STUDY PROTOCOL AND STATISTICAL ANALYSIS PLAN

Official Title: Acute Effects of Cannabis on Cognition and Affect

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SECTION 1: STUDY PROTOCOL

Objectives and Purpose of the Study

There are three objectives to this study:

1. To examine the acute effects of cannabis on various aspects of executive functioning (primary outcome) and to explore neural correlates of these effects.
2. To examine the acute effects of cannabis on affect (secondary outcome) and to explore moderators of those effects.
3. To examine the acute effects of cannabis on feeding behavior (secondary outcome) and explore effects of feeding on intoxication.

An abundance of previous research has established that acute cannabis intoxication produces impairments in memory, but the effects of acute cannabis use on executive functioning are less well understood. We plan to administer multiple measures of executive functioning tapping different components (task switching/cognitive flexibility, inhibition, planning, working memory) to determine which aspects of executive functioning are impaired and which are spared by acute cannabis intoxication. Moreover, few studies have examined brain activity during completion of executive function tests to determine the underlying mechanisms of the acute effects of cannabis on different components of executive functioning.

Additionally, most previous research on the acute effects of cannabis has focused on detrimental effects and less is known about potential beneficial effects of cannabis. We plan begin to fill this gap by examining whether cannabis increases positive affect, experiences of awe, connectedness to nature, connectedness to humanity, and connectedness to close others, in response to a nature video.

Responses to cannabis can vary with some people experiencing increased anxiety while others experience reduced anxiety and elevations in mood. Despite this, very little is understood about what may underlie these differential responses to acute cannabis intoxication. To help understand individual differences in responses to acute cannabis intoxication, we will examine whether baseline depression, anxiety, ADHD symptoms, difficulties with emotion regulation, and/or cannabis use motives moderate the acute effects of cannabis on mood/anxiety/affect/and executive functioning.

Finally, very little empirical research has been conducted on the "munchies" phenomenon, and little is known about which types of foods people prefer to eat when they are intoxicated (e.g., high carb, high fat), or whether eating helps to make them feel sober faster. We will help fill these gaps in knowledge by observing feeding behavior while participants sober up. We will also measure use of GLP-1 drugs to examine whether they block the munchies phenomenon.

Protocol/Procedures

Design: We will use a double-blind, placebo-controlled, cross-over design. Specifically, participants will be randomly assigned to be administered either cannabis vapor (20 mg THC) or placebo vapor (0 mg THC control) in session 1 and the opposite product in session 2. Participants and research assistants will be blinded to the condition (cannabis or placebo).

Cannabis Procurement, Storage, and Transport: Cannabis will be obtained from the National Institute on Drug Abuse (NIDA). We will obtain cannabis containing 13.7% THC (barrel #1592). Our plan for dosing considers potency (grams of flower x 1000 x %THC = mg THC) so participants will be administered .15g of 13.7% THC cannabis flower. Note: most dispensaries sell 0.5 - 1-gram joints that exceed 20% THC (100-200 mg of THC), so this is still a modest dose. The placebo will also be obtained from NIDA. The cannabis contains 13.7% Δ^9 THC and 1.2% cannabidiol (CBD). The placebo (Lot #1004-1904-01) contains <0.025% Δ^9 THC, 0.03% Δ^8 THC, 0.14% CBD, <0.025% CBC, and <0.01% CBG, CBN, and THCV.

