

Contents lists available at ScienceDirect

Transportation Research Interdisciplinary Perspectives

journal homepage: www.sciencedirect.com/journal/transportationresearch-interdisciplinary-perspectives





Development of a simulation-based experimental research framework for the characterization of cannabis-related driving impairment

Zayne Thawer ^a, Jennifer L. Campos ^{b,c}, Behrang Keshavarz ^{c,d}, Robert Shewaga ^c, Andrea D. Furlan ^{c,e}, Geoff Fernie ^{c,f,g}, Bruce Haycock ^{c,h,*}

- ^a Faculty of Applied Science and Engineering, University of Toronto, Toronto, ON Canada
- ^b Department of Psychology, University of Toronto, Toronto, ON, Canada
- ^c KITE-Toronto Rehabilitation Institute, University Health Network, Toronto, ON, Canada
- ^d Department of Psychology, Ryerson University, Toronto, ON, Canada
- e University of Toronto Department of Medicine, Toronto, ON, Canada
- f University of Toronto Institute for Biomedical Engineering, Toronto, ON, Canada
- g University of Toronto Department of Surgery, Toronto, ON, Canada
- ^h University of Toronto Institute for Aerospace Studies, North York, ON, Canada

ARTICLE INFO

Keywords: Driving simulator Scenarios Driving skills Drugs Performance

ABSTRACT

Recreational use of cannabis has been recently legalized in Canada, however, its impact on driving performance and safety is not well-defined. One experimental tool that can be implemented to better examine the link between cannabis use and driving impairment is driving simulation. Customized driving scenarios can be created to target and evaluate hypothesized effects of cannabis on driving behaviors. This paper presents a framework for the evidence-based design of driving scenarios that aim to characterize cannabis-related driving impairment. The framework begins by considering the effects of cannabis on sensory, motor, and cognitive abilities, as well as how impairments in these abilities could negatively affect driving performance. Next, we examine how these negative effects on driving could be measured in a controlled, repeatable, and safe manner using simulators, to map the specific effects of cannabis on particular aspects of driving performance. Last, we describe how customized driving simulator scenario elements could be designed to challenge the targeted driving abilities that are affected by cannabis. In addition to detailing this experimental framework, a prototype scenario developed for DriverLab at KITE - Toronto Rehabilitation Institute is presented, but the expectation is that the proposed approaches could be broadly implemented across a range of simulators.

1. Introduction

The use of cannabis has been legalized in varying degrees across the globe, with Canada legalizing it for recreational use in 2018. As a result, there has been an increased urgency to better understand its impact on driving performance and safety. Cannabis affects cognitive, sensory, and motor functions (Bondallaz et al., Nov. 2016; Kalant and Porath-Waller, 2017) that are important for safety–critical tasks such as driving, including judgement, working memory, response time, coordination, and concentration (Bondallaz et al., 2016; Kalant and Porath-Waller, 2017; Ramaekers et al., 2006; Hartman and Huestis, 2013; Salomonsen-Sautel et al., 2014; Ogourtsova et al., 2018; Ashton, 2001; Capler et al., 2017).

The cannabis plant is composed of over 400 chemical compounds, including over 60 cannabinoids (Ashton, 2001; Appendino et al., 2011). The primary psychoactive component is delta-9-tetrahydrocannabinol (THC). This ingredient, along with its psychoactive and non-psychoactive metabolites, is responsible for the majority of the behavioural and pharmacological effects of cannabis use (Mechoulam and Hanuś, 2000; Perez-Reyez et al., 1991; Grotenhermen, 2003; Goledzinowski, 2017; Wolff, 2013; Kochanowski and Kała, 2005; Jager, 2012). However, there is limited scientific consensus on identifying THC concentration levels that objectively define levels of impairment (Robertson et al., 2019; Armentano, 2013), due to a poor concentration–response relationship between THC levels in bodily fluid samples (e.g., blood, urine, saliva) and driving performance (Ramaekers et al., 2006;

^{*} Corresponding author at: KITE-Toronto Rehabilitation Institute, University Health Network, Toronto, ON, Canada. *E-mail address:* bruce.haycock@uhn.ca (B. Haycock).

Papafotiou et al., 2005; Sewell et al., 2009; O'Kane et al., 2002; Arkell et al., 2021). Thus, it is important to develop methods that will aid in determining whether cannabis use affects driving performance and in what ways.

2. Cannabis composition and pharmacology

The two most prevalent methods for cannabis consumption are inhalation (i.e., smoking) and oral ingestion (i.e., edibles) (Grotenhermen, 2003; Wolff, 2013). Cannabis inhalation results in a fast peak of THC concentration in blood and saliva within the first 5-15 min after smoking (Grotenhermen, 2003; Ronen et al., 2008; Huestis and Cone, 2004), as well as a fast decrease due to the half-life of THC being approximately 1.5-2 h depending on individual usage history and other factors (Moffat et al., 2011). On the other hand, after oral ingestion absorption of THC into the bloodstream is significantly slower, with peak blood THC levels observed 1 to 5 h after administration (Wolff, 2013; Niedbala et al., 2001; Lemberger et al., 1971). Inhalation results in onset of impairment within a few minutes and recovery within a few hours, while the impairing effects from ingestion begin within 1-2 h and end up to 12 h after use (Ashton, 2001; Grotenhermen, 2003; Wolff, 2013; Kochanowski and Kała, 2005). It is also important to note that blood or saliva THC levels are not necessarily directly associated with the degree of behavioural impairment (Ramaekers et al., 2006; Ashton, 2001; Wolff, 2013; Robertson et al., 2019; Papafotiou et al., 2005; Sewell et al., 2009; O'Kane et al., 2002). Individuals can have THC detected in their blood or saliva without experiencing any psychotropic effects or exhibiting impairments. Following the use of cannabis, THC and its metabolites can be detected for long periods of time in plasma and urine, ranging from approximately 7 days for occasional users (Goledzinowski, 2017; Jager, 2012; Huestis et al., 1992) and up to 30 days for frequent users (Ashton, 2001; Lowe et al., 2009). The extent to which the behavioural impairments of cannabis use are present depends on a variety of drug- and user-related factors due to the bidirectional and biphasic nature of the drug (Jager, 2012). These considerations include route of administration, dosage of THC, titration of dose, user tolerance, user intake frequency, environment of administration, and cannabinoid absorption, metabolism, and excretion rates (Wolff, 2013; Jager, 2012; Robertson et al., 2019; Sharma et al., 2012; Fischer et al., 2017).

