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# Mapping short-term brain changes in cannabis users

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28/04/2020

**Recruitment status**
No longer recruiting

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12/05/2020

**Overall study status**
Completed

**Last Edited**
05/11/2025

**Condition category**
Mental and Behavioural Disorders

[ ] Prospectively registered
[X] Protocol
[ ] Statistical analysis plan
[X] Results
[ ] Individual participant data

## Plain English summary of protocol

Background and study aims
Cannabis is currently the most commonly used and arguably the most frequently debated illicit drug globally, with about 188 million people worldwide reporting use. A significant portion of cannabis users smoke daily-to-weekly and endorse Cannabis Use Disorder (CUD).
Heavy cannabis use is associated with adverse psychosocial and mental health outcomes. This includes cannabis dependence, reduced performance at work, school and some cognitive tasks, engaging in risk-taking behaviour (e.g. smoking while driving), and higher symptoms of mood, anxiety, and psychotic disorders. Worryingly, only about 36% of those experiencing problems with cannabis use seek treatment, and many of those who receive treatment for CUD fail to reduce their use or to quit. Emerging evidence suggests that mindfulness-based strategies that target core features of CUD – such as the experience of craving and withdrawal – may mitigate brain, mental health and cognitive harms associated with CUD.
The first aim of this study is to use MRI scans to map how brain, cognitive performance and mental health differs between people with a CUD (moderate-to-severe) compared to people who don't use cannabis. The second aim of this study is to examine how brain, cognitive performance and mental health harms in people with a CUD are mitigated after a brief 2-week mindfulness intervention, compared with a 2-week relaxation intervention and a 2-week no intervention period. The intervention has been successfully tested in hazardous drinkers by Co-Investigators Prof. Kamboj and Dr Freeman. Finally, this study will explore how brain alterations in CUD are associated with the level of cannabis use (e.g. dosage, duration of use), depression, anxiety and psychosis symptoms, and cognitive performance (e.g. attentional bias, impulsivity and working memory).

Who can participate?
People aged 18 to 55 from the general community, including frequent cannabis users and people who don't use cannabis

What does the study involve?
Frequent cannabis users are assessed at the start of the study and 2-week follow-up and will be divided into three groups to be allocated to either a 2-week daily mindfulness intervention and brief questionnaires, a 2-week daily relaxation intervention and brief questionnaires, or a 2-week no intervention period with daily brief questionnaires. People who don't use cannabis will be

assessed at the start of the study only for comparative purposes. Frequent cannabis users undergo an MRI scan at the start of the study and follow up.

What are the possible benefits and risks of participating?
Possible benefits from participating include a potential reduction in cravings for cannabis use and improved mood. The study is considered to be low risk.

Where is the study run from?
Assessments will be run at the Monash Biomedical Imaging facility (MBI) (Australia). The participant will complete the intervention online, at a location convenient for them.

When is the study starting and how long is it expected to run for?
November 2018 to September 2022

Who is funding the study?
Australian Catholic University (Australia)

Who is the main contact?
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# Contact information

### Type(s)
Public, Scientific

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# Additional identifiers

### Clinical Trials Information System (CTIS)
Nil known

### Protocol serial number

Nil known

# Study information

### Scientific Title
Mapping short-term brain changes in cannabis users: an fMRI study

### Study objectives
It is hypothesized that:
1. People with a moderate-to-severe cannabis use disorder (CUD) compared to non-cannabis using controls, will show altered structure (e.g. volumes and thickness) and function (e.g. activity and connectivity) within brain pathways ascribed to addiction-relevant cognitive processes, including:
1.1. Reward processing (e.g. striatum, orbitofrontal cortex)
1.2. Stress/negative affect (e.g. amygdala)
1.3. Cognitive control (e.g. parietal cortex, dorsolateral prefrontal cortex, cerebellum)
1.4. Learning and memory (e.g. hippocampus)
1.5. Interoception (e.g. insula).
2. Brain function will change in brain pathways regions implicated in:
2.1. Reward processing, cognitive control and interoception, pre-to-post a brief ~2-week mindfulness-based intervention, which targets cannabis craving compared to no intervention, as shown in early work examining normative samples (Fox et al., 2016; Reese, Zielinski, & Veilleux, 2015).
2.2. Stress and interoception, pre-to-post a brief, ~2-week active placebo-controlled relaxation intervention, compared to no intervention, as shown by emerging work investigating normative samples (Sevinc et al., 2018).
3. The researchers will explore the association between changes in measures of brain integrity and level of cannabis use severity, psychopathology symptom scores (e.g. depression, anxiety and psychotic-like experiences) and cognitive performance (e.g. attentional bias, impulsivity and working memory).

