**Title**:

Impact of Cannabis and Low Alcohol Concentration on Divided Attention Tasks during Driving

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**Data Availability Statement:**

The data that support the findings of this study are available from the corresponding author, [author initials], upon reasonable request.

**STRUCTURED ABSTRACT**

**Objective**: To assess divided attention performance when driving under the influence of cannabis with and without alcohol. Three divided attention tasks were performed following administration of placebo, cannabis and/or alcohol.

**Methods**: Healthy adult cannabis users participated in 6 sessions, receiving combinations of cannabis (placebo/low-THC/high-THC) and alcohol (placebo/active) in randomized order, separated by washout periods of ≥1 week. At 0.5 hours post-dosing, participants performed simulator drives in the University of Iowa National Advanced Driving Simulator (NADS-1), a full vehicle cab simulator with a 360° horizontal field of view and motion base that provided realistic feedback. Drives contained repeated instances of three tasks: a side-mirror task (reaction to a triangle appearing in the side-mirrors), an artist-search task (select a specified artist from a navigable menu on the vehicle’s console), and a message-reading task (read aloud a message displayed on the console). Blood THC and breath alcohol concentration (BrAC) were interpolated using individual power curves from samples collected approximately 0.17, 0.42, 1.4, and 2.3 hours post-dose. Driving measures during tasks were compared to equal-duration control periods occurring just prior to the task. Performance shifts, task completion, and lane departures were modeled relative to blood THC and BrAC using mixed-effects regression models.

**Results**: Each 1 µg/L increase in blood THC concentration predicted increased odds of failing to complete the artist-search task (OR: 1.05, 95% CI: 1.01-1.11, p=0.046), increased odds of selecting at least one incorrect response (OR: 1.05, 95% CI: 1.00-1.09, p=0.041), declines in speed during the side-mirror task (0.005 m/s, 95% CI: 0.001-0.009, p=0.023), and longer lane departure durations during the artist-search task (0.74% of task-period, 95% CI: 0.12-1.36 p=0.020). BrAC (approximately 0.05%) was not associated with task performance, though each 0.01g/210 L increase predicted longer departure durations during the side-mirror task (1.41% of task-period, 95% CI: 0.08-2.76, p=0.040), and increased standard deviation of lane position in the message-reading task (0.61 cm, 95% CI: 0.14-1.08, p = 0.011).

**Conclusions**: With increasing medical and legal cannabis use, understanding the impact of acute cannabis use on driving performance, including divided attention is essential. These data indicate that impaired divided attention performance is a safety concern.

**Keywords**: Cannabis, THC, driving, alcohol, divided attention, Marijuana

**INTRODUCTION**

Alcohol and cannabis are the most common legal and illegal drugs detected in drivers worldwide. The detrimental effects of alcohol are well-documented and include delayed reaction times, impaired visual function, and slower information processing. Alcohol slows braking times, impairs drivers’ ability to maintain lane positions, and decreases the detection of potential hazards on the roadway (Martin et al. 2013). Recent meta-analyses showed blood alcohol concentration was associated with increased standard deviation of lane position (SDLP) and standard deviation of speed (SDS), two established measures of lateral and longitudinal control respectively (Irwin et al. 2017, Hartman et al. 2015, Hartman et al. 2016).

The effects of cannabis are less clear. The principal psychoactive compound in cannabis, Δ9-tetrahydrocannabinol (THC), impairs executive function and decision making, decreases perceptual motor speed and accuracy, worsens concentration, and alters the activity of the brain networks involved in cognition (Ramaekers et al. 2009). Previous research observed that cannabis use increases lane weaving, decreases driving speed, and increases variability in headways and lane positioning (Anderson et. al 2010, Downey et al. 2013). While many studies linked blood THC concentration with increased crash risk and driver culpability, the degree to which cannabis use increases crash risk is less clear, with recent meta-analyses finding highly variable and sometimes contradictory results. Additionally, cannabis is frequently used in tandem with other drugs, complicating risk attribution. Li et al. (2013) and Asbridge et al. (2012) reported that cannabis was a significant contributor to fatal crash risk, regardless of the presence of alcohol or other drugs.

The present study examines the influence of cannabis, with and without alcohol, on the performance of drivers engaged in divided attention tasks, including tuning the radio or using navigation maps, as is increasingly common in modern driving. For non-impaired drivers, a recent meta-analysis found 80% of 350 identified studies reported detrimental effects of secondary divided attention task engagement on driving performance (Ferdinand et al. 2014). Given the established effects of cannabis and alcohol, performance declines may be more pronounced in intoxicated drivers; however, we are unaware of existing research into this hypothesis. This research seeks to evaluate the relationship between THC, alcohol, and divided attention tasks performed while driving, and is part of a series of manuscripts evaluating cannabis and alcohol’s effects on driving with the NADS-1. Earlier publications evaluated the effects of cannabis and/or alcohol on lateral control (Hartman et al. 2015), and longitudinal control (Hartman et al. 2016).

**METHODS**

Note: Additional references for this manuscript can be found in the bibliography in the Appendix.

**Participants**

Healthy individuals aged 21-55, with self-reported cannabis use ≥1-3x/month but ≤3days/week over the past 3 months were recruited. Eligibility criteria required all participants to be licensed drivers for ≥2 years, with valid unrestricted licenses, and self-reported driving ≥1300 miles in the past year. Exclusion criteria were a past or current clinically significant medical illness; history of clinically significant adverse events related to cannabis or alcohol or motion sickness; a ≥450 mL blood donation in the 2 weeks before drug administration; currently pregnant or nursing; an interest in drug abuse treatment within the past 60 days; currently taking drugs contraindicated with cannabis or alcohol or known to impact driving; need for non-standard driving equipment; or prior participation in a similar driving simulator study. The study was approved by the University of Iowa IRB; all participants gave written informed consent before starting the study.

**Dosing**

Each participant attended 6 sessions, separated by washout periods ≥1 week, receiving different combinations of cannabis (placebo, low THC, high THC) and alcohol (placebo, active) in randomized order. Participants spent 10-16 h at the research clinic prior to controlled drug administration to ensure they were not acutely intoxicated. Sessions began with the participant drinking either 90% grain alcohol in fruit juice until reaching 0.065% peak breath alcohol concentration (BrAC, Alco-Sensor FST, Intoximeters, St. Louis MO), or a placebo drink with an alcohol-swabbed rim. After drinking, participants inhaled 500 mg placebo (0.008±0.002% THC), low THC (2.9±0.14%), or high THC (6.7±0.05%) vaporized cannabis (NIDA Chemistry and Physiological Systems Research Branch) ad libitum over 10 minutes using a Volcano® desk-top vaporizer (Storz & Bickel, Tuttlingen, Germany).

**Data Collection**

Simulated drives occurred 0.5-1.3 h after dosing in the University of Iowa National Advanced Driving Simulator (NADS-1), a full vehicle cab simulator with a 360° horizontal field of view and a motion base that provides realistic feedback. Following a short practice drive, participants embarked on a challenging 45-min main drive containing varied road segments and numerous programmed events. Event orders were randomized to minimize familiarity across the 6 sessions. During each drive, NADS-1 recorded driver inputs and vehicles states, which were processed and recorded as 60 Hz time-series data files.