The current state of enforcement in Canada for roadside testing of cannabis-induced impairment includes the use of Standardized Field Sobriety Tests (SFST) and handheld drug screening devices that can detect the presence of cannabis in saliva. While the SFST has been wellvalidated for impairment due to alcohol, they have been shown to have little sensitivity to impairment from cannabis (Spindle et al., 2021). If the SFST or handheld saliva device results indicate potential impairment, the administrating officer could demand a qualitative evaluation by a drug recognition evaluator and potentially a blood test at a police station to justify a charge of impaired driving. The minimum blood THC level that results in a criminal offence is 2 ng of THC per milliliter of blood within 2 h of driving (Government of Canada, 2019). However, as discussed above, blood THC levels do not directly correlate with levels of behavioural impairment as manifested in driving performance deficits. In essence, measuring THC levels at roadside does not allow comprehensive conclusions to be drawn regarding cannabis-related impairment, thus alternative measures are needed.

Much of the previous research examining the link between cannabis use and driving safety consists of epidemiological and observational studies (Salomonsen-Sautel et al., 2014; Asbridge et al., 2014; Bédard et al., 2007; Laumon et al., 2005). Reviews of these studies have consistently shown an increased crash risk for drivers who were under the influence of cannabis compared to drivers who had not consumed cannabis (Capler et al., 2017; Mura et al., 2003; Asbridge et al., 2012; Mann et al., 2010; Li et al., 2013; Drummer et al., 2004; Dussault et al., 2002; Biecheler et al., 2008; Brubacher et al., 2019), with indications that driving after cannabis consumption is twice as likely as sober

driving to result in a collision (Szumilas, 2010). However, these studies have several limitations including potentially compromised data validity such as inaccurate blood THC levels reported due to delays between the time of crash and the time of driver blood toxicology analysis and information bias, such as drug presence presumptuously assumed to result in drug impairment (Salomonsen-Sautel et al., 2014; Asbridge et al., 2014; Bédard et al., 2007; Laumon et al., 2005; Lilienfeld, 1983; World Health Organization, 2016). Another way to determine whether associations and/or causal relationships are observed between cannabis use and driving performance is to investigate this link experimentally within controlled settings, including using driving simulators.

3. Driving simulators for cannabis research

Simulators are an attractive proxy for the real-world operation of vehicles, as many of the practical, ethical, and safety issues involved with testing human operators under the influence of drugs in the real world are avoided (Caird et al., 2011; Fisher et al., 2017; Bruck et al., 2021). Sophisticated simulation technology also provides the ability to reproduce conditions in a controlled environment, capture precise measurements of quantitative variables, receive real-time qualitative assessment from trained evaluators, and design targeted test scenarios and conditions, including challenging driving situations. Compared to real world, on-road driving assessments, simulators allow for the safe testing of driving performance without requiring impaired individuals to join live traffic and potentially endanger themselves and others. Simulators ensure that all participants experience the same driving scenario without introducing a wide range of conditions that differ across individuals, such as differences in traffic, road structure, or environmental conditions.

Several previous driving simulation studies have demonstrated associations between cannabis use and changes to driving performance (Ogourtsova et al., 2018; Papafotiou et al., 2005; Ronen et al., 2008; Micallef et al., 2018; Sexton, et al., 2000; Anderson et al., 2010; Downey et al., 2013; Hartman et al., 2015; Lenné et al., 2010; Burt et al., 2021). For instance, it has been shown that poorer lane-keeping, slower reaction times, and slower driving speeds are observed following THC consumption (Ogourtsova et al., 2018; Papafotiou et al., 2005; Ronen et al., 2008; Micallef et al., 2018; Sexton, et al., 2000; Anderson et al., 2010; Downey et al., 2013; Hartman et al., 2015; Lenné et al., 2010) relative to pre-consumption. These effects on driving performance measures have also been shown to increase in a dose-dependent manner (Bondallaz et al., 2016; Ogourtsova et al., 2018; Ronen et al., 2008; Micallef et al., 2018; Verstraete et al., 2006). However, reduced speed and minor within-lane weaving in a generic scenario representing common, everyday driving is not necessarily indicative of performance impairments that compromise driving safety across the wide range of common and challenging situations drivers face in everyday settings. This is likely due to the use of preconfigured scenarios, not customized to this specific research question.

To our knowledge, there have been no formally described approaches to provide guidance on how to construct customized driving simulation scenarios that strategically test abilities shown to be affected by cannabis. Here, we define "driving scenarios" as the terrain, driving route, situations encountered, and environmental conditions (e.g., nighttime, poor weather) represented within a simulated drive. If not designed in an evidenced-informed manner, driving scenarios may not allow for a sensitive and reliable measurement of cannabis-related effects on safe driving performance. Driving simulators also provide the ability to introduce graded challenges to test driving abilities under typical and increasingly more difficult driving situations. Therefore, in this paper we offer a framework for developing simulated driving scenarios to test for cannabis-related impairment in a controlled, repeatable, safe way, and offer a prototype driving simulation scenario as an example of this approach. This approach takes into consideration the pharmacological effects of cannabis, the resulting effects on sensory, motor, and cognitive abilities, and how impairments in these abilities could negatively affect driving.

Scenarios can be developed to strategically target particular abilities, such as the abilities that are most likely to be influenced by cannabis. Numerous quantitative data variables can be measured over time and results can be compared between control and experimental groups and among experimental conditions. Driving simulators often also include either a passenger seat or an operator station, thereby allowing for realtime qualitative assessments by trained driving evaluators and/or postdrive evaluations conducted using playback modes. However, the advantages of simulators can only truly be realized for this purpose if the scenarios are designed in ways that, a) target the sensory, motor, and cognitive abilities predicted to be affected by cannabis by, b) design terrain elements, environmental conditions, and events that require these abilities, c) allows meaningful, reliable, and valid outcome measurements to be extracted. For example, cannabis is known to result in reduced speed of processing. Speed of processing is required during driving tasks requiring rapid responses to unexpected events. Response time can be measured using braking performance. Therefore, introducing events within the driving scenario that require drivers to react quickly, such as a pedestrian entering the roadway or a leading car suddenly braking, will allow researchers to determine whether cannabis use results in poorer driving performance as evidenced through slower braking times. For many scenario elements, a range of difficulties should be included, since it may be that some measures are only sensitive to cannabis-related effects if the difficulty level is sufficiently high. This graded-difficulty process further highlights the advantages of customized simulation scenarios in that it allows researchers to safely test challenging situations and analyze performance patterns across different difficulty levels within individual participants and across participants. Factors such as route of administration and dosage of THC (as described above), should be considered when developing driving simulation scenarios and experimental protocols. For example, the length of the driving scenario should target a time window within which impairment would most likely occur (e.g., based on method of consumption).