Brain function will be assessed during rest, and during fMRI tasks including (i) a cue reactivity fMRI task that involves exposure to cannabis pictures and carefully matched neutral pictures (Cousijn, Goudriaan, Ridderinkhof, van den Brink, Veltman, & Wiers, 2013), (ii) a monetary incentive delay fMRI task (van Hell, Vink, Ossewaarde, Jager, Kahn & Ramsey, 2010), and (iii) an avoidance learning fMRI task (Kim, Shimojo, & O'Doherty, 2006).

### Ethics approval required
Old ethics approval format

### Ethics approval(s)
Approved 10/06/2019, Australian Catholic University (ACU) Human Research Ethics Committee (HREC) (Level 16, Tenison Woods House, 8-20 Napier Street, North Sydney, NSW 2060, Australia; +61 (0)2 9739 2646; Res.Ethics@acu.edu.au), ref: 2019-71H

### Study design
Double-blind active-placebo-controlled design

### Primary study design
Interventional

## Study type(s)
Treatment

## Health condition(s) or problem(s) studied
Moderate-to-severe Cannabis Use Disorder (CUD), as defined by the Diagnostic and Statistical Manual of Mental Disorders, Fifth Edition (DSM-5)

## Interventions
Blinding details:
The study includes “blinded” and “unblinded” testers, with distinct roles described below.
1. Selected researchers will administer face-to-face clinical and cognitive assessment, and MRI to the participant, without knowing which intervention condition cannabis users have been allocated to. These researchers will be referred to as “blinded” testers.
2. Selected researchers will be unblinded to each CUD participant’s allocation to the three intervention conditions. These will be referred to as “unblinded” testers.
Unblinded testers will not administer any testing other than the intervention. Specifically, “unblinded” testers will:
1.1. Allocate CUD participants to one of the three distinct intervention conditions in a pseudo-randomised fashion. This is to ensure group matching for age and sex across all three intervention conditions and the non-using control group, and for the number of CUD symptoms at baseline across the three intervention conditions.
1.2. Administer the intervention at baseline and follow up face-to-face assessments.
1.3. Administer scales immediately before and after the intervention at baseline and follow up face-to-face assessments, to monitor its effectiveness.
1.4. Give participants information and material relevant to the online practice of the intervention.
1.5. Monitor the participant’s completion of the online daily intervention for the 2-week intervention period (e.g. VAS scales and/or audio tracks).
1.6. Communicate with the participants about any issues during the intervention period.
1.7. Debrief the participants on the intervention.

OVERALL STRUCTURE OF THE ASSESSMENT AND INTERVENTION PROTOCOL
1. THREE MAIN PHASES
The testing protocol comprises three main phases:
1.1. Face-to-face baseline assessment, ~4 hours (here on referred to as ‘baseline assessment’)
1.2. ~2-week daily off-site, online intervention, ~10-15 minutes daily
1.3. Face-to-face follow up assessment, ~3 hours (~2-weeks post baseline) (here on referred to as ‘follow up assessment’)

2. ROLES OF BLINDED AND UNBLINDED TESTERS
Both blinded and unblinded testers will be present at the start of the two (baseline and follow up) assessments and will drive distinct part of the assessment. Specifically:
2.1. A blinded tester will run all experimental procedures and assessments of socio-demographic variables, substance use, mental health and cognitive performance.
2.2. An unblinded tester will administer all information specifically pertaining to the intervention (the intervention itself and pre-to-post intervention related scales).
2.3. An unblinded tester will be responsible for debrief at baseline and at follow up with queries on intervention and obtaining consent at follow up.
2.4. An unblinded tester will be responsible for daily monitoring of the online tasks/intervention (e.g. VAS scales and/or audio tracks) and SMS reminders if these are missed, as well as communicating with the participant about any issues during the intervention period.