Peripheral venous blood collection was performed 0.17, 0.42, 1.4, and 2.3 hours post-inhalation, and blood THC concentration was quantified by a previously-published method (Schwope et al. 2011). 0.5 mL blood was protein-precipitated with ice-cold acetonitrile, and supernatants diluted and solid-phase extracted. THC concentrations and BrAC were interpolated using individual power curves derived from these four measurements (Hartman et al. 2015), thereby, providing estimated concentrations at every point during the drive.

**Divided Attention Tasks**

During each drive, participants were prompted to complete multiple instances of three different divided attention tasks.

The *side-mirror* task required participants to push a button whenever a red triangle appeared in one of their side-mirrors. If ignored, the triangle disappeared after 5 seconds, resulting in an incompletion for that instance of the task. Otherwise, the length of time the triangle was visible prior to completion was recorded. The side-mirror task occurred 14 times during each drive.

The *artist-search* task required participants to select the correct artist from a 3-page navigable touchscreen menu on the vehicle’s console, each page listing 12 artists. The task occurred 3 times during each drive, and participants had 10 seconds to provide a correct response before failing that instance of the task. Completion time and a count of incorrect selections were recorded.

The *message-reading* task required participants to read aloud a text message shown on the car’s display. Messages were designed to be of equal difficulty, containing an average of 18 words (min=15, max=24) and 111 characters (min=93, max=141). The task occurred 6 times in each drive, with each message displayed for 10 seconds.

**Statistical Analyses**

Data were analyzed separately for each divided attention task. Three different aspects of performance were evaluated while engaged in each task: changes in speed and lateral control; prevalence and duration of lane departures; and performance on the task itself.

We define the task period as the time interval beginning when a task first became available and ending when the task terminated (either due to completion or time-out). For evaluating changes in speed and lateral control, we paired each task period with an equal duration control period immediately prior to the task becoming available. Across the task and control periods, paired differences in SDLP, average speed (Speed), and SDS were then modeled in response to blood THC concentration, BrAC, and their possible interaction using mixed effects linear regression models.

For the second series of analyses, lane departures and departure durations were derived using the width of the NADS-1 vehicle chassis, the lane width of the roadway segment, and the position of the vehicle’s center of mass within the lane. Departures were characterized using three nested categories of severity: minor departures –any portion of the vehicle was out of lane, major departures – ≥25% of the vehicle’s width was out of lane, and extreme departures – ≥50% of the vehicle’s width was out of lane. The presence of each category of departure during a task period was modeled in response to blood THC concentration, BrAC, and their possible interaction using mixed effects logistic regression models. Among task periods where a departure was observed, the duration of the departure (defined as a fraction of the task period) was also modeled in response to blood THC concentration, BrAC, and their possible interaction using mixed effects linear regression models.

Task performance was measured by successful task completion, prevalence of an incorrect response, and time taken to complete the task. Each outcome was modeled in response to blood THC concentration, BrAC, and their possible interaction. No completion or time data were available for the message-reading task due to the high costs of manually coding and verifying these outcomes.

All models included subject-specific random intercepts and were fit using maximum likelihood via the lme4 package (Bates et al. 2015) in R version 3.5.1 (R Core Team. 2018). For quantitative dependent measures, the Gaussian distribution and identity link function were used; for binary measures, the binomial distribution and logit link were employed. Performance shift and task performance models each included covariates that adjusted for task-specific difficulty factors, such as page number in the artist-search task or message length in the message-reading task, as well as road segment (urban, rural, or interstate). Lane departure models included covariates that adjusted for speed and initial lane position at the onset of the task period. For each model, the Akaike Information Criterion (AIC) was used to determine whether an interaction between THC and BrAC warranted inclusion in the model. In each analysis, we report model coefficients for the estimated effects of THC, BrAC, and their interaction (if selected), as well 95% Wald confidence intervals and p-values.

**RESULTS**

**Participants**

Fifty-five healthy adults enrolled, of whom nineteen completed the study (68% male, ages 21-37 years, 74% white). Of these, sixteen reported consuming cannabis ≥2x/month, but ≤3days/week, and three reported consuming cannabis ≤1x/month. Fifteen reported their most recent use as less than one week prior to admission (mean=12.5, median=4.0, sd=27.9). Self-reported driving experience ranged from 6-23 years (mean=10, median=10, sd =4), and all participants reported driving ≥1x/week. The first visit of one participant (#18) was excluded from analyses on the side-mirror task due to completing 0 of 14 task instances on that drive. The high-THC/placebo drive for one participant (#7) did not have data for the message-reading task and was also excluded. Otherwise, all participants had at least one recorded event for each task, and 94.8%, 98.3% and 99.1% of the programmed instances of the side-mirror, artist-search, and message-reading tasks, respectively, were included in our analyses.

**Dosing**

Blood THC concentration showed high variability by dosing condition (Fig. 1). Several subjects had greater blood THC concentrations on the low-THC condition than on the high-THC condition, prompting our decision to base our statistical analyses on blood THC concentration, rather than assigned THC dose group.

**Divided Attention Tasks**

Completion rates varied considerably by task (p<0.001), with higher completion rates for the side-mirror task (93.3 %) and lower completion rates for the artist-search task (61.8%). Average completion times were 1.85 seconds for the side-mirror task and 5.89 seconds for the artist-search (p<0.001). Summaries of participants’ THC and BrAC concentrations, Speed, SDLP, and SDS during task periods by dosing condition and drive segment are in Tables A1-A3 in the appendix.

**Task Performance**

A summary of task performance models is in Table 1. For the artist-search task, each 1 µg/L increase in THC concentration led to 5.4% increased odds of failing to complete the task (OR 1.054, 95% CI: 1.01-1.11, p=0.046). Blood THC concentration was a significant predictor of incorrect responses; each 1 µg/L increase in THC concentration led to 4.7% increased odds of selecting an incorrect artist (OR 1.047, 95% CI: 1.00-1.09, p=0.041). THC concentration was associated with significantly longer time spent on the artist-search task (0.05 sec per 1 µg/L increase, 95% CI: 0.00-0.10, p=0.041), but there was no such association when considering only completed instances of the task. Neither THC concentration nor BrAC were significantly associated with completion times for the side-mirror task.

**Changes in Driving Performance**

A summary of modeling results for changes in driving performance across paired task and control periods is presented in Table 2. AIC did not select an interaction between THC and BrAC for any model/outcome.

During the message-reading task, participants tended to decrease speed, slowing on average by 1.02 m/s (95% CI: 0.59-1.45, p<0.001) relative to control periods. THC concentration was inversely related to the degree of slowdown, with each 1 µg/L increase in blood THC concentration lessening the decrease in speed by 0.02 m/s (95% CI: 0.00-0.04, p=0.026). In contrast, for the side-mirror task, each 1 µg/L increase in THC concentration predicted a 0.005 m/s (95% CI: 0.001-0.009, p=0.020) decrease in speed. BrAC was not associated with speed in any of the 3 tasks.

Blood THC concentration was not associated with changes in SDLP or SDS in any of the 3 tasks. BrAC was associated with a significant increase in SDLP (0.613 cm per 0.01 g/210 L BrAC) during the message-reading task (95% CI: 0.143-1.084, p=0.011), but had no detectable effects on change in SDLP or SDS in the other two tasks.