4. Proposed framework for developing simulated driving scenarios

Impairment of any magnitude in drivers' sensory, cognitive, or motor abilities can potentially lead to unsafe driving (Leufkens et al., May 2007; Dewar and Olson, 2007; Simms, Dec. 1985; Frittelli et al., 2009). Michon's hierarchical model classifies driving behaviors into three distinct levels of performance, namely the "operational level" (e. g., controlling the steering, throttle, and brakes,), "tactical level" (e.g., maneuvering around obstacles, merging into traffic), and "strategic level" (e.g., mapping out goals and routes) (Michon, 1985). Cannabinoids can affect all hierarchical levels of driving behaviours. For instance, cannabinoids affect various parts of the central nervous system, including the basal ganglia (psychomotor control), the hippocampus (memory), and the neocortex (higher cognitive functions) (Iversen, Jun. 2003). These effects can result in reduced abilities in the domains of visual acuity, coordination, reaction time, concentration, tracking of moving objects, divided attention, sustained attention, critical tracking, working memory, and decision-making ability (Bondallaz et al., 2016; Kalant and Porath-Waller, 2017; Ramaekers et al., 2006; Hartman and Huestis, 2013; Salomonsen-Sautel et al., 2014; Ogourtsova et al., 2018; Ashton, 2001; Capler et al., 2017). As such, simulated driving scenarios should incorporate elements that target each driving behavioural level (Campos et al., 2017). For instance, operational performance elements should be implemented to assess drivers with impaired sensory processing and motor coordination abilities, while strategic performance elements may be useful to assess higher-level cognitive impairments such as problems navigating to the desired destination. In order to present graded difficulty levels, increased sensory, motor, or cognitive loads can be introduced, such as by including, for example, low visibility

environmental conditions (sensory), unexpected events (rapid motor response), or multitasking requirements (cognitive) (Campos et al., 2017). Below we highlight several representative cannabis-related effects and corresponding scenario elements and driving measures that can be used to help quantify and characterize cannabis-related driving impairments. These effects and associated scenario elements are summarized in Table 1, although the examples listed are not mutually exclusive or exhaustive.

4.1. Processing speed and reaction time

Slower processing speed has been consistently reported in

Table 1
Scenario features and dependent measures to target acute effects of cannabis use.

Effects of Cannabis Use	Performance Dependent Measures	Representative Scenario Components(Icons for events in Fig. 2 where applicable)*
Slower processing speed and response times	Braking reaction time Steering reaction	Abrupt stoppage of preceding vehicle
	time	Unexpected pedestrian crossing
		Vehicle pulling out in path or opening door
Sensory impairments	Mean headway Headway variability Mean speed Speed variability Task completion time	Follow a preceding vehicle Overtake a slow-moving vehicle Merge on a highway Turn across active bicycle lane

Poorer sustained and divided attention, poor situational awareness

Variability in lane position Mean speed Speed variability Reacting to new or unpredictable events Task completion time Extended road including straight sections and gentle curves with limited surrounding entities

Potential hazard due to vehicle that may turn in front of the driver



Unexpected object (e.g., animal) in the driving scene



Right-of-way determination



^{*} Note the examples presented in this table are not mutually exclusive or exhaustive, e.g. perceptual impairments could affect lane deviations.

individuals under the influence of cannabis (Ramaekers et al., 2006; Ogourtsova et al., 2018; Sewell et al., 2009; O'Kane et al., 2002; Ronen et al., 2008; Hart et al., 2001). For instance, a study by Ramaekers et. al tested the abilities of individuals who had inhaled a single dose of cannabis with 500 μ g/kg THC prior to complete a stop signal task and found that processing speed was significantly impaired within the first 2 h after inhalation compared to the placebo conditions (Ramaekers et al., 2006). A study performed by Ronen et. al found that participant response times were significantly higher (i.e. slower response) after inhaling a 17 mg dose of THC compared to controls (Ronen et al., 2008). These findings could reasonably be evidenced during a driving task through poorer recognition of and reaction time to safety-critical tasks. One example of a driving scenario element that can be used to measure reaction time is to introduce an unexpected event, such as the abrupt stoppage of preceding vehicles, a hidden pedestrian unexpectedly walking in front of the participant's vehicle, or a car suddenly pulling out of a parking space. The drivers' reaction times can be measured by the onset of braking or steering responses following the triggering event.

4.2. Impaired sensory abilities

Sensory impairments from cannabis use are known to result in poorer visual processing speed and depth perception (Bondallaz et al., 2016; Kalant and Porath-Waller, 2017; Ashton, 2001; O'Kane et al., 2002; Sexton, et al., 2000; Downey et al., 2013; Kurzthaler et al., 1999). Reductions in these abilities may detrimentally affect driving tasks such as maintaining headway (Bondallaz et al., 2016; Salomonsen-Sautel et al., 2014; Ogourtsova et al., 2018; Ronen et al., 2008; Sexton, et al., 2000; Anderson et al., 2010; Lenné et al., 2010), lane keeping (Bondallaz et al., 2016; Salomonsen-Sautel et al., 2014; Ogourtsova et al., 2018; Sewell et al., 2009; O'Kane et al., 2002; Ronen et al., 2008; Ronen et al., 2008; Raes et al., 2008), and speed (Ronen et al., 2008; Lenné et al., May 2010; Sexton, et al., 2000; Anderson et al., 2010; Downey et al., 2013). For example, in terms of maintaining headway, cannabis use has been associated with compensatory behaviours such as keeping a larger and more variable (Bondallaz et al., 2016; Salomonsen-Sautel et al., 2014; Ogourtsova et al., 2018; Ronen et al., 2008; Sexton, et al., 2000; Anderson et al., 2010; Lenné et al., 2010) headway from preceding vehicles, however the effect on driving safety is unclear. This can be tested using a simulated driving framework with an uneventful stretch of continuous driving where the driver must follow a preceding vehicle. To titrate difficulty, curved road segments, unpredictable leading-vehicle speed changes, and changing speed limits can be introduced.

