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Review article

Mechanisms of cannabis impairment: Implications for modeling driving performance

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ABSTRACT

Past research on cannabis has been limited in scope to THC potencies lower than legally available and efforts to integrate the effects into models of driving performance have not been attempted to date. The purpose of this systematic review is to understand the implications for modeling driving performance and describe future research needs. The risk of motor vehicle crashes increases 2-fold after smoking marijuana. Driving during acute cannabis intoxication impairs concentration, reaction time, along with a variety of other necessary driving-related skills. Changes to legislation in North America and abroad have led to an increase in cannabis' popularity. This has given rise to more potent strains, with higher THC concentrations than ever before. There is also rising usage of novel ingestion methods other than smoking, such as oral cannabis products (e.g., brownies, infused drinks, candies), vaping, and topicals. The PRISMA guidelines were followed to perform a systematic search of the PubMed database for peer-reviewed literature. Search terms were combined with keywords for driving performance: driving, performance, impairment. Grey literature was also reviewed, including congressional reports, committee reports, and roadside surveys. There is a large discrepancy between the types of cannabis products sold and what is researched. Almost all studies that used inhalation as the mode of ingestion with cannabis that is around 6% THC. This pales in comparison to the more potent strains being sold today which can exceed 20%. Which is to say nothing of extracts, which can contain 60% or more THC. Experimental protocol is another gap in research that needs to be filled. Methodologies that involve naturalistic (real world) driving environments, smoked rather than vaporized cannabis, and non-lab certified products introduce uncontrollable variables. When considering the available literature and the implications of modeling the impacts of cannabis on driving performance, two critical areas emerge that require additional research: The first is the role of cannabis potency. Second is the route of administration. Does the lower peak THC level result in smaller impacts on performance? How long does potential impairment last along the longer time-course associated with different pharmacokinetic profiles. It is critical for modeling efforts to understand the answers to these questions, accurately model the effects on driver performance, and by extension understand the risk to the public.

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1. Introduction

Research from the past half a century has shown that alcohol and cannabis independently or in combination can impair a driver's ability to operate a vehicle safely [1–6]. While great efforts have been made to reduce alcohol impaired driving by education, stricter legislation, and swaying of public opinion, this same progress has not been made with cannabis. With the proliferation of cannabis in North America and especially in Western Europe, it has become increasingly common for drivers to operate a vehicle under its influence [7,8]. This is despite the fact that impaired driving is illegal regardless of the legality of the substance being used. While prohibition of driving after cannabis use would be simpler, studies have indicated that drivers with a variety of use patterns frequently report driving within two hours post-dose [9]. This is a further challenge because many users report no negative effects associated with cannabis use and driving. In order to convince the general populous of the risks, rigorous scientific studies are needed to provide the foundational data to convey the scope of potential risk associated with cannabis use and driving across the spectrum of use patterns.

Early research in cannabis impairment was not definitive. Crancer's 1969 paper measured simulated driving performance after administration of 1.7 g of cannabis in the form of a cigarette. They concluded that impairment is not a function of dosage or prior experience [10]. By the seventies, studies began to disagree with both notions, finding that performance is, in fact, a function of dosage and prior experience [11–15].

Delta-9-tetrahydrocannabinol (THC), one of over several hundred cannabinoids, is the primary psychoactive ingredient found in the cannabis species of plant. It is, by extension, the culprit of cannabis' impairing properties and the resulting "high" that comes with it. It has been shown to degrade driving performance by impairing psychomotor functions. Examples include, but are not limited to, increased response time, decreased lateral control, and impairing divided-attention along with critical-tracking tasks. Another notable cannabinoid used in consumer products is cannabidiol (CBD). It is, and has long been, believed to be non-intoxicating. This is not to suggest that it does not play a role in impairment, as research has shown it may in fact attenuate it, along with other cannabinoids [16]. Flower is a term for the growing bud part of the female cannabis plant. Both these cannabinoids are found in flower, with most concentrated in trichomes, tiny hairs which form crystal resin that coats the cannabis plant to protect from predation and prevent seed desiccation. However, they can also be found in the leaves and stems of the plant.