**Lane Departures**

In general, lane departures of all severity types were more common during task periods and less common in the placebo-placebo dosing condition, but were not systematically different among the active dosing conditions (Appendix Table A4). Extreme departures were rare, occurring in only 12 of the 5250 task/control periods, primarily during task periods (8 of 12), and exclusively in dosing conditions with active THC, with 3 in the low THC/placebo condition, 2 in the low THC/alcohol condition, and 7 in the high THC/alcohol conditions.

After adjusting for driver speed and initial lane position, blood THC concentration and BrAC were not significant predictors of lane departures of any severity in any of the 3 tasks (Table 3). However, for the artist-search task, THC concentration was associated with significantly increased duration of minor departures (p=0.02, Table 4), with each 1 µg/L increase predicting an additional 0.74% of the task period to be out of lane (95% CI: 0.12-1.36). BrAC was associated with longer durations (1.41% of the period per 0.01 g/210 L increase) of minor departures in the side-mirror task (95% CI: 0.08-2.76, p=0.040), but shorter durations (1.19% of the period per 0.01 g/210 L increase) of minor departures in the message-reading task (95% CI: 0.34-2.04, p=0.006). AIC did not select an interaction between THC and BrAC for any model/outcome.

**DISCUSSION**

This study evaluated the effects of cannabis and alcohol on performance during three different divided attention tasks using a placebo-controlled, within-subject experiment conducted with a highly realistic driving simulator. Our results are consistent with existing literature supporting decreased capacity to multi-task under the influence of cannabis. We found higher blood THC concentrations predicted lower odds of completing an artist-search task, increased odds of providing an incorrect response, longer times spent on the task, and slower recoveries from minor lane departures. Although these effects were not detected with the side-mirror and message-reading tasks, during the side-mirror task participants compensated by slightly decreasing speed.

Task complexity played a noticeable role in the manifestation of THC-related effects. Declines in task completion were prominent in the cognitively demanding artist-search task, but were not observed in the less demanding side-mirror task. This finding aligns with prior research showing greater detrimental effects of cannabis in tasks requiring substantial divided attention (Hartman et al. 2013, Lenné et. al. 2010, Anderson et al. 2010). Alternatively, these lower completion rates might be attributable to intoxicated drivers actively choosing not to attempt the task and instead concentrating on their driving performance in recognition of their impairment.

While the prevalence of lane departures during task segments were not significantly associated with THC concentration or BrAC, we did find evidence that THC concentration was associated with longer departure durations during the artist-search task. This indicates either slower recoveries from departures, or decreased awareness of the vehicle’s lane position while engaged in divided-attention tasks. It bears consideration that the magnitude of BrAC effect on lane departure duration during divided attention tasks was substantially higher per g/210 L (approximately equivalent to g/dL [%] blood alcohol concentration) than blood THC concentration per µg/L. However, THC concentrations vary considerably more and over shorter periods than do alcohol concentrations during normal use, changing rapidly within a short duration after inhalation (Hartman et al. 2016). Distracted driving alone has severe detrimental effects on driving performance (Caird et al. 2014); adding the effects of intoxication raises significant safety concerns for both the driver and other vehicles on the roadway.

We observed a tendency for participants to decrease speed even without cannabis and alcohol when engaged in a divided attention message-reading task. We also found evidence that THC concentration may be associated with minor speed decreases during the side-mirror task. While this finding seems to be contradicted by results for the message-reading task, the inconsistency is likely due to the absence of completion data for the message-reading task. Because we could not filter out non-attempts, individuals who ignored the task — thus having no reason to slow down—had data mixed in with those who actively engaged in the task. This might also explain the unexpected finding of higher BrAC predicting shorter lane departure durations during the message-reading task. It is also possible that the message-reading task requires more overall attention than detecting lights (side-mirror task) or even skimming for a certain value (artist-search task)—resulting in less overall attention paid to the primary driving task and thus, less attempt to compensate for intoxication through decreased speed.

No effect on SDLP or SDS was observed for any variable, with the exception of BrAC predicting increased SDLP during the message-reading task. The lack of effects on SDS was consistent with our findings from the full drive (Hartman et al 2016). However, given our results from the full drive (Hartman et al 2015), we expected to observe both THC and BrAC effects on SDLP. This inconsistency is likely explained by the fact that the short durations of the events result in less stable measures (LaVelle et al. 2019), which might also explain the low magnitudes of change in speed (-0.005 m/s and <-0.001 m/s per µg/L THC for side-mirror and artist-search tasks, respectively).

The effects of THC and BrAC were not synergistic in any of our analyses. This is consistent with our previous findings on lateral control (Hartman et. al 2015). Because cannabis was inhaled ad libitum, several participants in the low-THC condition had higher blood THC concentrations than participants in the high-THC condition. This is due to participants titrating their dose to their preferred level of drug high and tachycardia, as previously demonstrated (Hartman et al 2015). The availability of blood THC concentrations is a strength of the study, enabling analysis by the active THC blood concentration rather than by dose, as many previous studies did.

**Limitations**

The short duration of task periods in this study, while more realistic, made it difficult to detect differences in driving behavior. Despite BrAC having a well-established relationship to driving performance, the only significant performance shift attributable to alcohol in this study was in the message-reading task. This task had the second-longest duration, and was arguably the most cognitively demanding. Future research in this area might require more occurrences of each task, or tasks which are longer in duration.

While the study population was restricted to occasional to moderate cannabis smokers and took steps to preclude prior intoxication, some participants had low detectable blood THC concentrations under placebo conditions from previously self-administered cannabis. Another limitation is that concentrations at time-points within the drive were estimated by individual modeling (rather than directly measured) via interpolation from collection times pre- and post-drive. Continuous blood collection during driving was not feasible and would be prohibitively disruptive to the driving and divided attention tasks.

Possible bias may have been introduced by participants recognizing that their driving performance was under observation and altering their behavior accordingly. In addition, while the study used placebo conditions, it is probable that some participants were aware of dosing conditions due to their prior familiarity with cannabis and alcohol. Such awareness of study conditions may have led drivers to exhibit greater caution or focus, particularly given the vested interest some participants might have in demonstrating that cannabis does not impair driving performance. This notion is at least partially supported by survey data, which shows public attitudes towards driving under the influence of cannabis are less negative than attitudes towards driving under the influence of alcohol (McCarthy et al. 2007).