Cannabis-related deficits in speed and distance estimation (Ronen et al., 2008; Lenné et al., 2010; Robbe, 1998) may also influence the gap judgements required for the safe overtaking of other vehicles, turning left through a trafficked intersection, or merging into an active lane. This requires the driver to use a more carefully constructed spatio-temporal strategy than simply waiting for an excessively large gap. For both overtaking, turning, and merging, the size of the gap selected to act on may be examined, as well as evaluating speed variability, lane deviations, and time to initiate passing/turning maneuvers. Such constructs can be initiated either through examiner instructions, such as directions to overtake a slow-moving or large vehicle when they deem it safe to do so, or manipulating the scenario to ensure that the desired maneuver must be completed to continue. An example of this manipulation could be a stoppage of the preceding vehicle. The difficulty of this task can be increased by including oncoming traffic, active environmental conditions, and curved segments with visual occlusions such as trees and buildings.

Previous literature has demonstrated that cannabis use can also result in reductions in average speed and greater speed variability compared to control groups (Salomonsen-Sautel et al., 2014; Sewell et al., 2009; Ronen et al., 2008; Sexton, et al., 2000). One way to capture this effect within the framework of a driving scenario is to have participants first drive along a stretch of road with very few entity features

(e.g., environmental conditions, other vehicles, trees, buildings, pedestrians, or cyclists). To increase the challenge of maintaining a specified speed, curved road segments, turns, and variable speed limits/requirements (e.g., traffic, road signs) can be introduced.

4.3. Sustained and divided attention and situational awareness

Negative effects of cannabis use include an impaired ability to successfully sustain attention and perform divided attention tasks (Ashton, 2001; Bondallaz et al., 2016; Kalant and Porath-Waller, 2017; Ramaekers et al., 2006; Hartman and Huestis, 2013). Accurate maintenance of lane positioning requires the driver to constantly attend to the current lateral position, thus cannabis is expected to induce greater variability in this positioning, possibly to the extent of inappropriate lane crossings (Bondallaz et al., 2016; Salomonsen-Sautel et al., 2014; Ogourtsova et al., 2018; Sewell et al., 2009; O'Kane et al., 2002; Ronen et al., 2008; Ronen et al., 2008; Raes et al., 2008). For instance, a driving simulatorbased study by Ronen et al. found that the root mean square of drivers' lane position increased significantly after inhaling both 13 mg and 17 mg doses of THC as compared to controls (Ronen et al., 2008). This finding of significantly increased variation in lane position was likewise drawn from another simulation-based study performed by Micallef et. al., in which cigarettes containing 20 mg of THC (Micallef et al., 2018) were administered. This was observed through drivers' lane keeping behaviours using simulator measures such as the standard deviation of lane position and number of lane deviations. To target this ability within a driving scenario, the driver could be asked to drive along an extended, reasonably straight stretch of road while avoiding turns or requiring intentional lane changes. To titrate difficulty, this stretch of road could be made more complex by including curved road segments, turns, and lane changes, as well as active environmental conditions such as rain and reduced visibility. To specifically examine the effects of poorer divided attention due to cannabis use, a secondary task (Ronen et al., 2008; Lenné et al., 2010; Ramaekers et al., 2009; Ramaekers et al., 2016) could be introduced, such as, requiring interactions with the infotainment systems or navigation systems, or completing specific cognitive tasks during driving (e.g., n-back working memory task, having a conversation). Situational awareness (Gugerty, 1997), is important for recognizing scenario elements that, while not an immediate threat, may pose a hazard in the short term such as animals or turning vehicles in the periphery.

4.4. Sample complete scenario

As a working example we have developed a simulated driving scenario that reflects the considerations and resulting features discussed above for use in DriverLab at the Kite Research Institute (Fig. 1). DriverLab features a 7 degrees-of-freedom motion system with a hydraulic hexapod carrying a full passenger vehicle mounted on a turntable with a 360-degree visual projection dome (Haycock et al., 2016). Features for generating challenging conditions include a rain simulator producing real water droplets on the windshield and a glare simulator for recreating the harsh glare of oncoming headlights at night (Campos et al., 2017; Haycock et al., 2019). While DriverLab is a very high-fidelity driving simulator enabling a wide range of driving situations and measures, the proposed framework can also be applied to driving simulators with lower levels of fidelity by selecting suitable components within the capabilities of that particular system.

The scenario contains a 24 km route with distinct terrain segments (Fig. 2) intended to be completed when participants are at or near their peak behavioural impairment due to cannabis consumption. This drive takes approximately 30 min to complete in order to provide a variety of features over the course of a reasonably natural drive, including specific scenario elements shown via icons from Table 1. Several scenario elements are innocuous or include only subtle challenges in an effort to look for a range of impairments without continual unrealistic



Fig. 1. DriverLab at the Kite Research Institute.

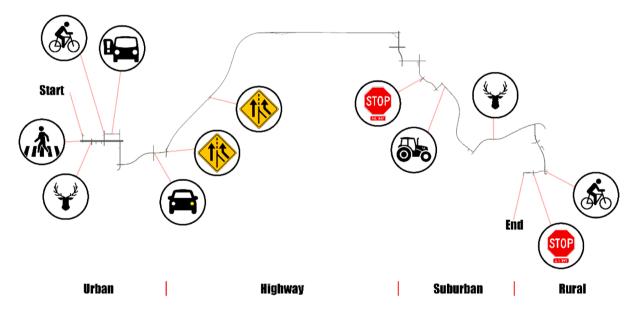


Fig. 2. Overview of terrain segments in a sample driving scenario.

disruptions. The drive begins with 6 km of driving through the downtown core of a city with many pedestrians, vehicles, and entity features (e.g., high-rise and low-rise buildings, animals, trees, crosswalks, bus stops, and traffic lights). The scenario then transitions to a 9 km stretch of divided highway driving with significantly fewer entities, followed by a 6 km stretch of driving through the countryside with some traffic signals, vehicles, and weather changes including the onset of rain. The scenario concludes with 3 km of driving in a residential neighbourhood. To date, the scenario has been piloted using non-impaired drivers, demonstrating good tolerance, feasibility, and validated procedures for extracting simulated driving performance measures. In addition to pure driving metrics from the simulator (such as measures based on driver inputs, or vehicle dynamic states), other measures can also be examined such as eye tracking (gaze direction, pupillometry), heart rate, respiration rate, expert observer ratings, and subjective ratings or questionnaires. Testing with impaired drivers awaits regulatory approval.