Humans have an endocannabinoid system with receptors found throughout the body. CB1 receptors are found throughout the central nervous system and CB2 receptors can be found in other systems including the gastrointestinal, immune and reproductive systems [17]. THC is metabolized to 11-hydroxy THC, which maintains pharmacologic activity. This product is metabolized to carboxy-THC and carboxy-THC-glucuronide, which is no longer pharmacologically active but has a long half-life of elimination in humans.

The risk of motor vehicle crashes increases 2-fold after smoking marijuana [7]. Driving during acute cannabis intoxication impairs concentration, reaction time, along with a variety of other necessary driving-related skills [18–33]. Changes to legislation in North America and abroad have led to an increase in cannabis' popularity. This has given rise to more potent strains, with higher THC concentrations than ever before. There is also rising usage of novel ingestion methods other than smoking, such as oral cannabis products (e.g., "edibles," brownies, infused drinks, candies), vaping, and topicals [7,34,35].

Although empirical research can provide insights into how driver impairment impacts particular crash situations, the ability to generalize to the broader crash situations can be challenging. The use of driver modeling and simulation has the potential to allow for the extrapolation of research findings in the literature to better estimate that true impact of driver impairment in general and cannabis impaired driving in particular. As driver modeling efforts in crash situations have been successful in the past [36–39], the addition of an impairment module that reflects the impact on driver perception and response will facilitate the examination of the role impairment plays in specific crash situations. Past research on cannabis has been limited in scope to THC potencies lower than legally available and efforts to integrate the effects into models of driving performance have not been attempted to date. There is also limited research on more novel forms of cannabis, such as edibles and concentrates that have different pharmacokinetic profiles that need to be considered. The purpose of this systematic review is to understand the implications for modeling driving performance and describe future research needs.

2. Methods

2.1. Literature search and selection

The PRISMA guidelines [40] were followed to perform a systematic search for peer-reviewed literature using the PubMed database which was selected based on preliminary review of journal publishing literature in this field. Search terms were divided into

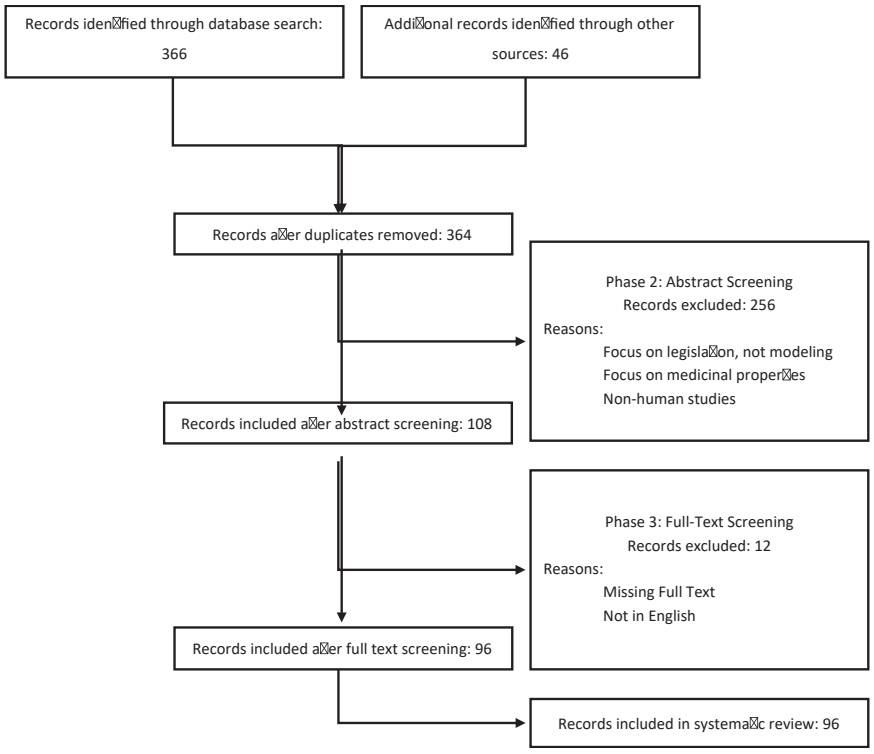

Fig. 1. Adapted from PRISMA flow-chart [40].

