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Cannabis effects on driving lateral control with and without alcohol

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ABSTRACT

Background: Effects of cannabis, the most commonly encountered non-alcohol drug in driving under the influence cases, are heavily debated. We aim to determine how blood Δ^9-tetrahydrocannabinol (THC) concentrations relate to driving impairment, with and without alcohol.
Methods: Current occasional (≥1×/last 3 months, ≤3days/week) cannabis smokers drank placebo or low-dose alcohol, and inhaled 500 mg placebo, low (2.9%)-THC, or high (6.7%)-THC vaporized cannabis over 10 min *ad libitum* in separate sessions (within-subject design, 6 conditions). Participants drove (National Advanced Driving Simulator, University of Iowa) simulated drives (~0.8 h duration). Blood, oral fluid (OF), and breath alcohol samples were collected before (0.17 h, 0.42 h) and after (1.4 h, 2.3 h) driving that occurred 0.5–1.3 h after inhalation. We evaluated standard deviations of lateral position (lane weave, SDLP) and steering angle, lane departures/min, and maximum lateral acceleration.
Results: In $N = 18$ completers (13 men, ages 21–37years), cannabis and alcohol increased SDLP. Blood THC concentrations of 8.2 and 13.1 μg/L during driving increased SDLP similar to 0.05 and 0.08 g/210 L breath alcohol concentrations, the most common legal alcohol limits. Cannabis-alcohol SDLP effects were additive rather than synergistic, with 5 μg/L THC + 0.05 g/210 L alcohol showing similar SDLP to 0.08 g/210 L alcohol alone. Only alcohol increased lateral acceleration and the less-sensitive lane departures/min parameters. OF effectively documented cannabis exposure, although with greater THC concentration variability than paired blood samples.
Conclusions: SDLP was a sensitive cannabis-related lateral control impairment measure. During drive blood THC ≥8.2 μg/L increased SDLP similar to notably-impairing alcohol concentrations. Despite OF's screening value, OF variability poses challenges in concentration-based effects interpretation.
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1. Introduction

Reducing drugged driving is a U.S. and worldwide priority (ONDCP, 2013). Cannabis is the most frequently detected illicit drug in drivers (Berning et al., 2015; Lacey et al., 2009; Legrand et al., 2013; Pilkinton et al., 2013); 12.6% of weekend nighttime drivers were positive for Δ^9-tetrahydrocannabinol (THC, primary psychoactive phytocannabinoid), in 2013–2014, a 48% increase since 2007 (Berning et al., 2015). Although blood THC is associated with increased crash risk and driver culpability (Asbridge et al., 2012; Drummer et al., 2004; Gjerde et al., 2011; Laumon et al., 2005; Li et al., 2012), cannabis effects on driving remain heavily debated. Road tracking and ability to remain within the lane are crucial driving skills. Lane weaving, an observable effect of drug-impaired driving, is a common measure for assessing driving performance. Standard deviation of lateral position (SDLP) is a sensitive vehicular control indicator, often employed in drugged driving research (Anderson et al., 2010; Lenné et al., 2010; Ramaekers et al., 2006a;

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Verster et al., 2006). In previous studies, cannabis increased SDLP and straddling lanes, but results were assessed by dose rather than blood THC concentrations (Ramaekers et al., 2000; Robbe, 1998; Downey et al., 2013).

To date, 23 states and the District of Columbia (DC) approved medical marijuana; four states and DC legalized recreational cannabis for adults (ProCon.org, 2014). Cannabis legalization is a crucial road safety issue. Since legalizing medical marijuana (2000), Colorado observed increased driving under the influence of cannabis (DUIC) cases (Urfer et al., 2014), and fatal motor vehicle crashes with cannabis-positive drivers; whereas no significant change was observed in 34 states without legalized medical marijuana (Salomonsen-Sautel et al., 2014). Establishing evidence-based *per se* laws for DUIC remains challenging, with varying laws across the US (Armentano, 2013; Grotenhermen et al., 2007; Lacey et al., 2010). Many are concerned that implementing concentration-based cannabis-driving legislation will unfairly target individuals not acutely intoxicated, because residual THC can be detected in blood for up to a month of sustained abstinence in chronic frequent smokers (Bergamaschi et al., 2013). Appropriate blood THC concentrations that universally reflect driving impairment remain elusive. Determining blood THC concentrations associated with lateral control impairment in occasional users would benefit forensic interpretation.

There is interest in linking driving impairment with oral fluid (OF) THC concentrations. OF is easy to collect, non-invasive, and associated with recent cannabis intake (Bosker and Huestis, 2009; Drummer, 2006; Wille et al., 2014). OF-based DUIC legislation exists in some jurisdictions (Drummer et al., 2007; Huestis et al., 2011; Van der Linden et al., 2012); however, limited simultaneous driving and OF concentration data preclude direct association with impairment.