5. Future directions

Here, we presented a framework for the assessment of cannabis use

on driving behaviors using driving simulation technologies. The proposed framework incorporates various events and scenarios that are based on theoretical and practical considerations specifically targeting cannabis-related impairment integrated into a single driving session. To fully establish this framework, it is crucial to validate it by comparing its efficacy to other generic driving scenarios for detecting and/or characterizing cannabis-related effects, including a careful determination of the level of sensitivity and specificity, so data collection for this purpose is the next logical step. Once validation has been successfully completed, this approach can then be applied to study more specific questions regarding cannabis-related driving impairment, such as the effects of dose, route of administration, history of use, age, and association with blood/saliva concentration levels. One key application, and the motivating factor behind the development of this framework, is quantitative determinations of cannabis-induced driving impairment to inform potential improvements with roadside impairment testing. While the current work has focused specifically on impairment due to cannabis, interaction effects with alcohol use are also relevant and could be examined in a similar fashion as these two substances are often taken together, beginning with a consideration of the expected impairments

from this combination.

Establishing the proposed framework has implications for both regulation and research purposes. Upon successfully validation, the presented framework can be adopted and modified by other researchers in the field in order to study driving impairment as a result of cannabis or other drugs/medications in a targeted manner. In working through this process, simulator capabilities such as the field of view and availability of motion must be considered, as introducing some scenario features, such as hard braking, may inadvertently introduce side-effects or produce unrepresentative behaviour. In the context of regulation, a careful and detailed evaluation of the key metrics capturing driving performance deficits related to the use of cannabis could inform the development of simplified roadside testing tools for authorities to determine driving impairment more accurately. It can also be extended to safety-critical fields other than driving, such as piloting aircrafts or operating heavy machinery. This would entail following the procedure set forth in this text, beginning with the identified acute effects of cannabis use or the identification of acute effects from usage of the drug under investigation. Next, the safe operating abilities within the desired field must be determined to establish independent test measures and dependent variables that can capture hypothesized deficits in performance. Overall, hypothesis-driven approaches to simulation scenario developments should be guided by targeting the sensory, motor, and cognitive processes of interest, incorporating task requirements that require these processes, and that are designed to extract outcome measures that address meaningful application-related implications.

Funding sources

This research was funded by Ontario Centres of Excellence, grant number 30092.

CRediT authorship contribution statement

Zayne Thawer: Investigation, Data curation, Writing – original draft. Jennifer L. Campos: Conceptualization, Writing – review & editing. Behrang Keshavarz: Conceptualization, Writing – review & editing. Robert Shewaga: Investigation, Software, Writing – review & editing. Andrea D. Furlan: Conceptualization, Writing – review & editing. Geoff Fernie: Conceptualization, Writing – review & editing, Supervision, Funding acquisition. Bruce Haycock: Conceptualization, Software, Investigation, Writing – review & editing, Supervision, Project administration, Funding acquisition.

Declaration of Competing Interest

The authors declare that they have no known competing financial interests or personal relationships that could have appeared to influence the work reported in this paper.

References

- Bondallaz, P., Favrat, B., Chtioui, H., Fornari, E., Maeder, P., Giroud, C., Nov. 2016. Cannabis and its effects on driving skills. Forensic Sci. Int. 268, 92–102. https://doi.org/10.1016/j.forsciint.2016.09.007.
- Kalant H., Porath-Waller, A. J. 2020. "Clearing the Smoke on Cannabis," Canadian Centre on Substance Abuse, Ottawa, ON, 5, 2017. Accessed: Jun. 02, [Online]. Available: https://prod.ccsa.ca/sites/default/files/2019-04/CCSA-Medical-Use-of-Cannabis-Report-2016-en.pdf.
- Ramaekers, J.G., Moeller, M.R., van Ruitenbeek, P., Theunissen, E.L., Schneider, E., Kauert, G., Nov. 2006. Cognition and motor control as a function of Δ9-THC concentration in serum and oral fluid: Limits of impairment. Drug Alcohol Depend. 85 (2), 114–122. https://doi.org/10.1016/j.drugalcdep.2006.03.015.
- Hartman, R.L., Huestis, M.A., Mar. 2013. Cannabis Effects on Driving Skills. Clin. Chem. 59 (3), 478–492. https://doi.org/10.1373/clinchem.2012.194381.
- Salomonsen-Sautel, S., Min, S.-J., Sakai, J.T., Thurstone, C., Hopfer, C., Jul. 2014. Trends in fatal motor vehicle crashes before and after marijuana commercialization in Colorado. Drug Alcohol Depend. 140, 137–144. https://doi.org/10.1016/j. drugalcdep.2014.04.008.