three categories: (1) CANNABIS AND DRIVING: cannabis, marijuana; (2) THC/CBD CONCENTRATION: concentration, THC, CBD; (3) MODES OF USE: oil, edibles, dabbing, vaporized. All three categories of search terms were combined with keywords for driving performance: driving, performance, impairment. Categories were combined with the previously mentioned performance keywords using the Boolean operator 'AND,' while the terms within each category were separated by a combination of 'OR' and 'AND.' The PRISMA flowchart in Fig. 1 shows the number of sources found and subsequent exclusions. Grey literature was also reviewed, including congressional reports, committee reports, and roadside surveys.

2.2. Selection criteria

For peer-reviewed literature, only papers in English with the full-text available were considered. Search results were screened by their abstracts for relevancy. Subsequently, the full text was assessed for eligibility. There were three outcomes of interest: cannabis' effect on driving performance, how mode of use (e.g., edibles, combustion, vaporizing) impacts said effect, and the impact of THC/CBD concentrations. To be included in this review, the studies had to investigate at least one of the aforementioned topics.

3. Changes in cannabis availability

In recent years there has been an explosion in the popularity of medical and recreational cannabis [41]. Cannabis, a term used to describe both the chemical compounds (e.g., THC and CBD) and the products for sale, has become more potent and accessible than ever. Canada has outright legalized it recreationally, along with more novel products, such as edibles, topicals, and extracts [42]. Effective January 2020, Australia legalized recreational growth and consumption of cannabis [43]. Europe's most famous example is the Netherlands, where cannabis can be found at "coffee shops" for recreational use. Medically, products manufactured by Bedrocan BV can be prescribed by doctors for use in vaporizers or tea. This same company exports to Germany, Finland, Italy, and Norway [44]. The United Kingdom (UK) has a similar arrangement with a competing company, Sativex. In the United States, although categorized as a schedule 1 controlled substance and illegal by the federal government, medical use is legal in thirty-three states and of those, recreationally legal in eleven [45]. Between 2014 and 2018, state tax revenue from cannabis sales in the United States increased nearly 16-fold to the sum of 1.3 billion dollars [46]. This is changing not only the accessibility of cannabis but also the way it is used. State's with medical marijuana laws show 'state-level patterns' of using alternative methods of ingestion (e.g., edibles, topicals, and vaping) with a significantly higher probability of vaping [34]. In Washington State, between 2014 and 2016, extract sales have increased by 145.8% and now account for 21.2% of sales [35].

3.1. Influence of potency on consumption patterns and behavior of users

If the THC level is high, then users could smoke less or increase the ratio of tobacco to cannabis. It is assumed experienced users are capable of titrating the effects of cannabis and will adjust their smoking habits to achieve this [47]. If users are titrating their usage to achieve a particular level of "high" then these high potency products may be of less concern for regular or experienced users. However, for occasional or inexperienced users who lack the ability, or knowledge, to titrate the effects of cannabis could easily inhale a large dose and risk and adverse reaction.

"Smoking topography," which relates to the factors of volume/depth of inhalation, duration of breath holding and the flow of air/smoke into and out of the lungs. All of these influence the amount of THC the user is exposed to (and absorbs) during the smoking process. Users can do this even without mixing tobacco into a cannabis cigarette. Experienced users do this already, but it is a potential problem for novice users. This is somewhat analogous to the issue some edible users experience when they consume and expect a rapid effect but because of delayed oral absorption and reduced bioavailability, they do not "feel" anything and take more.