Cannabis will be stored in the PI's secure cannabis storage facilities in room 218E of the Veterinary and Biomedical Research (VBRB) building. These highly secure storage facilities have been approved by the Drug Enforcement Agency (DEA). More specifically, access to VBRB 218E requires the activation of a proximity detector by a programmed security badge at all times (including working hours). In addition, access to the hallways where room 218E resides is limited and requires a valid swipe by a programmed security identification card at all times. Outside of working hours, entrance to the building requires activation of a proximity detector by a programmed security badge. Cannabis is stored in a locked, wall-mounted stainless steel drug storage cabinet dedicated to Dr. McLaughlin's laboratory located in 218E. The drug storage cabinet (29" W x 29" H x 14" D) has two locked doors and there are six individually locked drug storage compartments (4.5" W x 9" H x 9" D) behind each door. Cannabis is also stored in a lockable refrigerator. A different physical key opens each cabinet door and each of the 12 storage compartments. These keys are locked in a number combination locket that is attached to the drug cabinet. The refrigerator is equipped with a separate number combination lock. Only DEA authorized members of the lab know the code of each lock and the code can be reset as needed. A maximum of 24 hours prior to a scheduled testing session an individual authorized by the DEA (the PI) will transport a small amount of cannabis or placebo (corresponding to 20 mg THC) from the secure VBRB storage facilities to Johnson Tower (JT) 122 where the cannabis will be vaped by participants. The product will be stored in the chamber of a Volcano Vaporizer in a locked room (JT 122).

Recruitment: Cannabis users (n = 92) will be recruited from the Pullman and neighboring communities. Advertisements will be placed in local cannabis dispensaries and on social media (e.g., Facebook Free & For Sale, Reddit, Instagram). We will also email chronic cannabis users who have participated in our former cannabis studies (and who indicated they would be willing to be contacted with invitations for subsequent studies) to invite them to participate. These advertisements and emails will contain a link to an online Qualtrics survey that will be used to determine eligibility.

Inclusion/Exclusion Criteria: This screening survey will be used to screen for serious psychiatric conditions (psychosis, bipolar I, panic disorder), a family history of psychosis, neurological disorders, chronic medical conditions (e.g., heart disease, diabetes), learning disabilities, intellectual disabilities, history of multiple concussions or head injury that may impact cognition, pregnancy or lactation, and history of adverse experiences with cannabis (psychosis, panic attacks), use of illicit drugs in the past 6 months, heavy alcohol use (> 4 drinks, > 4 times/week), and smoking/nicotine use. Eligible participants will need to have used cannabis at least once a week for at least one year, and they will need to indicate that they typically inhale cannabis and are willing to abstain from using any cannabis on the day of their scheduled testing session (minimum of 8 hours of abstinence). This survey will be used to obtain contact information from interested and eligible candidates. Eligible candidates will be contacted using the contact information they provided to schedule the testing sessions. Ineligible participants will not be given the opportunity to input their contact information, so sensitive information will only be collected from eligible individuals.

Consent & Drug Screen: Participants will meet the research assistant in The Health & Cognition (THC) lab in the Department of Psychology at WSU (JT 331 or 333). After obtaining written informed consent, participants will be asked when they last ate, drank (anything other than water), and used cannabis. Participants who report using cannabis that day will be rescheduled and will be reminded that they must abstain from any cannabis use on the day of the testing session. To further verify abstinence from cannabis on the day of the testing session, they will be asked to complete a THC saliva test (this simply involves briefly sucking on a cotton pad at the end of a test strip). They will then be asked to complete a 12-panel urine drug test to ensure they test negative for illicit drugs. To collect the urine sample, participants will take a sterile urine cup and brown paper bag to the private restroom down the hall from the THC lab and provide a small urine sample in the cup. The urine will be tested (by the RA) for recent drug use using a commercially available 12-panel drug test (dip test strips into urine). The results will be recorded on paper (with participant ID code only) and then the urine will be dumped in the toilet, and the cup and drug test will be placed in the brown paper bag and then placed in the restroom garbage. Participants who test positive for illicit drugs are not eligible and will not be permitted to complete the study.