2.5. During the MRI scan:
2.5.1. A blinded tester will interact with the participant and read scripts relating to the delivery of the assessment
2.5.2. An unblinded tester will support the running of the technical aspects of the MRI that do not require direct interaction with the participant (e.g. open and save relevant fMRI task files and logs, to ensure timely completion of the MRI).

3. OVERVIEW OF BASELINE FACE-TO-FACE ASSESSMENT
3.1. First, at the start of the baseline assessment, a blinded tester will ask the participant to review and clarify all study details explained in the Participant Information Letter and to provide written informed consent to participate in the study.
3.2. Second, a blinded tester will ask the participant to provide a urine sample to confirm the presence and absence of THC metabolites in cannabis users and non-users, respectively, and the absence of any other drug metabolites.
3.3. Then, a blinded tester will administer to the participant a battery of validated cognitive tasks (to assess IQ, attentional bias, working memory, disinhibition), semi-structured interviews and self-report questionnaires (relating to mindfulness, substance use, and mental health); as well as an MRI scan to measure brain structure and function.
3.4. Finally, an unblinded tester will administer the intervention (i.e. press play on the intervention audio track and/or provision of VAS scales and debrief the participant). Non-cannabis using controls will be reimbursed and debriefed for their participation at this stage.

4. OVERVIEW OF THE ~2-WEEK OFF-SITE INTERVENTION PERIOD
4.1 Online delivery of the daily tasks
The ~2-week intervention will be run off-site, during the period between baseline and follow up assessment. The participant will be able to practice the intervention tasks via either an online link or via relevant files on the USB, both of which will be provided at the end of baseline testing by an unblinded tester.

4.2 Content of the daily tasks
Daily tasks will be given to the three CUD groups and will differ based on the intervention condition:

Those allocated to any intervention condition, will complete:
1. A 1-point VAS scale to indicate the levels of: craving for cannabis, relaxation, tension, and mindful attention.
2. A short questionnaire to indicate compliance, risk behaviour, mood, cravings, and cannabis use level.

Those allocated to the mindfulness and relaxation groups, will:
1. Listen to the 7-minute audio track with the allocated intervention
2. Complete a short questionnaire to indicate if they practiced the psychological strategy explained during the audio track, when they experience cannabis craving in moments other than during the audio track.

4.3. Monitoring of participants' compliance with daily tasks
An unblinded tester will monitor the participant's completion of daily tasks through Qualtrics and send reminders if the participant does not complete the tasks. Reminders will be provided as follows:
4.3.1. A SMS reminder, after the participant does not complete their tasks for 1 day
4.3.2. A SMS reminder, after the participant does not complete their tasks for 2 days
4.3.3. Phone call the participant to confirm if they are experiencing any issues to do the daily

tasks, if the participant does not complete their tasks for > two consecutive days
4.3.4. Daily (either SMS or phone) reminders from an unblinded tester if the participant remains non-compliant

Regardless of the level of compliance, the follow-up assessment will take place. The amount of intervention completed (e.g. total number of days or total number of minutes practiced) may be used as predictors of the outcomes of interest.

5. OVERVIEW OF THE FOLLOW UP FACE-TO-FACE ASSESSMENT
The follow-up assessment takes place ~2 weeks after the baseline assessment. These assessments are identical, with some exceptions. Specifically, at follow up:
5.1. The intervention is administered at the start of the assessment after participant' written informed consent is provided. This is to boost the effect that the 2-week intervention might have on the outcomes of interest.
5.2. The debrief includes additional questions about their experience of the intervention (e.g. if the participant found it useful and when they practiced it).
5.3. "Trait" variables already assessed at baseline will be not be measured, as these are unlikely to change over time (e.g. socio-demographic data, menstrual cycle details for females, CAPE, CUI, AUDIT, MMQ, CUD module of the SCID, and SF-36).
5.4. The WASI testing of IQ will not be administered, as this is already measured at baseline.
5.5. Measures that are irrelevant are not administered (i.e. the planning session for the 2-week intervention period).