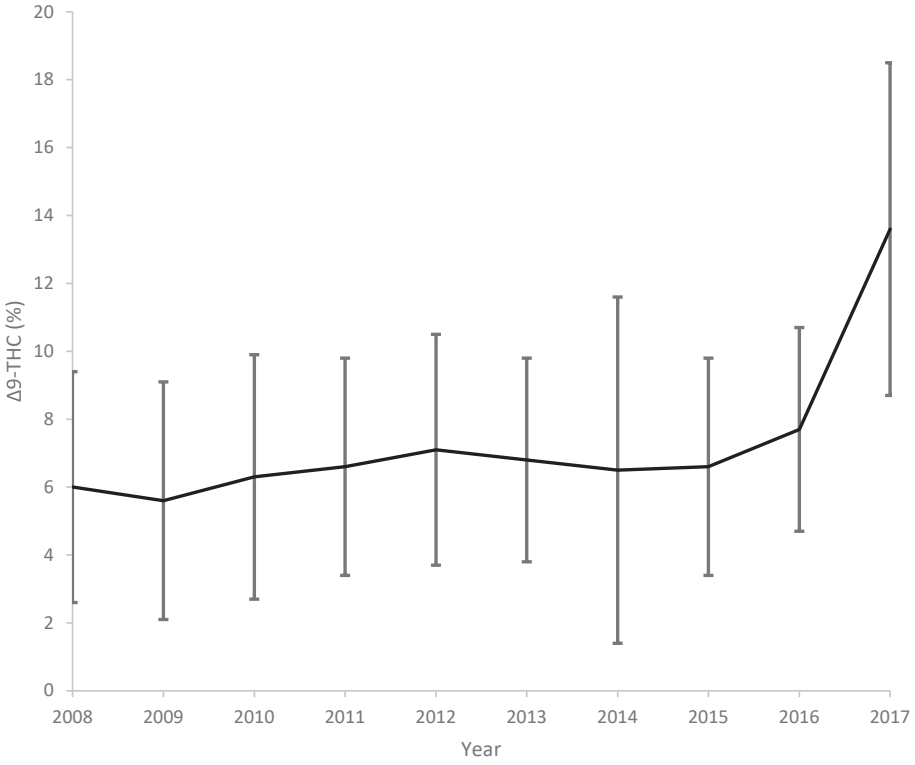

Fig. 2. Mean and standard deviation of Δ9-THC (%) potencies from 2008 to 2017 [63]. It has increased by nearly 127% since 2008, peaking at 13.6% Δ9-THC in 2017.

Eventually, it catches up with them as they experience an intense highness accompanied by bothersome side effects such as tachycardia, paranoia, nausea etc.

It is also important to consider the fact that a drug may affect an individual differently based on biological and genetic differences, psychological vulnerabilities. This can create confounds in the driving data. One recommendation would be to capture information on risk-taking and other behaviors. This points to the importance of a within-subject design.

3.2. Pharmacodynamics and pharmacokinetics of cannabis

THC can be detected in blood, plasma, oral fluid, hair, and urine. However, unlike alcohol, the relationship between blood/plasma concentration and intoxication is unclear. Its pharmacokinetics (the absorption, distribution, metabolism and elimination from the body) differ significantly with that of alcohol. Blood alcohol concentrations (BAC) decrease at a linear rate after peaking, with similar inter-user levels of impairment at a given BAC. On the other hand, measuring THC's impairment via blood, plasma, or oral fluid has a poor correlation with impairment. First, rather than a linear decline after inhalation, THC exponentially decreases in concentration [48]. THC will rapidly decrease shortly after peaking, making time-based measurements difficult. The implication being it is challenging in everyday practice to back-extrapolate concentrations to time of driving event such as road accident. This is not to say it is impossible, as there has been some success in predicting time of cannabis exposure from plasma concentrations of both THC and its metabolite THCCOOH [49,50], but it is complicated by the challenges of different use patterns with models performing better with those who had been abstaining than for those who were daily users [51]. Second, with chronic use the performance degrading effects of cannabis are not easily represented by THC concentration in blood. Chronic users will maintain elevated levels of THC in blood plasma even after abstinence and will also experience continued, lower-level impairment [52–54]. Research has shown blood plasma concentrations above 2–5 ng/ml are associated with discernable impairment [24,25,29,32,55–58].

Although CBD is considered non-intoxicating. Some research has shown it may interact with the way THC is metabolized in the body [16]. For example, one study found that when compared to a THC dominant strain of cannabis, a THC/CBD equivalent results in higher peak plasma THC concentration and worse performance in attention tasks [59]. Furthermore, low doses of CBD in conjunction with THC may result in greater intoxication due to CBD inhibiting enzymes that metabolize THC [60]. However, some research indicates that high levels of CBD might have less of an impairing effect [61].