Survey and Baseline Assessments: Participants who pass the drug test (test negative for recent cannabis or illicit drugs) will be fitted with an EEG headband (Muse S Athena, commercially available). They will then rate how high they feel using a scale from 0 = “not high at all” to 10 = “extremely high.” Next, they will complete standardized, valid, and reliable measures of their cannabis consumption patterns (Daily Sessions, Frequency, Age of Onset, and Quantity of Cannabis Use Inventory), depression (Center for Epidemiologic Studies Depression Scale [CES-D]), anxiety (Beck Anxiety Inventory [BAI]), ADHD symptoms (Barkley Adult ADHD Rating Scale - IV), motives for cannabis use (Marijuana Motives Questionnaire), emotion regulation (Difficulties in Emotion Regulation Scale [DERS]), and affect (Daniels Five-Factor Measure of Affective Well-Being [D-FAW], the Dispositional Positive Emotions Scale [DPES]), as well as provide demographic information. The information from this survey will be used to characterize the sample, determine covariates that should be controlled for in analyses, and examine the potential moderating effects of depression, anxiety, affect, and emotion regulation on cannabis induced changes in cognition and affect.

Drug Administration: Once the baseline assessments have been obtained the researcher will bring the participant down to room 122 of Johnson Tower for the vaping session. This is a secluded room (none of the neighboring rooms are currently in use) in the basement of Johnson Tower and has a functioning fume hood. The researcher will position the Volcano Vaporizer pre-loaded with cannabis containing 20 mg of THC or placebo (the researcher and participant will be blind to the product) near the participant. The researcher will turn the vaporizer on and will wait until it heats up to 210 degrees Celsius. This temperature is ideal as it is not hot enough for the plant material to burn, so many of the toxins associated with smoking are not released. The researcher will set up a Zoom videoconferencing session on an iPad/computer positioned in front of the participant and will text Dr. McLaughlin (PI) or Dr. Cuttler (Co-PI) to join the Zoom call. Importantly, this Zoom session will NOT be recorded. The researcher will then go to an adjacent room and wait until the cannabis session is complete to aid with blinding the researcher to drug condition. Once one of the PIs joins the Zoom call, they will instruct the participant to begin inhaling the vapor and exhaling into a “sploofy” carbon filter. They will be asked to try to inhale for a minimum of 2 seconds, and hold for 2 seconds, before exhaling into the sploofy. The PI or Co-PI will count the total number of puffs the participant inhales and will time the duration of their inhalations and holds. Once the participant has inhaled 30 puffs, they will be asked to exhale into the air and to look to see if there is any visible vapor. If they see visible vapor, they will continue to take more puffs and exhale into the sploofy. Every 5-10 puffs they will exhale into the air to check for any visible vapor. This will continue until they don’t see any vapor upon exhalation. The PI will text the RA once the vaping session is complete and the RA will return to JT 122, clean the mouthpiece with rubbing alcohol, put the Volcano Vaporizer away, and turn on the fume hood. The RA will then bring the participant back to JT 331 or JT 333 to complete the cognitive tests.

Subjective Ratings: Participants will rate how high they feel using a scale from 0 = “not high at all” to 10 = “extremely high.” They will also rate the level of good drug effects they are experiencing and their liking of those drug effects using similar 0 to 10 scales. Participants will be asked to rate their affect using the D-FAW.

Cognitive Tests: Participants will be asked to complete measures of task switching/cognitive flexibility, inhibition, planning, and working memory.

Intradimensional/Extradimensional Set Shifting Task. Participants are instructed to select between paired visual stimuli (e.g., geometric shapes/lines) based on learned rules and use feedback to determine the correct response. The relevant stimulus features and rules change across task stages, and participants must determine what the correct selection rule is based on the provided feedback. The goal is to demonstrate cognitive flexibility, as indicated by how well participants can adapt to these rule changes, which are often measured by the number of perseverative errors across task stages.

Prospective Memory Tests*.* Participants will be assigned two prospective memory tasks. Specifically, participants will be asked to remember to rate how difficult they found each test immediately after it is completed, using a 0 (not at all difficult) to 10 (extremely difficult) scale. The primary outcome of interest

is the number (or percentage) of difficulty ratings they remember to provide. Other outcomes of this task are the self-reported difficulty of each task completed.