**Conclusion**

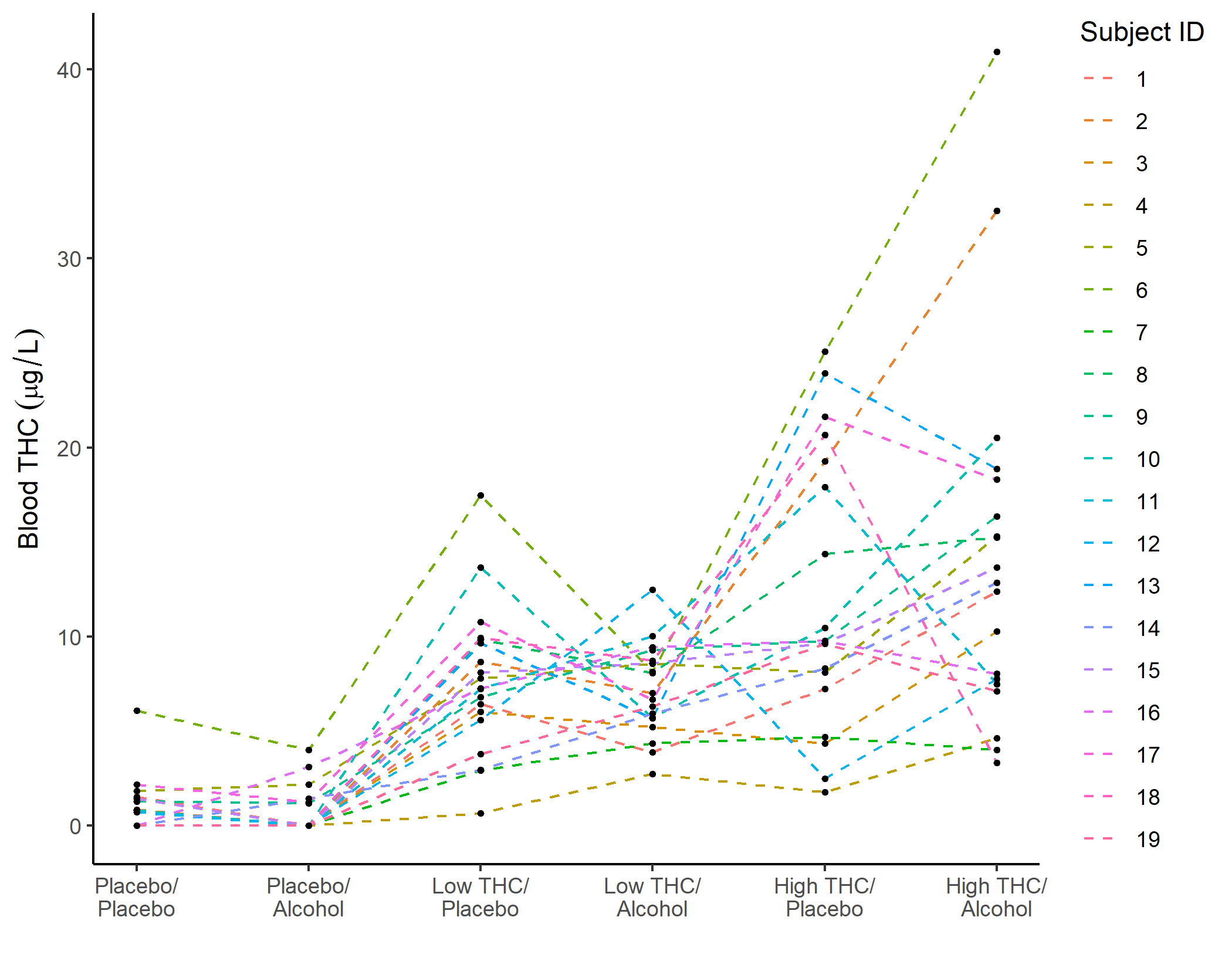
Due to THC’s effect on higher cognitive performance, evaluating divided-attention tasks in drivers with cannabis impairment is important—especially given the current high prevalence of cellular phone use and other driving distractions. Our research suggests that divided attention is an area of concern following acute cannabis exposure, particularly for complex tasks. More research is needed to understand the effects across the spectrum of divided attention while driving, including with longer distraction. The interaction of cannabis use and distraction raises significant safety concerns, exemplified by increased durations of lane departures during an artist-search task. As cannabis legalization increases across the US, additional research on THC’s impact on driving performance is essential.

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**REFERENCES**

1. Asbridge M, Hayden JA, Cartwright JL. 2012. Acute cannabis consumption and motor vehicle collision risk: systematic review of observational studies and meta-analysis. BMJ, 334, e536.
2. Anderson BM, Rizzo M, Block RI, Pearlson GD, O’leary DS. 2010. Sex differences in the effects of marijuana on simulated driving performance. Journal of Psychoactive Drugs, 42, 19-30.
3. Bates D, Maechler M, Bolker B, Walker S. 2015. Fitting Linear Mixed Models using lme4. Journal of Statistical Software, 67 (1), 1-48.
4. Caird JK, Johnston KA, Willness CR, Asbridge M, Steal P. 2014. A meta-analysis of the effects of texting on driving. Accid Anal Prev. 71:311-8
5. Downey LA, 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. Accident Analysis & Prevention, 50, 879–886.
6. Ferdinand A, Menachemi N. 2014. Associations between driving performance and engaging in secondary tasks: a systematic review. American Journal of Public Health, 104, e39–e48.
7. Hartman RL, Brown TL, Milavetz G, Spurgin A, Gorelick DA, Gaffney G, Huestis MA. 2015. Controlled cannabis vaporizer administration: blood and plasma cannabinoids with and without alcohol. Clinical Chemistry, 61, 850– 869.
8. Hartman RL, Brown TL, Milavetz G, Spurgin A, Pierce RS, Gorelick DA, Huestis MA. 2015. Cannabis effects on driving lateral control with and without alcohol. Drug and Alcohol Dependence, 154, 25-37
9. Hartman RL, Brown TL, Milavetz G, Spurgin A, Pierce RS, Gorelick DA, Huestis MA. 2016. Cannabis effects on driving longitudinal control with and without alcohol. Journal of Applied Toxicology, 36, 1418-1429.
10. Hartman RL, Brown TL, Milavetz G, Spurgin A, Gorelick DA, Gaffney GR, Huestsis MA. 2016. Effect of blood collection time on measured Δ9-Tetrahydrocannabinol concentrations: implications for driving interpretation and drug prevention. Clin Chem, 62(6), 895.
11. Irwin C, Iudakhina E, Desbrow B, McCartney D. 2017. Effects of acute alcohol consumption on measures of simulated driving: a systematic review and meta-analysis. Accident Analysis & Prevention, 102, 248-266.
12. LaVelle A, Brown T, Schwarz C. 2019. Effect of data window statistical analysis on driver performance. Paper presented at: Road Safety and Simulation; Iowa City, IA.
13. Lenné MG, Dietze PM, Triggs TJ, Walmsley S, Murphy B, Redman JR. 2010. The effects of cannabis and alcohol on simulated arterial driving: influences of driving experience and task demand. Accident Analysis & Prevention, 42, 859-866.
14. Li MC, Brady JE, DiMaggio CJ, Lusardi AR, Tzong KY, Li G. 2012. Marijuana use and motor vehicle crashes. American Journal of Epidemiology, 34, 65–72.
15. Martin TL, Solbeck PA, Mayers DJ, Langille, RM, Buczek Y, Pelletier MR. 2013. A review of alcohol-impaired driving: The role of blood alcohol concentration and complexity of the driving task. Journal of Forensic Sciences, 58, 1238 –1250.
16. McCarthy DM, Lynch AM, Pederson SL. (2007). Driving after use of alcohol and marijuana in college students. Psychology of Addictive Behaviors, 21, 425–430.
17. Ramaekers J, Kauert G, Theunissen E, Toennes S, Moeller M. 2009. Neurocognitive performance during acute THC intoxication in heavy and occasional cannabis users. Journal of Psychopharmacology, 23, 266–277.
18. Romano E, Torres-Saavedra P, Voas RB, Lacey JH. 2014. Drugs and alcohol: Their relative crash risk. Journal of Studies on Alcohol and Drugs, 75, 56-64.
19. R Core Team, 2018. R: A language and environment for statistical computing. R Foundation for Statistical Computing, Vienna Austria. https://www.R-project.org/
20. Schwope D, Scheidweiler K, Huestis M. 2011. Direct quantification of cannabinoids and cannabinoid glucuronides in whole blood by liquid chromatography–tandem mass spectrometry. Analytical and Bioanalytical Chemistry, 401, 1273–1283.