INTERVENTION CONDITIONS
There will be three intervention conditions, all of which will be accessible via online weblinks in Qualtrics:
1. A 2-week mindfulness-based intervention, consisting of a guided mindfulness audio track and VAS scales (e.g. stress, anxiety, substance use levels on the day of completion; see OUTCOMES section 2 below for detailed explanation of measures).
2. A 2-week active placebo-controlled relaxation-based intervention, consisting of a guided relaxation audio track and VAS scales (e.g. stress, anxiety, substance use levels on the day of completion).
3. A 2-week passive placebo no intervention consisting of VAS scales only (e.g. stress, anxiety, substance use levels on the day of completion).
Note: Non-cannabis using controls will not be administered an intervention. This group will undergo only the baseline face-to-face assessment, which will be identical to that of cannabis users.

The allocated intervention (i.e. VAS scales and/or audio tracks) will be administered in three different phases outlined below.

PHASE I (BASELINE FACE-TO-FACE ASSESSMENT)
The first delivery of the intervention will occur at the end of the baseline face-to-face assessment. An unblinded tester will run this component of the assessment, which will include:
1. VAS and Toronto Scale (administered pre- and post-intervention), and the Credibility /Manipulation Check (administered post-intervention). See OUTCOMES section 2 below for detailed explanation of measures.
2. Audio track with the content of the intervention. The unblinded tester will start the track (i.e. press play) so the participant will hear the audio track via headphones connected to a laptop.
3. The first audio track will encapsulate 4 parts:
Part 1: A 30-second introduction. This explains the aim of the intervention. This part is identical for both the mindfulness and the relaxation intervention conditions;

Part 2: A 3-minute explanation of the psychological strategy that they will be asked to practice;
Part 3: A 4-minute preliminary experiential practice;
Part 4: The 7-minute "main" track that encapsulates the intervention that the participant will be asked to practice daily (either mindfulness or relaxation). The word 'mindfulness' will not be mentioned in either intervention to minimise expectancy effects.
4. During the first delivery of the intervention at baseline face-to-face testing, assessment of credibility and expectance will be run using The Credibility/Expectancy Questionnaire (CEQ; Devilly & Borkovec, 2000). These are described in detail in the section 'Secondary Outcome Measures – Mindfulness and Interventions Measures'.
5. At the conclusion of the first delivery of the intervention, an unblinded tester will:
5.1. SMS the participant with the online web-link to access the intervention in order to complete it at home
5.2. Give the participant a USB stick with back-up files necessary to practice the intervention (i.e. VAS scales in a word document, and/or MP4 audio tracks), to facilitate the compliance of people with limited access to online data.

2.2 PHASE 2 (ONLINE, OFF-SITE DAILY INTERVENTION)
The participant will be required to practice the intervention (using the online link or the USB files) daily offsite for ~2-weeks, between the baseline and the follow up face-to-face testing.

The allocated intervention will consist of the VAS scales (the sole component in the "no intervention condition"), followed by 7-minute long audio tracks (i.e. described above) for either the mindfulness or relaxation intervention condition.

An unblinded tester will measure compliance via monitoring the participant's daily completion of the intervention, through the study's online Qualtrics server.

PHASE 3 (FOLLOW UP FACE-TO-FACE ASSESSMENT)
The final delivery of the intervention will occur at the start of the follow up face-to-face assessment (immediately after informed consent). This is in order to boost the ~2-week intervention effect on the outcomes of interest at follow up. An unblinded tester will run this component of the assessment, which will include:
1. VAS and Toronto Scale (administered pre- and post-intervention). See OUTCOMES section 2 below for a detailed explanation of measures
2. Audio track with the content of the intervention. The unblinded tester will start the track (i.e. press play) so the participant will hear the audio track via headphones connected to a laptop. The intervention will be the 7-minute track as used across the previous 2-weeks and at baseline (see 2.1.3.4).
Audio-tracks containing the interventions will be made available to all participants after the completion of the study.