They will also be asked to try to remember to request a token every 10 minutes. A clock will be positioned face down on the table for them to refer to the time and we will record their clock checking behavior throughout each 10-minute block. The primary outcome is the number (or percentage) of times they remember to request the token, out of the total time of the cognitive assessment session.

Go-No/Go Task. Participants are presented with basic visual stimuli and are asked to tap to respond when a target stimulus appears and refrain from responding when a non-target stimulus appears. The primary outcome of interest is the number of accurate trials. Greater accuracy on the task will be indicative of greater inhibitory control. Other outcomes will be the number of commission errors, defined as responses made to No-Go stimuli. Higher commission error scores indicate poorer inhibitory control. The Muse S Athena wearable EEG device will also capture time-locked event-related potential (ERP) data during this task which will be explored.

N-Back Test. Participants are shown strings of letters one at a time and are instructed to tap the screen whenever a letter appears that matches the letter shown two letters ago. This is a measure of working memory/cognitive flexibility. The primary outcome is the percentage of correct responses made, also called the hit rate (i.e., the number of times they correctly recognize that the current letter matches the one from two trials before, etc.). Other outcomes include the mean reaction time (milliseconds) for correct responses on the task. The Muse S Athena wearable EEG device will also capture time-locked ERP data during this task which will be explored.

Color Word Interference Test (Stroop Test). For this test participants will be shown words whose letters are in a specific color (e.g., the word Blue shown in red) and they will have to select the button corresponding to the color that the letters are presented in. The primary outcome of interest is the interference score, which reflects the difference in reaction times between the incongruent (e.g., the word Blue shown in red) and congruent trials (e.g., the word Blue shown in blue). Other outcomes on this task include the percentage of correct responses on incongruent trials. The Muse S Athena wearable EEG device will also capture time-locked ERP data during this task which will be explored.

Probabilistic Reversal Learning. Cognitive flexibility will be assessed using a decision-making task where participants will choose between two response options and receive feedback indicating reward or no reward. One option is more likely to be rewarded (on 80% of trials), but feedback is probabilistic, so correct choices are not always reinforced. After a series of correct responses, the reward contingencies will reverse without warning, requiring participants to adjust their behavior based on changing feedback patterns. The goal is to measure flexibility in adapting to shifting reinforcement contingencies, indexed by switching behavior following reversals and sensitivity to feedback. The primary outcome of interest will be the proportion of trials on which participants select the stimulus associated with the higher probability of positive feedback. Higher advantageous-choice accuracy indicates more effective learning from probabilistic feedback. Other outcomes will be the proportion of trials on which participants repeat a previously rewarded choice (“win-stay”), the proportion of trials on which participants switch choices following negative feedback (“lose-shift”), and reversal errors, defined as incorrect choices made following a reversal in the stimulus–outcome contingencies.

The Zoo Maps Test. Participants are shown a map of a zoo and they are required to show how they would visit a series of designated locations while following certain rules (e.g., they must start at the entrance and end at the picnic area and use designated paths only once). The primary outcome of interest is the total achievement score, representing accuracy when generating a self-directed route under the provided constraints. Other outcomes on this task include the number of rule violations on the task and the overall completion time.

Verbal Fluency (Category Switching). Participants are given two categories (e.g., fruits and furniture) and are asked to name as many things as possible that belong to those categories in alternating order. The primary outcome of interest is category switching accuracy, which is the number of correct

switches between the categories. Other outcomes on this task include the category fluency score (the number of correct words generated), repetitions, and intrusion errors (i.e., non-category words).

***Digit Span Backwards Test*.** Participants are read lists of digits (of increasing lengths) and are asked to recall them in reverse order. The primary outcome of interest is the total number of correct trials.

***The Tower Test*.** Participants are given a wooden base with three columns and a set of disks of different sizes. They must construct a series of different towers using the disks. Their task is to create the towers by moving only one disk at a time and never placing a larger disk on top of a smaller disk. The primary outcome of interest is the total achievement score across the tower problems, which reflects planning effectiveness. Other outcomes on this task include the number of rule violations (e.g., stacking a larger disk on top of a smaller one) and the time taken to complete each tower problem.