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**Figure 1.** Estimated blood THC concentrations by administered cannabis and alcohol doses during the first occurrence of the side-mirror task for each of the 19 participants.

**Table 1**: Results from models used to analyze performance on divided attention tasks performed while driving, including coefficient estimates, odds ratios (OR), 95% confidence intervals, and p-values.

|  |  |  |  |  |  |  |
| --- | --- | --- | --- | --- | --- | --- |
| Task | Outcome | Model | BrAC (0.01 g/210 L) | | Blood THC concentration (µg/L) | |
| β, OR | p-value | β, OR | p-value |
| Artist-search | Completion | GLMM | -0.01,  0.99 (0.90, 1.09) | 0.802 | **-0.05,**  **0.95 (0.90, 0.99)** | **0.046 \*** |
| Incorrect | GLMM | -0.01,  0.99 (0.90, 1.09) | 0.858 | **0.05,**  **1.05 (1.00, 1.09)** | **0.041 \*** |
| Time (engaged), sec | LMM | -0.02 (-0.11, 0.07) | 0.697 | **0.05 (0.00, 0.10)** | **0.041 \*** |
| Time (completed), sec | LMM | 0.00 (-0.07, 0.09) | 0.864 | 0.00 (-0.04, 0.04) | 0.967 |
| Side-mirror | Completion | GLMM | 0.03,  1.03 (0.95, 1.11) | 0.461 | 0.02,  1.02 (0.98, 1.06) | 0.327 |
| Time (completed), sec | LMM | -0.00 (-0.01, 0.01) | 0.595 | -0.00 (-0.01, 0.00) | 0.250 |
| \*Denotes statistical significance at p<0.05.  BrAC: breath alcohol concentration; THC: Δ9-tetrahydrocannabinol;  GLMM indicates generalized linear mixed models using a binomial response, logit link, and subject-specific random intercepts; LMM indicates linear mixed models with a Gaussian response, identity link, and subject-specific random intercepts. AIC did not select an interaction between BrAC and THC for any outcomes. | | | | | | |

**Table 2**: Results of models used to analyze baseline driving performance, including fixed-effect intercepts, coefficient estimates, 95% confidence intervals, and p-values.

|  |  |  |  |  |  |  |  |
| --- | --- | --- | --- | --- | --- | --- | --- |
| Task | Outcome | Intercept (fixed effect) | | BrAC (0.01 g/210 L) | | THC (µg/L) | |
| β (95% CI) | p-value | β (95% CI) | p-value | β (95% CI) | p-value |
| Side-Mirror | Δ SDLP (cm) | 0.13  (-2.09, 2.35) | 0.910 | -0.07  (-0.36, 0.22) | 0.648 | 0.00  (-0.14, 0.14) | 0.996 |
| Δ Speed (m/s) | -0.007  (-0.127, 0.113) | 0.908 | 0.007  (-0.002, 0.016) | 0.143 | **-0.005**  **(-0.009, -0.001)** | **0.020 \*** |
| Δ SDS (m/s) | 0.027  (-0.014, 0.069) | 0.200 | -0.113  (-0.620, 0.394) | 0.664 | 0.001  (-0.001, 0.004) | 0.417 |
| Artist-Search | Δ SDLP (cm) | -2.69  (-35.39, 30.02) | 0.872 | -0.17  (-1.33, 0.99) | 0.772 | -0.39  (-0.99, 0.22) | 0.206 |
| Δ Speed (m/s) | -0.640  (-2.326, 1.045) | 0.455 | 0.019  (-0.041, 0.079) | 0.529 | -0.000  (-0.031, 0.031) | 0.999 |
| Δ SDS (m/s) | -0.117  (-0.500, 0.266) | 0.548 | -0.003  (-0.016, 0.011) | 0.688 | 0.003  (-0.004, 0.010) | 0.383 |
| Message-Reading | Δ SDLP (cm) | -4.18  (-10.13, 1.76) | 0.168 | **0.61**  **(0.14, 1.08)** | **0.011 \*** | -0.01  (-0.24, 0.22) | 0.959 |
| Δ Speed (m/s) | **-1.019**  **(-1.450, -0.588)** | **<0.001\*\*\*** | -0.011  (0.045, 0.022) | 0.515 | **0.019**  **(0.002, 0.036)** | **0.026 \*** |
| Δ SDS (m/s) | 0.005  (-0.088, 0.098) | 0.917 | -0.003  (-0.015, 0.009) | 0.599 | 0.004  (-0.002, 0.010) | 0.186 |
| \*Denotes statistical significance at p<0.05.  BrAC: breath alcohol concentration; THC: Δ9-tetrahydrocannabinol;  All models used a Gaussian response, identity link, and subject specific random intercepts. AIC did not select an interaction between BrAC and THC for any outcomes. | | | | | | | |

**Table 3:** Results from models used to analyze the prevalence of lane departures during divided attention task periods, including coefficient estimates, odds ratios (OR), 95% confidence intervals, and p-values.

|  |  |  |  |  |  |
| --- | --- | --- | --- | --- | --- |
| Task | Outcome | BrAC (0.01 g/210 L) | | THC (µg/L) | |
| β, OR (95% CI) | p-value | β, OR (95% CI) | p-value |
| Side- Mirror | Minor departures | -0.02,  0.99  (0.93, 1.05) | 0.632 | -0.00,  0.99  (0.96, 1.03) | 0.851 |
| Major departures | -9.72,  0.99  (0.81, 1.01) | 0.089 | -0.02  0.91  (0.92, 1.05) | 0.637 |
| Severe departures | 0.20,  1.22  (0.58, 3.43) | 0.600 | -0.00,  1.00  (0.52, 1.27) | 0.982 |
| Artist-Search | Minor departures | 0.02,  1.03  (0.91, 1.15) | 0.673 | 0.00,  1.00  (0.95, 1.06) | 0.924 |
| Major departures | -0.00,  1.00  (0.82, 1.21) | 0.981 | -0.05,  0.95  (0.84, 1.06) | 0.375 |
| Severe departures | 0.19,  1.21  (0.66, 2.22) | 0.534 | 0.03,  1.03  (0.73, 1.45) | 0.864 |
| Message-Reading | Minor departures | 0.01,  1.01  (0.94, 1.09) | 0.748 | -0.00,  1.00  (0.962, 1.031) | 0.826 |
| Major departures | -0.00,  1.00  (0.91, 1.10) | 0.963 | 0.00,  1.00  (0.95, 1.05) | 0.904 |
| Severe departures | 0.11,  1.11  (0.77, 1.15) | 0.549 | -0.01,  0.99  (0.78, 1.15) | 0.929 |
| \*Denotes statistical significance at p<0.05.  BrAC: breath alcohol concentration; THC: Δ9-tetrahydrocannabinol;  All models used a binomial response, logit link, adjusted for speed and initial lane position, and included subject-specific random intercepts. AIC selected an interaction between THC and BrAC for major departures during the side-mirror task (β = 0.293, p = 0.740), but not for any other tasks/outcomes. | | | | | |