INTERVENTION SCRIPTS
The scripts used for the mindfulness and relaxation intervention conditions have the following characteristics:
1. They do not contain the word 'mindfulness', to mitigate expectancy effects
2. They rely on already establish scripts used for delivering a similar intervention in hazardous drinkers, which was published by Co-Investigators Prof Sunjeev Kamboj and Dr Tom Freeman (PMID: 29016995).
3. They are delivered on high-quality audio tracks, which were read and recorded by Tamblyn Lord, who is a qualified mindfulness instructor with >20 years of experience, is the voice of the Smiling Mind application, and is a career voice artist/actor.
4. They are matched by the following parameters: length (15 minutes for the first delivery at

baseline, and 7-minutes for subsequent deliveries during the intervention and at follow up), number of smoking- and craving-related words, language complexity (Flesch-Kincaid grade level 8), keywords relating to craving and cannabis, sequence of components and readability scores.
5. They are matched by number of words for the mindfulness intervention i.e. 1,779 words. These include 946 words for the baseline assessment audio track and 833 words for subsequent at home intervention and follow up assessment audio tracks.
6. They are matched by number of words for the relaxation intervention: 1,783 words. These include 949 words for the baseline assessment audio tracks and 834 words for subsequent at home intervention and follow up assessment audio tracks.

Example phrases used for the interventions:
1. Relaxation script: During the explanation of the intervention, the participant is instructed that craving intensity can be reduced by “softening the muscles...and calming and unwinding the mind…releasing tension in your body” and that relaxation enables transformation of sensations into more calming, less unpleasant experiences. It is also emphasized that this is a way of gaining control over craving.
2. Mindfulness script: By contrast, instructions for the mindfulness script did not include any mention of reduced “craving or of controlling, transforming, or regulating internal experience. It was clarified that the aim was not to simply relax, but to be alert and attentive. The emphasis was on “open monitoring” of experience and particularly on “aware[ness] of feelings and bodily sensations” and to “experience craving in a different way.” The participant was told that by noticing bodily sensations they could “experience them as temporary events in the body,” helping the participant to “tolerate [bodily sensations] without acting on them.” To minimize expectancy effects relating to the increasing popularity and public discussion of complementary medicine approaches, there was no mention of the term “mindfulness” (or “relaxation”) in any experimental or recruitment material.

## Intervention Type
Other

## Primary outcome(s)
Structural and functional brain outcomes will be measured using Magnetic Resonance Imaging (MRI) at baseline and follow up.
1.1. Brain structure will be measured by assessing the volumes and thickness of the hypothesised brain regions of interest (see above for details)
1.2. Brain function will be measured while performing a number of fMRI tasks outlined below:
1.2.1. A cue reactivity fMRI task (10 minutes) will be run to examine brain function when the participant views cannabis-related pictures versus matched neutral pictures. There are two versions of this task, which are identical in procedure but contain different pictures (matched for picture complexity, object size, colours, and brightness) in order to minimise the confounding impact of memory and recognition on cue reactivity. The two task versions are delivered in counterbalanced order at baseline and follow up assessment, via a pseudorandomised procedure.
1.2.2. A Monetary Incentive Delay fMRI task (15 minutes) will be run to investigate brain function while:
1.2.2.1. Anticipation (vs receipt) of monetary outcomes
1.2.2.2. Anticipation of monetary outcomes (vs neutral outcomes)
1.2.2.3. Receipt (vs anticipation) of monetary outcomes
1.2.2.4. Receipt of neutral outcomes (vs monetary outcomes)
1.2.3. An Avoidance Learning fMRI task (15 minutes) will be run to measure brain function while:
1.2.3.1. Anticipating rewards and losses

1.2.3.2. Learning to avoid losses and obtain rewards
1.2.4. A resting-state fMRI task (10 minutes) will be run to investigate functional connectivity during rest (eyes open, while looking at a fixation cross)

## Key secondary outcome(s))

1.1. Repeated measures of craving, anxiety and other psychological states throughout the face-to-face baseline and follow up assessments. These measures are delivered online via Qualtrics:
1.1.1. Changes to cannabis craving, relaxation, tension, and mindful attention level:
1.1.1.1. The Visual Analogue Scale (VAS) will be used to measure on a 1-to-10 point scale current levels of cannabis craving, relaxation, tension, and mindful attention.
The number of VAS administrations will vary according to which group the participant is allocated to. Cannabis users allocated to the mindfulness or relaxation intervention group will complete five administrations of the VAS (I-V outlined below), cannabis users allocated to the no-intervention group will complete four administrations of the VAS (I-IV outlined below), and non-using controls will complete three administrations of the VAS (I-III outlined below).
(I) immediately pre-MRI scan
(II) during the MRI scan, immediately before the cue reactivity fMRI task (see 1.2.1 above)
(III) during the MRI scan, immediately after the cue post cue reactivity fMRI task
(IV) immediately before the delivery of the audio intervention
(V) immediately after the delivery of the audio intervention
1.1.1.2. A single item from the VAS will be used to measure on a 1-to-10 point scale the participant's current level of cannabis craving. This will be administered twice:
(I) immediately pre-attentional bias dot probe task (see 2.4.1.1 below)
(II) immediately post-attentional bias dot probe task