A critical component of modeling cannabis-induced impairment is inter-user variability. A user's frequency of use can have an enormous effect on plasma THC concentration. Heavy, chronic users were shown to have detectable levels of THC in plasma after a week of abstinence. Schwope et al. found that chronic smokers showed no psychomotor indications of impairment during acute intoxication [62]. However, other studies have shown that chronic use in and of itself causes impairment in the absence of acute intoxication and after three weeks of abstinence [54]. Lastly, there are differences in self-administration. For example, with a marijuana cigarette, two people can smoke the same amount of THC, but due to behavioral factors (inhalation volume, and the number, duration, and spacing of inhalations; "smoking topography"), will have different levels of THC in plasma [16].

3.3. THC and CBD Levels

In 1995, cannabis in the United States was approximately 4% THC. In the late 2010s, average potency for flower is between 14% and 20% with more expensive strains approaching 30% THC [35,63,64]. Fig. 2 shows mean potency from 2008 to 2017. In Washington state, a flower with lower than 10% THC accounts for less than 2% of flower sales. Extracts, a more potent, processed form of cannabis (e.g., hash and oil), have reached a mean potency of 69% THC [63]. Extracts have made headlines in the past few years because of their use in vaping

and the potential health consequences that come with that [65]. Higher THC concentration in cannabis, regardless of its form (e.g., flower, extract, edible), correlates to higher peak blood THC concentrations [29,32,55,57,66]. This significant increase in the percent THC has implications for modeling impairment.

CBD levels vary wildly by product. For flower, CBD levels peaked in the mid-2000s at 0.55%. Since then, concentration has been on the decline with an average of 0.15% in 2014 [67]. Very few products have more than 4% CBD, with 98.6% and 93.9% of all flower and extracts sold having less than 4% respectively [35].

3.4. Ingestion methods

With cannabis' proliferation, the popularity of novel ingestion methods (e.g., other than the traditionally smoked flower) has exploded [7,34,35]. The mode of ingestion, along with other factors (e.g., composition, frequency of use, and presence of other drugs such as alcohol), determine the time until onset, duration of effect, and peak level of impairment.

Smoking results in the immediate presence of THC in plasma after inhalation. During which it rapidly increases, peaking only slightly below that of intravenous administration [16]. Shortly after peaking, THC levels in plasma rapidly decrease.

Edibles, a.k.a. oral ingestion, take anywhere between 30 min and 3 h for its effects to be felt [20,66,68,69]. Edibles include cannabis in the form of either cannabis butter, hash oil, or cannabis tincture. Smoking, whether it be flower or extracts, results in near-immediate onset with blood THC peaking shortly after inhalation [48,52]. Absorption of THC after oral consumption has a delayed onset and lower blood levels, most likely due to degradation in the stomach and first-pass metabolism in the liver [70]. Some studies have found that an equal dose of THC via an edible has lower blood THC levels than that of inhalation [55]. Fig. 3 and 4 plot plasma THC over time for inhalation and ingestion, respectively. However, regardless of the mode of ingestion, increased cannabis THC potency correlates to greater impairment [32,55–58,66].

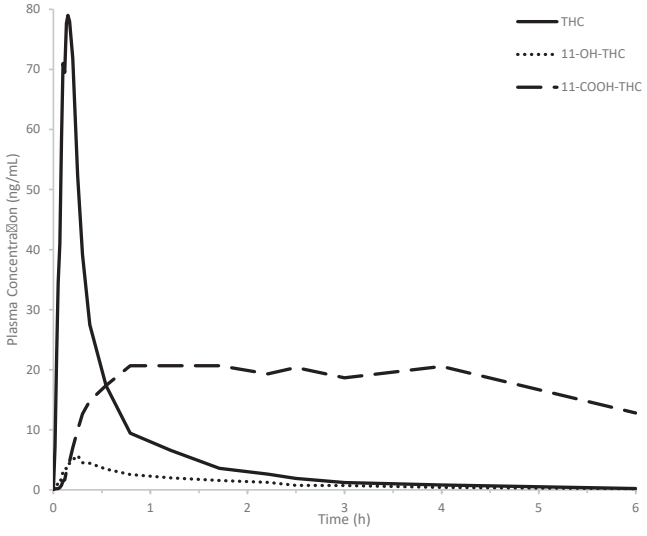

Fig. 3. Mean plasma concentrations of THC, 11-OH-THC, and 11-COOH-THC after smoking cannabis containing 15.8 mg THC (1.75%) [48]. THC rapidly peaks and decreases just as quickly.