Nature Video and Subjective States: Participants will then be brought to JT 330 where they will rate their affect using the D-FAW and the strength of their subjective high, good drug effects, and liking of the drug effects using 0 (not at all) to 10 (extremely) scales on an iPad. They will then watch a brief (approximately 4 min) nature video (there are two versions of this video that will be counterbalanced). After the nature video they will provide ratings of awe, their feelings of connectedness to nature, humanity, and close others, and they will re-rate their affect using the D-FAW.

Spontaneous Thought/Think Aloud Task. Participants will then be instructed to continuously verbalize the contents of their thoughts in real time for 5 minutes while alone in a quiet environment to assess spontaneous thought dynamics. They will be asked to speak freely about whatever comes to mind without filtering or structuring their responses, and no specific prompts or topics are provided during the task. Verbal responses will be audio recorded using the voice memo application on our lab's MacBook (university owned, password protected and encrypted) for later transcription and analysis using our lab's Python program. The goal is to capture the natural flow of spontaneous thought, including how flexibly individuals transition between ideas over time. Audio recordings will be transcribed and segmented into individual thought units, which are grouped into topics using natural language processing. Thought patterns will be characterized by the frequency and transitions between topics, including the degree of similarity between successive thoughts.

Subjective States: Finally, participants will rate the strength of their subjective high, good drug effects and liking of the drug effects. The EEG headband will then be removed.

Sobering and Food Consumption Monitoring: Participants will sit and entertain themselves in JT 330 until it has been at least 4 hours since their vape session ended, and they report feeling completely sober (i.e., a 0 on the intoxication scale). JT 330 is equipped with couches, chairs, a TV with streaming platforms, and a video game system. Snacks (e.g., fruit snacks, granola bars, hot pockets, chips, chocolate bars, nuts, jerky, soda, chocolate milk) will also be available for participants to consume while they wait. This room is equipped with a one-way mirror, and an RA will monitor participants via the window in the adjacent room to ensure the participants do not attempt to leave the lab, as well as monitor and record the snacks/beverages participants choose to consume (the calories, fat, protein and carbohydrate content of each) and the activities they choose to engage in while they sober up. Participants will be informed that the RA is in the adjoining room monitoring them and that they can call them for assistance at any time. The RA will enter the room every 30 minutes to collect intoxication ratings. Participants will also be asked to rate how much they enjoyed the taste of each food product or beverage they consumed in the prior 30 minutes using a 0 (dislike very much) to 10 (like very much) rating scale. Participants will permitted to leave the lab after it has been a total of 4 hours since their vape session ended, and they report feeling sober (give a 0 on the intoxication rating scale).

Session 2: One week later, participants will return for their second session which will be identical to the first, except those administered 20 mg of THC in session 1 will be administered placebo in session 2 and those administered placebo in session 2 will be administered 20 mg of THC in session 2.

Debriefing and Compensation: Participants will be debriefed and compensated at the end of session 2. They will receive $100 per session plus an additional bonus of $25 if they don't reschedule their second session for a total possible of $225.

SECTION 2: STATISTICAL ANALYSIS PLAN

Study Design and Analysis Population: A double-blind, placebo-controlled crossover trial will be conducted with 92 participants with a history of cannabis use. Recruitment will continue until 92 participants have completed both sessions. Each participant will complete two laboratory sessions approximately one week apart, receiving 20 mg Δ9-tetrahydrocannabinol (THC) during one session and a matched 0 mg THC placebo during the other. Product order will be randomized and counterbalanced across participants. Alternative forms (A and B) of cognitive tests with alternative forms available will be used and counterbalanced where applicable.