1.1.2. Changes to state anxiety and cannabis craving symptom scores pre-to-post the MRI scan:
1.1.2.1. The Marijuana Craving Questionnaire (MCQ). It has 45-items rated on a seven-point Likert-type scale ranging from "strongly disagree" to "strongly agree." The items relate to four distinct constructs: (1) compulsivity e.g. inability to control marijuana use; (2) emotionality, e.g. use of marijuana in anticipation of relief from withdrawal or negative mood; (3) expectancy, e.g. anticipation of positive outcomes from using marijuana; and (4) purposefulness, e.g. intention and planning to use marijuana for positive outcomes.
1.1.2.2. The State Anxiety Subscale of the Spielberger State-Trait Anxiety Inventory (STAI; Spielberger, Gorsuch, Lushene, Vagg, & Jacobs, 1983). It has 20 items rated on a 4-point scale (e. g., from 1 = "Almost Never" to 4 = "Almost Always").

1.1.3. Changes to state mindfulness levels before and after the mindfulness and relaxation audio interventions:
NOTE: Not completed by cannabis users allocated to the no intervention group or non-using controls.
1.1.3.1. The Toronto Mindfulness Scale (TMS). It has 42-items rated on a 5-point scale Likert scale from 0 = "Not At All" to 4 = "Very Much". It measures "state-like" experiences during meditation.
1.1.3.2. State Mindfulness Scale (SMS). It has 23-items rated on a 5-point Likert scale ranging from 1 = "Not At All" to 5 = "Very Well". It measures state mindfulness of both mind and body.

1.2. Substance use and related problems:
1.2.1. Semi-structured interviews (online and printed), administered at baseline only:
1.2.1.1. The Structured Clinical Interview for DSM-5 Research Version (SCID-5-RV). The SCID-5-RV is an 11-item semi-structured interview that measures cannabis dependence according to specific DSM-5 criteria for CUD. This will be used to confirm a diagnosis of moderate-to-severe CUD in cannabis users
1.2.1.2. Cannabis Use Interview (CUI) measures lifetime cannabis exposure. The CUI is adapted

from the Daily Sessions, Frequency, Age of Onset, and Quantity of Cannabis Use Inventory. It has been previously utilised for the testing of cannabis users in research settings.

1.2.2. Self-report online questionnaires (exception of the TLFB, completed face-to-face), administered at baseline and follow up:
1.2.2.1. The Timeline Follow Back (TLFB). The TLFB is administered in a paper- calendar-based format. It is a researcher administered semi-structured interview, to gather retrospective estimates of number of days of substance use and quantity of use over the previous 30 days (at baseline testing) or ~ 2-weeks (at follow up testing). The researchers will additionally collect information about the type, amount and strength of the cannabis use.
1.2.2.2. The Cannabis Withdrawal Scale (CWS). It has 19-items rated on a 10-point scale from 'Not at all' to 'Extremely'. The CWS is used in clinical and research settings to measure how cannabis withdrawal symptoms affect daily activities.
1.2.2.3. The Cannabis Use Identification Test-Revised (CUDIT-R). It has 8-items rated on a 5-point Likert scale. It is a screening tool as it has diagnostic cut-offs for the DSM-5 CUD severity, validated with clinical and normative samples.
1.2.2.4. The Obsessive Compulsive Drug Use Scale – Cannabis (OCDUS). It has 12-items rated on a 5-point Likert scale. It measures compulsive cannabis use.
1.2.2.5. Fagerström Test for Nicotine Dependence (FTND). It has 8-items rated on yes/no and Liker scales. It measures the severity of physical dependence to nicotine related to cigarette smoking.
1.2.2.6. One item on cannabis use to sleep i.e. "In the past two weeks have you used cannabis to help you sleep?".