**Table 4:** Results from models used to analyze the duration of lane departures during divided attention task periods, including coefficient estimates, 95% confidence intervals, and p-values.

|  |  |  |  |  |  |
| --- | --- | --- | --- | --- | --- |
| Task | Outcome | BrAC (0.01 g/210 L) | | THC (µg/L) | |
| β (95% CI) | p-value | β (95% CI) | p-value |
| Side-Mirror | Minor (percent of task out of lane) | **1.42**  **(0.08, 2.76)** | **0.040 \*** | 0.09  (-0.73,  0.90) | 0.834 |
| Major (percent of task out of lane) | 0.59  (-1.06, 2.23) | 0.487 | -0.26  (-1.28, 0.77) | 0.622 |
| Artist-Search | Minor (percent of task out of lane) | 0.47  (-1.03, 1.96) | 0.533 | **0.74**  **(0.12, 1.36)** | **0.020 \*** |
| Major (percent of task out of lane) | -0.73  (-2.92, 1.46) | 0.500 | -0.20  (-1.20, 0.80) | 0.685 |
| Message-Reading | Minor (percent of task out of lane) | **-1.19**  **(-2.04, -0.34)** | **0.006 \*** | -0.16  (-0.59, 0.26) | 0.451 |
| Major (percent of task out of lane) | 0.06  (-1.31, 1.42) | 0.935 | -0.10  (-0.94, 0.74) | 0.819 |
| \*Denotes statistical significance at p<0.05.  BrAC: breath alcohol concentration; THC: Δ9-tetrahydrocannabinol;  All models used a Gaussian response, identity link, adjusted for speed and initial lane position, and included subject-specific random intercepts. AIC did not select an interaction between BrAC and THC for any outcomes. There were not enough extreme lane departures to estimate model coefficients. | | | | | |

**APPENDIX**

**Table A1**: Average measures of driving and task performance for the side-mirror task by drive segment and dosing level.

|  |  |  |  |  |  |  |  |
| --- | --- | --- | --- | --- | --- | --- | --- |
| Segment |  | Placebo/  Placebo | Placebo/  Alcohol | Low/  Placebo | Low/  Alcohol | High/  Placebo | High/  Alcohol |
| Urban | Blood THC (µg/L) | 0.9 | 0.7 | 7.9 | 7.2 | 12.1 | 14.0 |
| BrAC (g/210 L) | 0 | 0.059 | 0 | 0.052 | 0 | 0.048 |
| % complete | 88.3 | 89.7 | 95.1 | 87.1 | 88.9 | 86.9 |
| Time (sec) | 1.85 | 1.91 | 1.74 | 2.02 | 1.91 | 1.81 |
| SDLP (cm) | 4.57 | 3.05 | 3.96 | 4.88 | 3.66 | 4.27 |
| Speed (m/s) | 12.74 | 13.10 | 13.19 | 13.19 | 12.34 | 12.65 |
| SDS (m/s) | 0.08 | 0.12 | 0.11 | 0.13 | 0.13 | 0.10 |
| Interstate | Blood THC (µg/L) | 0.9 | 0.6 | 6.1 | 5.6 | 9.4 | 10.5 |
| BrAC (g/210 L) | 0 | 0.057 | 0 | 0.052 | 0 | 0.049 |
| % complete | 95.5 | 94.7 | 97.9 | 97.9 | 92.6 | 98.0 |
| Time (sec) | 1.99 | 1.95 | 1.89 | 2.04 | 2.02 | 1.91 |
| SDLP(cm) | 13.72 | 17.68 | 14.63 | 15.54 | 19.81 | 19.20 |
| Speed (m/s) | 28.34 | 29.06 | 28.97 | 27.98 | 27.58 | 27.67 |
| SDS (miles/h) | 0.11 | 0.13 | 0.11 | 0.15 | 0.13 | 0.14 |
| Rural | Blood THC (µg/L) | 0.9 | 0.6 | 5.0 | 4.6 | 7.3 | 8.7 |
| BrAC (g/210 L) | 0 | 0.054 | 0 | 0.051 | 0 | 0.049 |
| % complete | 100 | 100 | 95.9 | 94.5 | 97.2 | 100 |
| Time (sec) | 1.73 | 1.65 | 1.67 | 1.76 | 1.75 | 1.67 |
| SDLP (cm) | 5.79 | 7.62 | 6.40 | 6.40 | 5.49 | 7.62 |
| Speed (m/s) | 22.40 | 23.69 | 22.26 | 23.29 | 21.41 | 22.49 |
| SDS (m/s) | 0.09 | 0.12 | 0.12 | 0.12 | 0.11 | 0.11 |
| Abbreviations: THC, Δ9-tetrahydrocannabinol; BrAC, breath alcohol concentration; SDLD, standard deviation of lateral position; SDS, standard deviation of speed. | | | | | | | |

**Table A2**: Average measures of driving and task performance for the artist-search task by dosing level. All instances of the artist-search task took place on the interstate.

|  |  |  |  |  |  |  |
| --- | --- | --- | --- | --- | --- | --- |
|  | Placebo/  Placebo | Placebo/  Alcohol | Low/  Placebo | Low/  Alcohol | High/  Placebo | High/  Alcohol |
| Blood THC (µg/L) | 0.8 | 0.6 | 6.0 | 5.6 | 9.3 | 10.8 |
| BrAC (g/210 L) | 0 | 0.057 | 0 | 0.052 | 0 | 0.048 |
| % complete | 66.7 | 71.4 | 64.3 | 49.1 | 57.9 | 61.4 |
| % incorrect | 15.8 | 17.9 | 32.1 | 26.3 | 15.8 | 12.3 |
| time (sec) | 6.18 | 5.43 | 6.14 | 5.78 | 5.31 | 6.30 |
| SDLP (cm) | 23.16 | 25.91 | 26.82 | 24.69 | 19.81 | 23.77 |
| Speed (m/s) | 29.77 | 29.01 | 30.00 | 27.67 | 27.76 | 27.27 |
| SDS (m/s) | 0.20 | 0.32 | 0.32 | 0.27 | 0.26 | 0.34 |
| Abbreviations: THC, Δ9-tetrahydrocannabinol; BrAC, breath alcohol concentration; SDLP, standard deviation of lateral position; SDS, standard deviation of speed. | | | | | | |

**Table A3**: Average measures of driving and task performance for the message-reading task by drive segment and dosing level.