- Ogourtsova, T., Kalaba, M., Gelinas, I., Korner-Bitensky, N., Ware, M.A., 2018. Cannabis use and driving-related performance in young recreational users: a within-subject randomized clinical trial. cmajo 6 (4), E453–E462. https://doi.org/10.9778/cmajo.20180164
- Ashton, C.H., Feb. 2001. Pharmacology and effects of cannabis: A brief review. Br. J. Psychiatry 178 (02), 101–106. https://doi.org/10.1192/bjp.178.2.101.
- Capler, R. Bilsker, D. Van Pelt, K. MacPherson, D. 2017. "Cannabis Use and Driving: Evidence Review," Canadian Drug Policy Coalition, Simon Fraser University, Mar. [Online]. Available: https://drugpolicy.ca/wp-content/uploads/2017/02/CDPC_ Cannabis-and-Driving_Evidence-Review_FINALV2_March27-2017.pdf.
- Appendino, G., Chianese, G., Taglialatela-Scafati, O., Mar. 2011. Cannabinoids: Occurrence and Medicinal Chemistry. Curr. Med. Chem. 18 (7), 1085–1099. https://doi.org/10.2174/092986711794940888.
- Mechoulam, R., Hanuś, L., Nov. 2000. A historical overview of chemical research on cannabinoids. Chem. Phys. Lipids 108 (1–2), 1–13. https://doi.org/10.1016/S0009-3084(00)00184-5
- Perez-Reyez, M., White, W.R., McDonald, S.A., Hicks, R.E., Jeffcoat, A.R., Cook, C.E., Nov. 1991. The pharmacologic effects of daily marijuana smoking in humans. Pharmacol. Biochem. Behav. 40 (3), 691–694. https://doi.org/10.1016/0091-3057 (91)90384-E.
- Grotenhermen, F., Feb. 2003. Pharmacokinetics and Pharmacodynamics of Cannabinoids. Clin. Pharmacokinet. 42 (4), 327–360. https://doi.org/10.2165/00003088-200342040-00003.
- M. Goledzinowski, "Pharmacokinetics and Detection of THC Impairment Traffic Safety Considerations in Canada: Alcohol Countermeasure Systems (ACS)," presented at the Canadian Council of Motor Transportation Administrators (CCMTA) Annual Meeting, Yellowknife, Northwest Territories, Canada, Jun. 2017. [Online]. Available: https://ccmta.ca/images/Annual_Meeting/2017_-Yellowknife/ presentations/Pharmacokinetics-and-Detection-of-THC-Impairment ACS.pdf.
- presentations/Pharmacokinetics-and-Detection-of-THC-impairment_ACS.pdf. Wolff, K., et al., Mar. 2013. Driving Under the Influence of Drugs. United Kingdom Department for Transport, London, UK.
- Kochanowski, M., Kala, M., 2005. Tetrahydrocannabinols in clinical and forensic toxicology. Przegl. Lek. 62 (6), 576–580.
- G. Jager, "Cannabis," in *Drug Abuse and Addiction in Medical Illness*, New York, NY: Springer, 2012, pp. 151–162. [Online]. Available: https://link.springer.com/chapter/10.1007/978-1-4614-3375-0 11#enumeration.
- Robertson, R. D. Woods-Fry, H. Vanlaar, W. G. M. Brown, T. G. Moore, C. 2019. "Drug-Impaired Driving: Research Needs," Transportation Research Board, Washington, D. C., E-C250, Sep. [Online]. Available: http://onlinepubs.trb.org/onlinepubs/ circulars/ec250.pdf.
- Armentano, P., 2013. Should Per Se Limits Be Imposed For Cannabis? Equating Cannabinoid Blood Concentrations with Actual Driver Impairment: Practical Limitations and Concerns. Humboldt J. Soc. Relat. 35, 41–51.
- Papafotiou, K., Carter, J.D., Stough, C., Dec. 2005. The relationship between performance on the standardised field sobriety tests, driving performance and the level of D9-tetrahydrocannabinol (THC) in blood. Forensic Sci. Int. 155 (2–3), 172–178. https://doi.org/10.1016/j.forsciint.2004.11.009.
- Sewell, R.A., Poling, J., Sofuoglu, M., 2009. The Effect of Cannabis Compared with Alcohol on Driving. Am. J. Addict. 18 (3), 185–193. https://doi.org/10.1080/ 10550490902786934.
- O'Kane, C.J., Tutt, D.C., Bauer, L.A., 2002. Cannabis and driving: A new perspective. Emerg. Med. 14 (3), 296–303. https://doi.org/10.1046/j.1442-2026.2002.00347.x.
- Arkell, T.R., Spindle, T.R., Kevin, R.C., Vandrey, R., McGregor, I.S., Feb. 2021. The fallings of per se limits to detect cannabis-induced driving impairment: Results from a simulated driving study. Traffic Inj. Prev. 22 (2), 102–107. https://doi.org/10.1080/15389588.2020.1851685.
- Asbridge, M., Mann, R., Cusimano, M.D., Trayling, C., Roerecke, M., Tallon, J.M., Whipp, A., Rehm, J., 2014. Cannabis and traffic collision risk: findings from a case-crossover study of injured drivers presenting to emergency departments. Int. J. Public Health 59 (2), 395–404. https://doi.org/10.1007/s00038-013-0512-z.
- Bédard, M., Dubois, S., Weaver, B., 2007. The Impact of Cannabis on Driving. Can. J. Public Health 98 (1), 6–11. https://doi.org/10.1007/BF03405376.
- Laumon, B., Gadegbeku, B., Martin, J.-L., Biecheler, M.-B., 2005. Cannabis intoxication and fatal road crashes in France: population based case-control study. BMJ 331 (7529), 1371. https://doi.org/10.1136/bmj.38648.617986.1F.
- Mura, P., Kintz, P., Ludes, B., Gaulier, J.M., Marquet, P., Martin-Dupont, S., Vincent, F., Kaddour, A., Goullé, J.P., Nouveau, J., Moulsma, M., Tilhet-Coartet, S., Pourrat, O., 2003. Comparison of the prevalence of alcohol, cannabis and other drugs between 900 injured drivers and 900 control subjects: results of a French collaborative study. Forensic Sci. Int. 133 (1-2), 79–85. https://doi.org/10.1016/S0379-0738(03)00052-5.
- Asbridge, M. Hayden, J. A. Cartwright, J. L. "Acute cannabis consumption and motor vehicle collision risk: systematic review of observational studies and meta-analysis," BMJ, vol. 344, pp. 1–9, 2012, doi: 10.1136/bmj.e536.
- Mann, R.E., Stoduto, G., Ialomiteanu, A., Asbridge, M., Smart, R.G., Wickens, C.M., 2010. Self-Reported Collision Risk Associated With Cannabis Use and Driving After Cannabis Use Among Ontario Adults. Traffic Inj. Prev. 11 (2), 115–122. https://doi. org/10.1080/1539589003536704
- Li, G., Brady, J.E., Chen, Q., 2013. Drug use and fatal motor vehicle crashes: A case-control study. Accid. Anal. Prev. 60, 205–210. https://doi.org/10.1016/j.com/2013.09.001.
- Drummer, O.H., Gerostamoulos, J., Batziris, H., Chu, M., Caplehorn, J., Robertson, M.D., Swann, P., 2004. The involvement of drugs in drivers of motor vehicles killed in Australian road traffic crashes. Accid. Anal. Prev. 36 (2), 239–248. https://doi.org/10.1016/S0001-4575(02)00153-7.