1.2.3. Self-report online questionnaires, administered at baseline only:
1.2.3.1. The Marijuana Motives Questionnaire (MMQ). It assesses motivation of marijuana use and related consequences. It has 25-items rated on a 4-point Likert scale from 'Never/Almost never' to 'Almost always/Always'.
1.2.3.2. The Alcohol Use Disorders Identification Test (AUDIT). It has 10-items. The AUDIT is screening tool developed by the World Health Organization. It assesses alcohol use and the level of hazardous drinking.
1.2.3.3. The Credibility/Expectancy Questionnaire (CEQ). It has 6-items rated on a Likert scale. It measures: the momentary belief that the received therapy will help to reduce anxiety; what the participant thinks will happen and what the participant feels will happens a result of the intervention.

1.3. Mindfulness and intervention-related measures. These include self-report online questionnaires, administered both at baseline and follow up assessment:
1.3.1. The Five Facet Mindfulness Questionnaire (5FMQ). This scale has 39-items, rated on a 5-point Likert scale. Items relate to 5 factors: (1) observing (2) describing (3) acting with awareness (4) non-judging of inner experience (5) non-reactivity to inner experience.
1.3.2. Motivation to Stop Scale (MSS). It has 1-item, which is rated on a 7-point Likert scale, which reflects desire and intention to stop substance use.
1.3.3. The Credibility/Manipulation Check (CMC). It has 9 intervention specific items, which assess the participant's compliance with the intervention and comprehension of the intervention.
1.3.4. Debrief/task feedback. It consists of 19 open and closed questions regarding the participants experience completing the daily tasks and if applicable, audio tracks.
NOTE: This is completed at follow up only.

1.4. Cognitive performance measures
1.4.1. Cognitive performance will be assessed via computerised cognitive tasks (administered at baseline and follow up):

1.4.1.1. A ‘dot probe’ task will be used to measure attentional bias towards cannabis-related pictures and pictures matched for composition. There are two identical versions of this task, delivered in counter balanced order at baseline and follow up assessment, via pseudorandomised procedure. The two task versions are identical in procedure, but contain different pictures (matched for picture complexity, object size, colours, and brightness) to minimise the confounding impact of memory and recognition on attentional bias.
1.4.1.2. A ‘2, 3, & 4-N-back task' will be run to assess working memory. Participants are shown a sequence of visual stimulus on a computer and must respond each time the current stimulus is identical to the one presented ‘n’ positions back in the sequence
1.4.1.3. A ‘Go/No-Go task’ will be run to test response inhibition. Participants are shown cues on a computer; the cues provide preliminary information regarding the type of target (i.e. go or stop) that is likely to follow. The cues have a high probability of signalling the correct target, to which the participant must response. The response time and accuracy of the participant is measured.
1.4.2. IQ will be assessed at baseline only
1.4.2.1. The Wechsler Abbreviated Scales of Intelligence, 2nd edition (WASI-II) is a short form standardised measure of intellectual ability. It provides an estimate of full-scale IQ using the two-subtest administration consisting of the Vocabulary and Matrix Reasoning subtests.

1.5. Mental health and wellbeing measures
1.5.1. Self-report online questionnaires, administered at baseline only:
1.5.1.1. The 36 Item Short Form Survey Instrument (SF-36; Ware, Sherbourne, & Davies, 1992). Items are rated on yes/no and Likert scale responses. It is a set of generic, coherent, and easily administered items measuring quality-of-life. It is widely utilized by managed care organizations and by Medicare for routine monitoring and assessment of care outcomes in adult patients.
1.5.1.2. Community Assessment of Psychic Experiences (CAPE) (Stefanis et al., 2002). It has 42 items rating the frequency (rated on a 4-point scale: Never, Sometimes, Often, Nearly Always) and distress (rated on a 4-point scale: Not distressed, A bit distressed, Quite distressed, Very distressed) of positive and negative psychotic symptoms.