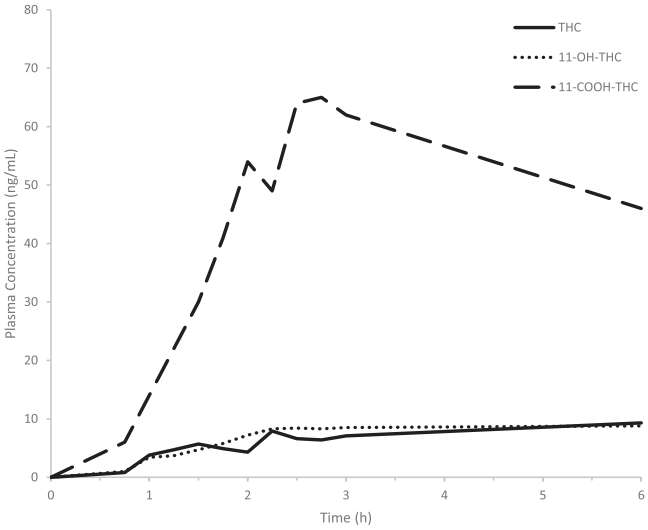

Fig. 4. Mean plasma concentrations of THC, 11-OH-THC, and 11-COOH-THC after ingesting 20 mg of THC [69]. THC levels taper to a peak over two hours after consumption.

4. Combination with other drinks

4.1. Co-consumption with alcohol

Alcohol with cannabis is the most common drug combination found in drivers [7]. However, research is inconclusive about how impairment differs when alcohol is in tandem with cannabis. Some studies suggest that alcohol and cannabis are neither synergistic nor additive [71,72]. One possible explanation for this are the methodologies of the studies. The Liguori paper used only brake latency and sense of balance as metrics of impairment. Furthermore, there were no measurements of THC content in blood or oral fluid and THC exposure was limited to a 3.33% THC cannabis cigarette. Wright and Terry focused on non-acute intoxication from regular use of cannabis, which is enlightening in and of itself but not helpful. A broader swathe of data shows that acute intoxication from alcohol, in combination with cannabis, is more impairing than either in isolation [22,24,25,28,73]. Most of the aforementioned research shows that the two are additive, rather than synergistic, with each impacting different aspects of driving performance [24]. Alcohol increases the standard deviation of speed and percent time speeding. Cannabis also decreases mean speed and increases follow distance to other vehicles. When combined, cannabis may mitigate some behaviors associated with alcohol, such as increased speed [22].

4.2. Infused drinks

Any drink that contains CBD or THC can be defined as an infused drink. In the United States, since the Farm Bill was signed into law in December 2018, hemp is no longer listed as a controlled substance [74]. Meaning, it is now possible to use CBD derived from hemp. As of 2019, the cannabis beverage market in the United States stands at 367 million dollars [75]. This is only bound to increase, with Coca-Cola investigating entering the industry in both Canada and the United States [76,77].

4.3. Mixed consumption of cannabis and synthetic cannabinoids

A relatively modern and less studied phenomena are synthetic cannabinoids. Synthetic cannabinoids, collectively referred to as "Spice" or "K2", are commercially available and can be taken alone or

sprayed onto the cannabis herb [78]. They are often used by those who want to avoid detection during a drug test, as standard urine toxicology does not test for synthetic cannabinoids. While synthetic cannabinoids stimulate the same receptors as their non-synthetic counterparts, the relative risk of requiring medical treatment is thirty times higher than natural cannabis [79]. This is because synthetic cannabinoids are full agonist whereas THC is a partial agonist [80]. Because of this higher reactivity, medical complications are more likely. Example complications include tachycardia, psychosis, and acute kidney injury [78,80].