- Dussault, C., Brault, M., Bouchard, J., Lemire, A.M., 2002. "The contribution of alcohol and other drugs among fatally injured drivers in Quebec: some preliminary results", presented at the 16th International Conference on Alcohol, Drugs and Traffic Safety -T2002. Montréal, Québec, Canada.
- Biecheler, M.-B., Peytavin, J.-F., the SAM Group, Facy, F., Martineau, H., 2008. SAM Survey on 'Drugs and Fatal Accidents': Search of Substances Consumed and Comparison between Drivers Involved under the Influence of Alcohol or Cannabis. Traffic Inj. Prev. 9 (1), 11–21. https://doi.org/10.1080/15389580701737561.
- Brubacher, J.R., Chan, H., Erdelyi, S., Macdonald, S., Asbridge, M., Mann, R.E., Eppler, J., Lund, A., MacPherson, A., Martz, W., Schreiber, W.E., Brant, R., Purssell, R.A., 2019. Cannabis use as a risk factor for causing motor vehicle crashes: a prospective study. Addiction 114 (9), 1616–1626.
- Szumilas, M., Aug. 2010. Explaining Odds Ratios. J. Canad. Acad. Child Adolesc. Psych. 19 (3), 227–229.
- Lilienfeld, A.M., Oct. 1983. Practical limitations of epidemiologic methods. Environ. Health Perspect. 52, 3–8. https://doi.org/10.1289/ehp.83523.
- World Health Organization, 2016. The health and social effects of nonmedical cannabis use. WHO Press, Geneva, Switzerland
- Caird, J., Horrey, W., 2011. In: Handbook of Driving Simulation for Engineering, Medicine, and Psychology. CRC Press. https://doi.org/10.1201/b10836-6.
- Fisher, D.L., Rizzo, M., Caird, J., Lee, J.D., 2017. Handbook of driving simulation for engineering, medicine, and psychology. Place of publication not identified, ROUTE FIGE.
- Bruck, L., Haycock, B., Emadi, A., 2021. A Review of Driving Simulation Technology and Applications. IEEE Open J. Vehicul. Technol. 2, 1–16. https://doi.org/10.1109/
- Ronen, A., Gershon, P., Drobiner, H., Rabinovich, A., Bar-Hamburger, R., Mechoulam, R., Cassuto, Y., Shinar, D., 2008. Effects of THC on driving performance, physiological state and subjective feelings relative to alcohol. Accid. Anal. Prev. 40 (3), 926–934. https://doi.org/10.1016/j.aap.2007.10.011.
- Micallef, J., Dupouey, J., Jouve, E., Truillet, R., Lacarelle, B., Taillard, J., Daurat, A., Authié, C., Blin, O., Rascol, O., Philip, P., Mestre, D., 2018. Cannabis smoking impairs driving performance on the simulator and real driving: a randomized, double-blind, placebo-controlled, crossover trial. Fundam. Clin. Pharmacol. 32 (5), 558–570. https://doi.org/10.1111/fcp.12382.
- Sexton B. F. et al., "The influence of cannabis on driving," Transport Research Library Limited, 2000. [Online]. Available: http://dev.norml.org.nz/downloads/ DrivingTRL477.pdf.
- Anderson, B.M., Rizzo, M., Block, R.I., Pearlson, G.D., O'Leary, D.S., Mar. 2010. Sex Differences in the Effects of Marijuana on Simulated Driving Performance. J. Psychoact. Drugs 42 (1), 19–30. https://doi.org/10.1080/02791072.2010.10399782.
- Downey, L.A., King, R., Papafotiou, K., Swann, P., Ogden, E., Boorman, M., Stough, C., 2013. The effects of cannabis and alcohol on simulated driving: Influences of dose and experience. Accid. Anal. Prev. 50, 879–886. https://doi.org/10.1016/j. aap.2012.07.016.
- Hartman, R.L., Brown, T.L., Milavetz, G., Spurgin, A., Pierce, R.S., Gorelick, D.A., Gaffney, G., Huestis, M.A., 2015. Cannabis effects on driving lateral control with and without alcohol. Drug Alcohol Depend. 154, 25–37. https://doi.org/10.1016/j. drugalcep. 2015. 06.015
- Lenné, M.G., Dietze, P.M., Triggs, T.J., Walmsley, S., Murphy, B., Redman, J.R., May 2010. The effects of cannabis and alcohol on simulated arterial driving: Influences of driving experience and task demand. Accid. Anal. Prev. 42 (3), 859–866. https://doi. org/10.1016/j.aap.2009.04.021.
- Burt, T.S., Brown, T.L., Schmitt, R., McGehee, D., Milavetz, G., Gaffney, G.R., Berka, C., 2021. Perceived effects of cannabis and changes in driving performance under the influence of cannabis. Traffic Inj. Prev. 22 (sup1), S8–S13.
- A. G. Verstraete and E. Raes, "Rosita-2 Project: Final Report," Ghent University, Ghent, Belgium, Mar. 2006. [Online]. Available: https://www.marker-test.de/_Resources/Persistent/c8378f55590704d3571a9692e49eb9b7b9ff1824/rosita-2-project-final-report.pdf.
- Huestis, M.A., Cone, E.J., Sep. 2004. Relationship of Δ9-Tetrahydrocannabinol Concentrations in Oral Fluid and Plasma after Controlled Administration of Smoked Cannabis. J. Anal. Toxicol. 28 (6), 394–399. https://doi.org/10.1093/jat/28.6.394.
- Moffat, A.C., Osselton, M.D., Widdop, B., Watts, J., 2011. Clarke's Analysis of Drugs and Poisons. 4th ed. Pharmaceutical Press.
- Niedbala, R.S., Kardos, K.W., Fritch, D.F., Kardos, S., Fries, T., Waga, J., Robb, J., Cone, E.J., 2001. Detection of Marijuana Use by Oral Fluid and Urine Analysis Following Single-Dose Administration of Smoked and Oral Marijuana. J. Anal. Toxicol. 25 (5), 289–303. https://doi.org/10.1093/jat/25.5.289.
- Lemberger, L., Axelrod, J., Kopin, I.J., 1971. Metabolism and Disposition of delta-9-tetrahydrocannabinol in Man. Pharmacol. Rev. 23 (4), 371–380.