|  |  |  |  |  |  |  |  |
| --- | --- | --- | --- | --- | --- | --- | --- |
| Segment |  | Placebo/  Placebo | Placebo/  Alcohol | Low/  Placebo | Low/  Alcohol | High/  Placebo | High/  Alcohol |
| Urban | Blood THC (µg/L) | 0.9 | 0.7 | 7.7 | 7.2 | 12.5 | 14.2 |
| BrAC (g/210 L) | 0 | 0.059 | 0 | 0.052 | 0 | 0.048 |
| SDLP (cm) | 17.22 | 19.35 | 20.60 | 17.31 | 15.12 | 23.68 |
| Speed (m/s) | 12.38 | 13.10 | 13.05 | 12.92 | 12.47 | 12.78 |
| SDS (m/s) | 0.41 | 0.38 | 0.42 | 0.43 | 0.37 | 0.42 |
| Interstate | Blood THC (µg/L) | 0.9 | 0.7 | 6.1 | 5.6 | 9.2 | 10.8 |
| BrAC (g/210 L) | 0 | 0.057 | 0 | 0.051 | 0 | 0.049 |
| SDLP (cm) | 31.70 | 32.31 | 32.00 | 32.61 | 25.66 | 30.48 |
| Speed (m/s) | 29.19 | 28.83 | 29.55 | 27.36 | 28.34 | 27.81 |
| SDS (m/s) | 0.38 | 0.57 | 0.47 | 0.45 | 0.46 | 0.50 |
| Rural | Blood THC (µg/L) | 0.8 | 0.6 | 4.9 | 4.6 | 8.1 | 8.8 |
| BrAC (g/210 L) | 0 | 0.054 | 0 | 0.516 | 0 | 0.048 |
| SDLP (cm) | 23.32 | 31.39 | 24.30 | 25.73 | 25.85 | 30.78 |
| Speed (m/s) | 21.55 | 22.17 | 21.99 | 21.10 | 19.71 | 22.31 |
| SDS (m/s) | 0.51 | 0.55 | 0.52 | 0.40 | 0.53 | 0.61 |
| Abbreviations: THC, Δ9-tetrahydrocannabinol; BrAC, breath alcohol concentration; SDLP, standard deviation of lateral position; SDS, standard deviation of speed. | | | | | | | |

**Table A4:** The prevalence of lane departures of each severity category by assigned dosing condition across all divided attention task instances.

|  |  |  |  |  |  |  |  |  |
| --- | --- | --- | --- | --- | --- | --- | --- | --- |
|  | Control Periods | | | | Task Periods | | | |
|  | None | Minor | Major | Extreme | None | Minor | Major | Extreme |
| Placebo/  Placebo | 370 | 49 | 28 | 0 | 341 | 78 | 38 | 0 |
| Placebo/  Alcohol | 359 | 66 | 31 | 0 | 328 | 97 | 40 | 0 |
| Low/  Placebo | 382 | 52 | 23 | 1 | 345 | 89 | 52 | 2 |
| Low/  Alcohol | 360 | 57 | 28 | 1 | 333 | 84 | 40 | 1 |
| High/  Placebo | 356 | 55 | 28 | 0 | 337 | 74 | 41 | 0 |
| High/  Alcohol | 359 | 65 | 22 | 2 | 338 | 86 | 36 | 5 |
| Lane departure categories are nested, and are determined by the proportion of the vehicle that is out of lane. Minor departures indicate any of the vehicle is out of lane, major departures indicate at least 25% of the vehicle chassis width is out of lane, and extreme departures indicate at least 50% of the vehicle chassis width is out of lane. | | | | | | | | |