Sample Size and Power: An a priori power analysis conducted using G*Power indicated that a sample of 90 participants would provide 80% power to detect small effects (d = 0.34) with α = .05. This analysis informed the planned sample size of 92 participants, to effectively counterbalance the four conditions (cannabis vs placebo and assessment forms A vs B). The original power analysis does not imply that all individual outcomes or exploratory moderator effects are independently powered to detect effects of this magnitude.

Descriptive Analyses: Participant characteristics will be summarized using frequencies and percentages for categorical variables and means and standard deviations for continuous variables. Adverse events and other relevant safety outcomes will be summarized descriptively by condition.

Data Quality, Scoring, and Missing Data: Data will be entered and then checked/verified by a second research assistant. Data will be screened for completeness, implausible values, and scoring errors before analysis. Task outcomes will be scored according to prespecified task-specific rules, with practice trials excluded where applicable. Reaction times (RTs) below 200 ms will be treated as anticipatory responses and excluded from RT analyses. Tasks' built-in response windows will determine when responses time out. Timeouts will be scored according to each task's scoring rules, and RT exclusions will not automatically exclude trials from accuracy analyses. Extreme values will be checked for errors. True outliers (defined as scores > 3.29 standard deviations from the mean) will be adjusted by making them 1 raw score above or below the nearest non-outlying value.

Participants who do not complete both experimental sessions will be excluded from the primary crossover analyses. Participants with sporadic missing or unusable outcome data in one session will not be excluded and may contribute available valid observations to mixed-effects models; analyses requiring complete paired scores will include only participants with usable data in both conditions.

General Analytic Approach: Continuous outcomes will be analyzed using linear mixed-effects models (LMMs), and binary, count, or proportion outcomes using appropriate generalized mixed-effects models (GLMMs). Models will include condition (THC vs. placebo), session (first vs. second), and product order (THC first vs. placebo first) as fixed effects, with a participant random intercept to account for repeated observations. See Equation 1 for a general model for a continuous outcome.

Equation 1. $Y_{ij} = \beta_0 + \beta_1 C_{ij} + \beta_2 P_{ij} + \beta_3 S_i + u_i + \varepsilon_{ij}$

Where:

- Y_{ij} = outcome for participant i during session j
- C_{ij} = drug condition (THC versus placebo)
- P_{ij} = session (first versus second)
- S_i = randomized product order
- β_0 = intercept
- β_1 = effect of drug condition, **the primary effect of interest**
- β_2 = period effect
- β_3 = sequence effect
- u_i = participant-specific random intercept
- ε_{ij} = residual error

Assessment form (A vs. B) will be included as a fixed effect for outcomes that had counterbalanced alternative versions (e.g., $\beta_4 V_i$ where β_4 = version effect and V_i = version). Models for repeated ratings

within a session will include time and condition × time effects, with participant-level random effects accounting for repeated observations. Model assumptions will be evaluated, and alternative specifications will be used where necessary. Effect estimates, 95% confidence intervals, and two-sided *p*-values will be reported.

Primary Outcomes

Cognitive flexibility. Intra-dimensional/extradimensional set-shifting task (IDED) extradimensional (ED)-shift errors (failures to shift response strategy in the extradimensional shift trials) and verbal fluency category-switching accuracy (number of correct category switches in 60 s) will be analyzed using a Poisson GLMM; IDED total accuracy and probabilistic reversal learning task (PRL) choice "accuracy" (the proportion of choices of the higher probability of reward stimulus) will be analyzed using a binomial GLMM, with trial-level data when available. Assessment form will be included as a fixed effect where applicable.

Inhibitory control. Stroop interference (mean correct-response RT on incongruent trials minus mean correct-response RT on congruent trials) will be analyzed using an LMM. Go/No-Go accuracy (the proportion of accurate trials out of eligible trials) will be analyzed using a binomial GLMM. Go trials with a response and No-Go trials without a response will be scored as correct; the converse will be scored as incorrect.

Planning. Tower Test Total Achievement and Zoo Maps Total Achievement scores will be analyzed using separate LMMs.