- Huestis, M.A., Henningfield, J.E., Cone, E.J., Sep. 1992. Blood Cannabinoids. I. Absorption of THC and Formation of 11-OH-THC and THCCOOH During and After Smoking Marijuana. J. Anal. Toxicol. 16 (5), 276–282. https://doi.org/10.1093/jat/ 16.5.276
- Lowe, R.H., Abraham, T.T., Darwin, W.D., Herning, R., Cadet, J.L., Huestis, M.A., Nov. 2009. Extended urinary Δ9-tetrahydrocannabinol excretion in chronic cannabis users precludes use as a biomarker of new drug exposure. Drug Alcohol Depend. 105 (1–2), 24–32. https://doi.org/10.1016/j.drugalcdep.2009.05.027.
- Sharma, P., Murthy, P., Bharath, M.M.S., 2012. Chemistry, Metabolism, and Toxicology of Cannabis: Clinical Implications. Iran. J. Psych. 7 (4), 149–156.
- Fischer, B., Russell, C., Sabioni, P., van den Brink, W., Le Foll, B., Hall, W., Rehm, J., Room, R., 2017. Lower-Risk Cannabis Use Guidelines: A Comprehensive Update of Evidence and Recommendations. Am. J. Public Health 107 (8), e1–e12. https://doi. org/10.2105/AJPH.2017.303818.
- Spindle, T.R., Martin, E.L., Grabenauer, M., Woodward, T., Milburn, M.A., Vandrey, R., Jul. 2021. Assessment of cognitive and psychomotor impairment, subjective effects, and blood THC concentrations following acute administration of oral and vaporized cannabs. J. Psychopharmacol. 35 (7), 786–803. https://doi.org/10.1177/ 0269811211021583
- Government of Canada: Department of Justice, 2019. "Legislative Background: reforms to the Transportation Provisions of the Criminal Code (Bill C-46)," *Criminal Justice: Impaired Driving Laws*, Aug. 30, https://www.justice.gc.ca/eng/cj-jp/sidl-rlcfa/c46/p3.html.
- Leufkens, T.R.M., Vermeeren, A., Smink, B.E., van Ruitenbeek, P., Ramaekers, J.G., May 2007. Cognitive, psychomotor and actual driving performance in healthy volunteers after immediate and extended release formulations of alprazolam 1 mg. Psychopharmacology 191, 951–959. https://doi.org/10.1007/s00213-006-0669-8.
- Dewar, R., Olson, P., 2007. Human Factors in Traffic Safety, 2nd ed. Lawyers & Judges Publishing Company, Incorporated, Tucson, Arizona
- Simms, B., Dec. 1985. Perception and Driving: Theory and Practice. Br. J. Occupat. Theor. 48 (12), 363–366. https://doi.org/10.1177/030802268504801204.
- Frittelli, C., Borghetti, D., Iudice, G., Bonanni, E., Maestri, M., Tognoni, G., Pasquali, L., Iudice, A., 2009. Effects of Alzheimer's disease and mild cognitive impairment on driving ability: a controlled clinical study by simulated driving test. Int. J. Geriat. Psych. 24 (3), 232–238. https://doi.org/10.1002/gps.2095.
- Michon, J.A., 1985. "A critical review of driver behavior models: what do we know, what should we do?", in *Human Behavior and Traffic Safety*. Plenum Press, New York, pp. 485–524.
- Iversen, L., Jun. 2003. Cannabis and the brain. Brain 126 (6), 1252–1270. https://doi. org/10.1093/brain/awg143.
- Campos, J.L., Bédard, M., Classen, S., Delparte, J.J., Hebert, D.A., Hyde, N., Law, G., Naglie, G., Yung, S., Aug. 2017. Guiding Framework for Driver Assessment Using Driving Simulators. Front. Psychol. 8 https://doi.org/10.3389/fpsyg.2017.01428.
- Hart, C.L., van Gorp, W., Haney, M., Foltin, R.W., Fischman, M.W., 2001. Effects of Acute Smoked Marijuana on Complex Cognitive Performance. Neuropsychopharmacology 25, 757–765. https://doi.org/10.1016/S0893-133X(01)00273-1.
- Kurzthaler, I., Hummer, M., Miller, C., Sperner-Unterweger, B., Gunther, V., Wechdorn, H., Battista, H.-J., Fleischhacker, W.W., 1999. Effect of cannabis use on cognitive functions and driving ability. The J. Clin. Psych. 60 (6), 395–399. https:// doi.org/10.4088/JCP.v600609
- Raes, E., Van den Neste, T., Verstraete, A.G., 2008. Drug use, impaired driving and traffic accidents. European Monitoring Centre for Drugs and Drug Addiction, Luxembourg.
- H. W. J. Robbe, "Marijuana's impairing effects on driving are moderate when taken alone but severe when combined with alcohol," Human Psychopharmacology, vol. 13, no. 2, pp. S70–S78, Dec. 1998, doi: 10.1002/(SICI)1099-1077(1998110)13:2+
 S70::AID-HUP50>3.0.CO:2-R.
- Ramaekers, J.G., Kauert, G., Theunissen, E.L., Toennes, S.W., Moeller, M.R., 2009. Neurocognitive performance during acute THC intoxication in heavy and occasional cannabis users. J. Psychopharmacol. 23 (3), 266–277. https://doi.org/10.1177/ 0269881108092393.
- Ramaekers, J.G., van Wel, J.H., Spronk, D.B., Toennes, S.W., Kuypers, K.P.C., Theunissen, E.L., Verkes, R.J., 2016. Cannabis and tolerance: acute drug impairment as a function of cannabis use history. Sci. Rep. 6 (1) https://doi.org/10.1038/ crep/26943
- Gugerty, L.J., Mar. 1997. Situation awareness during driving: Explicit and implicit knowledge in dynamic spatial memory. J. Exp. Psychol.: Appl. 3 (1), 42–66. https://doi.org/10.1037/1076-898X.3.1.42.
- Haycock, B., Campos, J., Keshavarz, B., Fernie, G., Potter, M., Advani, S., Sep. 2016. "DriverLab: A standards setting simulator for driving in challenging conditions", presented at the Driving Simulation Conference. France, Paris.
- Haycock, B.C., Campos, J.L., Koenraad, N., Potter, M., Advani, S.K., Feb. 2019. Creating Headlight Glare in a Driving Simulator. Transport. Res. Part F: Traff. Psychol. Behav. 61, 93–106. https://doi.org/10.1016/j.trf.2017.10.006.