As we were speaking just a moment ago, the Office of National Drug Control Policy has made this a major initiative and having gone to them and talked about the world's most advanced driving stimulator, which is at that University of Iowa, this was built by the National Highway Traffic Safety Administration to study issues, all kinds of issues, including texting and other distractions, cell phone distraction.

Unfortunately, this wonderful resource has never been used to test an illicit drug and its effects on driving, and so I'm going to ask Rebecca to tell you about our new study, that's underway, that is the first study of an illicit drug in driving impairment in this wonderful national resource.

Rebecca Hartman: Yes, we are very excited about this. We have spent a lot of time setting this up and taking some of the driving tasks that were used to examine other things and redesigning them as I mentioned earlier to better examine cannabis impairment.

So this study will examine cannabis in driving, looking at several different levels of cannabis administration, with and without a low dose alcohol, so it should be a very robust study examining cannabis by itself as well as that combination that's seen so frequently in the real world.

And we will be using the National Advanced Driving Simulator with simulations that we have spent a great deal of time working out what would be the appropriate scenarios that we would need to test in order to have it be sensitive to the effects of cannabis. And it's a substantial project that will encompass several different study sessions so that we can examine all these different combinations of cannabis and alcohol in the most robust way possible.

Bob Barrett: Dr. Marilyn Huestis is the Chief of the Chemistry and Drug Metabolism branch of the National Institute on Drug Abuse. Rebecca Hartman is a doctoral candidate at the University of Maryland. They have been our guests in this podcast from *Clinical Chemistry.*

I am Bob Barrett. Thanks for listening.