Alcohol is the most common drug identified in drivers (Berning et al., 2015; Legrand et al., 2013). Cannabis and alcohol, frequently detected together (Legrand et al., 2013), produced greater impairing effects together than either separately (Robbe, 1998; Ronen et al., 2010), but it is unclear whether effects are additive or synergistic.

This is the first in a series of manuscripts evaluating cannabis' effects, with and without concurrent alcohol, on driving. We present here effects, relative to THC concentrations, on drivers' lateral control. We hypothesized cannabis and alcohol would each impair lateral control, with synergistic effects when combined.

2. Methods

2.1. Participants

Healthy adults provided written informed consent for this Institutional Review Board-approved study. Inclusion criteria were ages 21–55 years; self-reported cannabis consumption ≥1×/3 months but ≤3 days/week over the past three months (Cannabis Use Disorders Identification Test [CUDIT]; Adamson and Sellman, 2003); self-reported "light" or "moderate" alcohol consumption according to a Quantity-Frequency-Variability (QFV) scale (Sobell and Sobell, 2003); or, if "heavy", not more than 3–4 servings on a typical drinking occasion; licensed driver for ≥2 years with currently valid unrestricted license; and self-reported driving ≥1300 miles in the past year. Exclusion criteria included past or current clinically significant medical illness; history of clinically significant adverse event associated with cannabis or alcohol intoxication or motion sickness; ≥450 mL blood donation in two weeks preceding drug administration; pregnant/nursing; interest in drug abuse treatment within past 60 days; currently taking drugs contraindicated with cannabis or alcohol or known to impact driving; requirements for nonstandard driving equipment; and prior participation in a similar driving simulator study.

2.2. Study design/procedures

Participants entered the clinical research unit 10–16 h prior to drug administration to preclude acute intoxication. Participants drank 90% grain alcohol in fruit juice to reach approximately 0.065% peak breath alcohol concentration [BrAC], or placebo (juice with alcohol-swabbed rim and topped with 1 mL alcohol to mimic alcohol taste and odor) *ad libitum* over 10 min. After drinking, they inhaled 500 mg placebo (0.008 ± 0.002% THC), low (2.9 ± 0.14%)-, or high (6.7 ± 0.05%)-THC vaporized (Volcano® Medic, Storz & Bickel, Tuttlingen, Germany) cannabis (NIDA Chemistry and Physiological Systems Research Branch) *ad libitum* over 10 min. Participants received all six alcohol/cannabis combinations in randomized order, with sessions separated by ≥1 week.

Simulated drives occurred 0.5–1.3 h after start of cannabis dosing. Blood collection times were 0.17, 0.42, 1.4, and 2.3 h post-inhalation. Blood was collected via indwelling peripheral venous catheter into grey-top (potassium oxalate/sodium fluoride) Vacutainer® tubes (Becton, Dickinson and Company, Franklin Lakes, NJ), and stored on ice ≤2 h. Specimens were stored in 3.6 mL Nunc® cryotubes (Thomas Scientific, Swedesboro, NJ) at −20 °C, and analyzed within three months, based on known cannabinoid stability (Scheidweiler et al., 2013). OF was collected simultaneously with blood (except 0.42 h), with the Quantisal™ collection device (Immunalysis, Pomona, CA). BrAC was measured via Alco-Sensor® IV (Intoximeters, St. Louis, MO) at the same times as blood, reporting alcohol in g/210 L breath (limit of quantification [LOQ] 0.006 g/210 L), equivalent to approximate blood alcohol concentration (BAC).

2.3. National Advanced Driving Simulator

Driving simulations were conducted in NADS-1, the high-fidelity, full-motion simulator at the National Advanced Driving Simulator (NADS), Iowa City, IA (Fig. 1). A 1996 Malibu sedan is mounted in a 7.3 m-diameter dome with a motion system providing 400 m^2 acceleration space, ±330° rotation, and high-frequency motion (Lee et al., 2010). Drivers experience acceleration, braking, steering cues, road conditions (e.g., gravel), and realistic sounds (e.g., wind, motor). NADS-1 produces a complete record of vehicle state (e.g., lane position) and driver inputs (e.g., steering wheel position).

2.4. Drives

The 45 min drive challenged multiple driving skills affected by cannabis, including SDLP. Each drive had urban, interstate, and rural nighttime segments. The urban segment involved a two-lane city roadway with posted speed limits 25–45 miles/h (40–72 km/h) and signal-controlled and uncontrolled intersections; interstate, a four-lane divided expressway with posted 70 miles/h (113 km/h) speed limit; rural, two-lane undivided road with curves, a gravel portion, and a 10 min timed straightaway. Because each participant drove six times, three scenarios with varied event orders were utilized to minimize practice effects. Each scenario contained the same number of curves and turns, in varied order and position. Other traffic, pedestrians, and potential hazards were present throughout the drive. Hundreds of performance variables were monitored; the lateral control (necessary for road tracking, lane keeping) subset is presented here.

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