Working memory. N-back performance will be assessed using a GLMM analyzing target "hit" rate (correct target selections divided by eligible target trials). Importantly, the first two trials of each block will be excluded, as the sequence restarts between blocks. Digit Span Backwards total correct will be analyzed using an LMM.

Prospective memory. Event-based prospective memory will be measured as the proportion of difficulty ratings remembered and provided after cognitive tasks. Time-based prospective memory will be measured as the proportion of scheduled 10-minute token requests correctly remembered and completed. Both outcomes will be analyzed using binomial GLMMs, modeling successful responses relative to eligible opportunities.

Secondary Outcomes

Subjective drug effects. Ratings of intoxication, good drug effects, and drug liking (0–10) will be assessed at T1 (immediately after vaping), T2 (after cognitive testing), and T3 (after the nature video). Separate LMMs will include condition, categorical time, and the condition × time interaction as fixed effects, along with session and product order. Significant interactions will be followed by contrasts comparing conditions at each time point, with Sidak adjustments applied to the time-specific contrasts within each outcome.

Post-video awe and connectedness outcomes. Awe and connectedness to nature, humanity, and close others (assessed after the nature video), will be analyzed in separate LMMs. Video version will be included as a fixed effect.

Affective well-being outcomes. The Daniels Five-Factor Measure of Affective Well-Being (D-FAW) will be completed at baseline (T0), T1, T2, and T3. The five subscales will be analyzed as separate secondary outcomes using LMMs with condition, categorical time, and the condition × time interaction as fixed effects, along with session and product order. Significant interactions will be followed by estimated marginal means contrasts comparing conditions at each time point, with Sidak adjustments applied to the time-specific contrasts within each subscale. Individual D-FAW items will be analyzed separately as exploratory outcomes.

Food consumption outcomes. Total calories, grams of carbohydrates, grams of fat, grams of protein consumed and taste ratings will be assessed every 30 minutes after they have access to food (after completion of the cognitive and affective measures). Separate LMMs will include condition, time

window, and the condition × time window interaction as fixed effects, along with session and product order. Significant interactions will be followed by contrasts comparing conditions at each time point, with Sidak adjustments applied to the time-specific contrasts within each outcome.

Exploratory Moderator Analyses: Sex, cannabis-use frequency, mental health outcomes (symptoms of depression, anxiety, and ADHD), and motives for use will be examined as exploratory moderators by adding condition × moderator interaction terms to relevant outcome models. These analyses will be interpreted as exploratory because the study is not specifically powered to detect moderator effects.

Multiple Comparisons and Reporting: The Benjamini–Hochberg false discovery rate (FDR) procedure will be applied separately within five primary outcome domains: (1) working memory, (2) planning, (3) inhibitory control, (4) cognitive flexibility, and (5) prospective memory. For subjective drug effects, FDR correction will be applied separately across the three omnibus condition × time interaction tests. Significant interactions will be followed by estimated marginal means contrasts comparing THC and placebo at each time point, with Sidak adjustments applied to the three time-specific contrasts for each subjective drug effect outcome. Thus, Sidak will adjust for follow-up comparisons while the FDR correction will control for multiple comparisons across the tests. FDR correction will also be applied across the four post-video outcomes. For the five D-FAW subscales, FDR correction will be applied across the five omnibus condition × time interaction tests. Significant interactions will be followed by estimated marginal means contrasts comparing THC and placebo at each time point, with Sidak adjustments applied to the four time-specific contrasts within each subscale. Individual D-FAW item analyses will be considered exploratory. For the food consumption and taste rating outcomes, FDR correction will be applied across the five omnibus condition × time interaction tests. Significant interactions will be followed by estimated marginal means contrasts comparing THC and placebo at each time point, with Sidak adjustments applied to the time-specific contrasts within each food consumption and taste rating outcome. Unadjusted and adjusted *p*-values, effect estimates, and 95% confidence intervals will be reported. Statistical tests will be two-sided, with $\alpha = .05$.