At the time of writing, there is a paucity of research concerning the effect of synthetic cannabinoids on driving performance. However, case studies provide insight into the implication of these novel, psychoactive substances. From DUI cases, it was found that synthetic cannabinoids shared similar psychomotor detriments as their natural counterparts [81,82].

5. Implications for driving

5.1. Driving performance

Epidemiological research from the past twenty years has consistently shown cannabis-impaired driving doubles the risk of a car crash [25]. This is due to THC impairing psychomotor abilities. This spans across multiple critical driving tasks such as divided attention, reaction time, decision making, and risk-taking. A blood plasma THC concentration of 2–5 ng/ml or more is associated with driving impairment, with a more substantial impact on occasional smokers [83]. Higher concentrations are associated with more significant detriments to driving performance, meaning impairment is a function of dosage [55,57,58,84–86]. There is, however, an upper limit above which it appears THC has a diminishing effect. While 2–5 ng/ml is the accepted range at which one is deemed impaired, there is even greater attenuation of driving skill from 5 to 10 ng/ml. More specifically the percentage of observations showing significant impairment jumps from 70/90% to 75–90%. Above 30 ng/ml, however, one hundred percent of observations are indicative of impairment [32]. A common theme in current and past studies is that research has focused on cannabis with THC concentrations well under 20%, typically closer to 6% [22,24,29,32,56,57,73,85,87]. Considering that acute intoxication from THC is dose-dependent, it makes studying higher potency strains all the more critical.

Lateral control is an umbrella term for a collection of driving performance metrics. Poor lateral control is represented by a high standard deviation of lane position (SDLP). Both alcohol and cannabis increase lane weaving and, in combination, produce an additive effect [21,24–26,88–90].

Longitudinal control (e.g., following distance and speed) is also impacted by cannabis. Acute intoxication results in increased following distance, decreased mean speed, and increased percent speed low [22]. Cannabis, in combination with alcohol, has a different outcome. While alcohol use alone increases mean speed, when used with cannabis this effect is mitigated. One possible explanation is that this is a compensatory behavior [22].

5.2. Perceived impact

Given the two-fold increase in automobile crash risk associated with cannabis use, one would think its users would be somewhat aware of the danger. Surprisingly, the impairing effect of cannabis on driving is not even close to being widely accepted among its users [9,91]. A study of the drug driving behaviors of New Zealanders found that only 57% would avoid driving after using cannabis. A study in the United States conducted an online survey found that the majority of respondents believe cannabis had no effect on driving while between 15% and 27% believe it in fact made them *drive better* [9].

5.3. Mismatches

The fact that many cannabis users believe that it has no effect on driving ability, or improves it, flies in the face of the research. Studies have shown a near 2-fold increase in risk of motor vehicle crash when under the influence of cannabis [7]. After smoking cannabis, drivers implement compensatory behaviors. This has been shown in both naturalistic and simulated studies, where drivers will drive slower, avoid risky maneuvers, and increase follow distances [92]. The usage of these compensatory maneuvers suggests an innate understanding that acute cannabis intoxication is, in fact, impairing.

6. Conclusion and future direction

6.1. Gaps in current research

There is a large discrepancy between the types of cannabis products sold and what is researched. Almost all studies that have inhalation as the mode of ingestion use cannabis that is around 6% THC. This pales in comparison to the more potent strains being sold today. In Washington State, over half of flower sold contains more than 20% THC [35]. Which is to say nothing of extracts, which contain around 60% or more THC and account for one fifth of cannabis sales in Washington State [35]. As of this writing, most research involved flower with less than 10% THC [22,24,29,32,52,55–57,73,85,87]. Consumable forms of cannabis other than flower, such as edibles, extracts, and beverages are also under-represented in the current body of research. As our discussion indicate, there is an increasing variety of cannabis use. Although acknowledging smoking is still the most popular method of ingestion, more novel modes of use are increasing in popularity. Between October 2014 and September 2016, extract (concentrate) sales in Washington State have increased by 145.8% [35].