**Bibliography**

1. Akaike, H. (1974). A new look at the statistical model identification. In Selected Papers of Hirotugu Akaike (pp. 215-222). Springer, New York, NY.
2. Anderson, B.M., Rizzo, M., Block, R.I., Pearlson, G.D., O’Leary, D.S. (2010). Sex differences in the effects of marijuana on simulated driving performance. Journal of Psychoactive Drugs, 19–30.
3. Arnedt, J. T., Wilde, G. J., Munt, P. W., & MacLean, A. W. (2001). How do prolonged wakefulness and alcohol compare in the decrements they produce on a simulated driving task?. Accident Analysis & Prevention, 337-344.
4. Asbridge M, Hayden JA, Cartwright JL. (2012). Acute cannabis consumption and motor vehicle collision risk: Systematic review of observational studies and meta-analysis. BMJ. 344:e536. [PubMed: 22323502]
5. Augsburger M, Donzé N, Ménétrey A, Brossard C, Sporkert F, Giroud C, Mangin P. (2005). Concentration of drugs in blood of suspected impaired Drivers. Forensic Science International, 11–15
6. Battistella, G., Fornari, E., Thomas, A., Mall, J. F., Chtioui, H., Appenzeller, M., & Giroud, C. (2013). Weed or wheel! FMRI, behavioural, and toxicological investigations of how cannabis smoking affects skills necessary for driving. PloS one, 8(1), e52545.
7. Bergamaschi MM, Karschner EL, Goodwin RS, Scheidweiler KB, Hirvonen J, Queiroz RH, Huestis MA. (2013). Impact of prolonged cannabinoid excretion in chronic daily cannabis smokers’ blood on per se drugged driving laws. Clinical Chemistry. 2013; 59:519–526. [PubMed: 23449702]
8. Brown I. (1970) Safer drivers. British Journal of Hospital Medicine, 441–450.
9. Downey LA, 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. (2013). Accident Analysis & Prevention, 50, 879–886. [PubMed: 22871272]
10. Drummer OH, Gerostamoulos J, Batziris H, Chu M, Caplehorn J, Robertson MD, Swann P. (2014). The involvement of drugs in drivers of motor vehicles killed in Australian road traffic crashes. Accident Analysis & Prevention, 36, 239–248. [PubMed: 14642878]
11. E. J.D. Ogden & H. Moskowitz (2004) Effects of Alcohol and Other Drugs on Driver Performance. Traffic Injury Prevention, 5, 185-198, DOI: 10.1080/15389580490465201
12. ElSohly MA, Mehmedic Z, Foster S, Gon C, Chandra S and Church JC (2016) Changes in Cannabis Potency Over the Last 2 Decades (1995-2014): Analysis of Current Data in the United States. Biological Psychiatry, pp. 1-7.
13. Ferdinand, A., & Menachemi, N. (2014). Associations between driving performance and engaging in secondary tasks: a systematic review. American Journal of Public Health, 104, e39–e48.
14. Gawron, V. J., & Ranney, T. A. (1988). The effects of alcohol dosing on driving performance on a closed course and in a driving simulator. Ergonomics, 31, 1219-1244
15. Gjerde, H., Normann, P.T., Christophersen, A.S., Samuelsen, S.O., Mørland, J. (2011). Alcohol, psychoactive drugs and fatal road traffic accidents in Norway: a case-control study. Accident Analysis & Prevention. 43, 1197– 1203. [PubMed: 21376919]
16. Grant, W. (1974) Toxicology of the Eye: Drugs, Chemicals, Plants, Venoms. C.C. Thomas, Springfield, IL
17. Hartman, R. L., Brown, T. L., Milavetz, G., Spurgin, A., Pierce, R. S., Gorelick, D. A., & Huestis, M. A. (2016). Cannabis effects on driving longitudinal control with and without alcohol. Journal of Applied Toxicology, 36, 1418-1429.
18. Hartman, R.L., Brown, T.L., Milavetz, G., Spurgin, A., Gorelick, D.A., Gaffney, G., Huestis, M.A. (2015). Controlled cannabis vaporizer administration: blood and plasma cannabinoids with and without alcohol. Clinical Chemistry, 61, 850– 869.
19. Hartman, R. L., Brown, T. L., Milavetz, G., Spurgin, A., Pierce, R. S., Gorelick, D. A., & Huestis, M. A. (2015). Cannabis effects on driving lateral control with and without alcohol. Drug and alcohol dependence, 154, 25-37
20. Hartman, R. L., & Huestis, M. A. (2013). Cannabis effects on driving skills. Clinical chemistry, 59, 478-492.
21. Irwin, C., Iudakhina, E., Desbrow, B., & McCartney, D. (2017). Effects of acute alcohol consumption on measures of simulated driving: a systematic review and meta-analysis. Accident Analysis & Prevention, 102, 248-266.
22. Jones AW, Andersson L. 2003. Comparison of ethanol concentrations in venous blood and end expired breath during a controlled drinking study. Forensic Science International, 132 18– 25.
23. King, L.A., Carpentier, C., Griffiths, P. (2004). An Overview of Cannabis Potency in Europe. European Monitoring Centre for Drugs and Drug Addiction: Lisbon.
24. King, L.A., Carpentier, C., Griffiths, P. (2005). Cannabis potency in Europe. Addiction, 100, 884–886
25. Kurzthaler, I., Hummer, M., Miller, C., Sperner-Unterweger, B., Günther, V., Wechdorn, H., & Fleischhacker, W. W. (1999). Effect of cannabis use on cognitive functions and driving ability. The Journal of clinical psychiatry, 395-399
26. 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, 331-1371. [PubMed: 16321993]
27. Lee, J.D., Fiorentino, D., Reyes, M.L., Brown, T.L., Ahmad, O., Fell, J., Ward, N., Dufour, R. (2010). Assessing the Feasibility of Vehicle-Based Sensors to Detect Alcohol Impairment. National Highway Traffic Safety Administration, Report No. DOT HS 811–358
28. Legrand, S.A., Isalberti, C., Der Linden, T.V., Bernhoft, I.M., Hels, T., Simonsen, K.W., Favretto, D., Ferrara, S.D., Caplinskiene, M., Minkuviene, Z., Pauliukevicius, A., Houwing, S., Mathijssen, R., Lillsunde, P., Langel, K., Blencowe, T., Verstraete, A.G. (2013). Alcohol and drugs in seriously injured drivers in six European countries. Drug Testing and Analysis, 5, 156–165. [PubMed: 22887894]
29. Lenne, M.G., Dietze, P.M., Triggs, T.J., Walmsley, S., Murphy, B., Redman, J.R. (2010). The effects of cannabis and alcohol on simulated arterial driving: influences of driving experience and task demand. Accident Analysis & Prevention. 42, 859–866.
30. Li, M.C., Brady, J.E., DiMaggio, C.J., Lusardi, A.R., Tzong, K.Y., Li, G. (2012). Marijuana use and motor vehicle crashes. American Journal of Epidemiology, 34, 65–72.
31. Li, G., Brady, J., & Chen, Q. (2013). Drug use and fatal motor vehicle crashes: A case-controlled study. Accident Analysis & Prevention, 60, 205-210
32. Liguori, A. (2009). Simulator studies of drug-induced driving impairment. In J. C. Verster, S. R. Pandi-Perumal, J. G. Ramaekers & J. J. De Gier (Eds.), Drugs, driving and traffic safety, (pp 75– 82). Basel, Switzerland: Birkhauser Verlag.
33. Marks, D. F., & MacAvoy, M. G. (1989). Divided attention performance in cannabis users and non-users following alcohol and cannabis separately and in combination. Psychopharmacology, 99, 397-401.
34. Martin, T. L., Solbeck, P. A., Mayers, D. J., Langille, R. M., Buczek, Y., & Pelletier, M. R. (2013). A review of alcohol-impaired driving: The role of blood alcohol concentration and complexity of the driving task. Journal of Forensic Sciences, 58, 1238 –1250.
35. McCarthy, D.M., Lynch, A.M., Pederson, S.L. (2007). Driving after use of alcohol and marijuana in college students. Psychology of Addictive Behaviors, 21, 425–430. [PubMed: 17874895]
36. Ramaekers, J., Kauert, G., Theunissen, E., Toennes, S., Moeller, M. (2009) Neurocognitive performance during acute THC intoxication in heavy and occasional cannabis users. Journal of Psychopharmacology, 23, 266–277. [PubMed: 18719045]
37. Ramaekers, J., Theunissen, E., De Brouwer, M., Toennes, S., Moeller, M., Kauert, G. (2011). Tolerance and crosstolerance to neurocognitive effects of THC and alcohol in heavy cannabis users. Psychopharmacology. 214, 391–401. [PubMed: 21049267]
38. Ramaekers, J. G., Kauert, G., van Ruitenbeek, P., Theunissen, E. L., Schneider, E., & Moeller, M. R. (2006). High-potency marijuana impairs executive function and inhibitory motor control. Neuropsychopharmacology, 31, 2296.
39. Ramaekers, J. G., Robbe, H. W. J., & O'Hanlon, J. F. (2000). Marijuana, alcohol and actual driving performance. Human Psychopharmacology: Clinical and Experimental, 15, 551-558.
40. Romano, E., Torres-Saavedra, P., Voas, R. B., & Lacey, J. H. (2017). Marijuana and the risk of fatal car crashes: what can we learn from FARS and NRS data?. The Journal of Primary Prevention, 38, 315-328.
41. Romano, E., Torres-Saavedra, P., Voas, R. B., & Lacey, J. H. (2014). Drugs and alcohol: Their relative crash risk. Journal of Studies on Alcohol and Drugs, 75, 56-64.
42. Salomonsen-Sautel, S., Min, S. J., Sakai, J. T., Thurstone, C., & Hopfer, C. (2014). Trends in fatal motor vehicle crashes before and after marijuana commercialization in Colorado. Drug and alcohol dependence, 140, 137-144.
43. Schwope, D., Scheidweiler, K., & Huestis, M. (2011). Direct quantification of cannabinoids and cannabinoid glucuronides in whole blood by liquid chromatography–tandem mass spectrometry. Analytical and Bioanalytical Chemistry, 401, 1273–1283. [PubMed: 21727996]
44. Starmer, G. (1989) Effects of low to moderate doses of ethanol on human driving performance. In Human Metabolism of Alcohol (Volume 1): Pharmacokinetics, Medicolegal aspects and General Interest, Crow K., Batt R. (eds.), pp. 101–133. CRC Press, Boca Raton, Florida
45. Steentoft, A., Simonsen, K.W., Linnet, K. (2010) The frequency of drugs among Danish drivers before and after the introduction of fixed concentration limits. Traffic Injury Prevention, 11, 329–333.
46. Toennes, S.W., Ramaekers, J.G., Theunissen, E.L., Moeller, M.R., & Kauert, G.F. (2008). Comparison of cannabinoid pharmacokinetic properties in occasional and heavy users smoking a marijuana or placebo joint. Journal of Analytical Toxicology, 32, 470–477. [PubMed: 18713514]
47. Urfer, S., Morton, J., Beall, V., Feldmann, J., Gunesch, J. (2014) Analysis of Delta9-tetrahydrocannabinol driving under the influence of drugs cases in Colorado from January 2011 to February 2014. J Anal Toxicol, 38, 575–581. [PubMed: 25217549]
48. Van Dyke, N., & Fillmore, M. T. (2014). Acute effects of alcohol on inhibitory control and simulated driving in DUI offenders. Journal of safety research, 49, 5-e1.
49. Wallgren H, Barry H. (1970) Actions of Alcohol, Vol I&II, pp. 287–292, Elsevier Publishing, Amsterdam-London-New York
50. Wright, K., & Terry, P. (2002). Modulation of the effects of alcohol on driving-related psychomotor skills by chronic exposure to cannabis. Psychopharmacology, 160, 213–219. [PubMed: 11875640]