Experimental protocol is another gap that needs to be filled. Methodologies that involve naturalistic (real world) driving environments, smoked rather than vaporized cannabis, and non-lab certified products introduce uncontrollable variables. Naturalistic drives are neither as controllable nor consistent to the same degree as simulated drives. The latter offers precision in timing of driving tasks, other vehicles, and road conditions. Smoking cannabis is similar in its shortcomings, in that it introduces uncontrollable variables. First, a higher proportion of the cannabis is lost to combustion compared to vaporization. Second, smoking technique plays a large role, with factors such as side-stream (smoke that is produced but not inhaled), number of puffs, and duration and volume of inhalation all affecting the resulting high. Smoking also has health implications, with vaporization of cannabis producing lower carbon monoxide exposure relative to smoking [93]. Furthermore, vaporization is less aggravating to those with respiratory irritation [94]. It is worthwhile to note that while there is varying performance between vaporizers, vaporization can be as effective a delivery system as smoking [95]. Lastly, studies that make use of non-lab certified products cannot be sure of the chemical composition, thus making a controllable dosage more difficult. Foundational research is needed to better understand these uncontrolled variables. In the absence of said foundational research, we recommend vaporization of lab certified products ad libitum, which is consistent with research in this area [52,73,96]. Given it is illegal to drive impaired, this foundational research can serve to provide the basis for educational messaging focused on changing behaviors to better align with the inherent risks.

6.2. Implications for modeling

Future modeling of cannabis impairment will need to consider the amount and potency of THC available to the public. Furthermore, understanding mode of consumption, quantity, and time elapsed since consuming cannabis will need to be considered. This is especially true when considering the pharmacokinetic difference between, for example, smoked versus ingested cannabis.

Understanding when people feel safe to drive after consumption of cannabis will be another important consideration. Because time elapsed since exposure is such a large factor in impairment, focusing experimental procedures on timeframes when people would normally drive will be more applicable to real-world scenarios.

Future modeling should also investigate the distinction between general control and higher-level functioning. Research has already shown cannabis impacts general control of a vehicle, correlating with increased reaction times and higher SDLP relative to placebo [22]. Adjusting task demand to see its effect on higher level functioning will be important for a more complete model of impairment.

6.3. Research needs

When considering the available literature and the implications of modeling the impacts of cannabis on driving performance, two critical areas emerge that require additional research: The first is the role that the potency of the cannabis product. The second is the route of administration or mode of use.

High potency marijuana (greater than 6% THC) has been studied less than strands with lower potencies that have been around for decades. Products being sold both medically and recreationally have THC concentrations far greater than what past research has used. The extent to which these high potency strands accentuate, or change, the effects on human performance is less known. If users are titrating their usage to achieve a particular level of “high” then this may be of less concern, but current research does not provide clarity in this area. Given modeling cannabis impairment is a function of dose, it is paramount to gain a better understanding of how such high potencies impact performance.

Modes of use (e.g., vaping, edibles, and topicals) are new methods for administration of cannabis that are becoming increasingly common. They are under-represented in research and leave many questions concerning the impact on performance. Does the lower peak THC level result in smaller impacts on performance? How long does potential impairment last along the longer time-course associated with the different pharmacokinetic profile. It is critical for modeling efforts to understand the answers to these questions to understand and accurately model the effects on driver performance and understand the risk to the public.

Finally, it should be noted that there is a wide range of strategies to assess the effects of cannabis on driving performance. Epidemiological studies, psychological tests, simulated driving studies, and naturalistic driving studies. Each of these approaches have their own advantages and limitations, and their combination likely provides the best overview of the effects of cannabis on driving performance.

CRediT authorship contribution statement

Thomas Burt: Conceptualization, Methodology, Investigation, Writing – original draft. **Timothy L. Brown:** Conceptualization, Supervision, Writing – review & editing. **Gary Milavetz:** Writing – review & editing. **Daniel V. McGehee:** Conceptualization, Supervision, Writing – review & editing.

Conflict of interest

This paper was funded by internal funds at the University of Iowa. All other authors report no other conflict of interest.

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