1.5.2. Self-report online questionnaires, administered at baseline and follow up:
1.5.2.1. The Emotion Regulation Questionnaire (ERQ). It has 10-items rated on a 7-point Likert-type scale ranging from 1 (strongly disagree) to 7 (strongly agree). It measures the tendency to regulate emotions via Cognitive Reappraisal and Expressive Suppression.
1.5.2.2. Beck’s Depression Inventory – 2nd edition (BDI-II). It has 21-items rated on a 4-point Likert scale. It measures the severity of depression and its total score has diagnostic cut-offs, i.e. 0–13: minimal depression, 14–19: mild depression, 20–28: moderate depression, 29–63: severe depression.
1.5.2.3. The Confidence Ladder (CL). This visual scale measures motivation/readiness to change. It has 11 rungs and 5 statements represent stages of change, rated on a scale from 0 (least motivated) to 10 (most motivated).
1.5.2.4. The Apathy Evaluation Scale (AES). It has 18 items rated on a 3-point Likert scale ranging from 1 (not at all) to 3 (somewhat a lot). It provides global measure of apathy.
1.5.2.5. The Perceived Stress Scale (PSS). It has 10 items rated on a 5-point Likert scale ranging from 0 (never) to 4 (very often). It measures how unpredictable, uncontrollable, stressful and overloaded respondents find their lives.
1.5.2.6. International Physical Activity Questionnaire (short form) (IPAQ). It has 9 items measuring the frequency and duration of vigorous activity, moderate activity, walking, and sitting over the previous seven days.
1.5.2.7. Urgency-Premeditation-Perseverance-Sensation Seeking-Positive Urgency – Short Form (S-UPPS-P). It has 20 items, rated on a 4-point Likert scale ranging from (1) agree strongly to (4) disagree strongly. It measures 5 distinct domains of impulsivity i.e., Negative Urgency, (lack of)

Premeditation, (lack of) Perseverance, Sensation Seeking, and Positive Urgency). Two more second-order factors can be extracted i.e. Emotion Based Rash Action (Positive & Negative Urgency) and Deficits in Conscientiousness (Premeditation and Perseverance).

### Completion date
30/09/2022

## Eligibility

### Key inclusion criteria
Inclusion criteria for all participants:
1. Aged 18 to 55 years
2. Normal-to-corrected vision
3. Fluent in English
4. Meeting safety criteria for MRI scan

Inclusion criteria for cannabis users:
1. Daily/almost daily (>3 days per week) cannabis use for >12 months
2. CUD 4+ DSM-5 symptoms
3. Tried to quit/reduce cannabis use at least once within the past 24 months

### Participant type(s)
Mixed

### Healthy volunteers allowed
No

### Age group
Adult

### Lower age limit
18 years

### Upper age limit
55 years

### Sex
All

### Total final enrolment
117

### Key exclusion criteria
Exclusion criteria for all participants:
1. Any illicit substance and alcohol use for 12 hours before assessment (confirmed by self- report)
2. Currently using prescription medication that affect the central nervous system
3. Current or past diagnosed psychiatric disorders
4. Any current severe psychiatric diagnosis, excepting diagnoses of depression or anxiety
5. History of any neurological disorders
6. History of acquired or traumatic brain injury

7. Currently pregnant
8. Suicidality

Exclusion criteria for cannabis users:
1. Significant use or dependence on alcohol and any illicit substances other than cannabis
2. Illicit drug use past 4 weeks (other than cannabis)

Exclusion criteria for non-cannabis using controls:
1. Significant use or dependence on alcohol and any illicit substances
2. Illicit drug use past 4 weeks

### Date of first enrolment
01/10/2019

### Date of final enrolment
05/09/2022

## Locations

### Countries of recruitment
Australia

### Study participating centre
**Australian Catholic University**
115 Victoria Parade
Fitzroy
Australia
3065

## Sponsor information

### Organisation
Australian Catholic University

### ROR
https://ror.org/04cxm4j25

## Funder(s)

### Funder type
University/education

### Funder Name
Australian Catholic University

### Alternative Name(s)
ACU Australian Catholic University, ACU

### Funding Body Type
Private sector organisation

### Funding Body Subtype
Universities (academic only)

### Location
Australia

## Results and Publications

### Individual participant data (IPD) sharing plan
The datasets generated during the current study will be available upon reasonable request from Dr Valentina Lorenzetti (Valentina.Lorenzetti@acu.edu.au), Principal Investigator. Data will include relevant group allocations and outcome variables and will be anonymised. Data will be available either as it is published, or on request (following completion of the data collection process, estimated end of 2021). A time limit will not be set on the duration of availability. Data will be shared with anyone who wishes to access it, for meta-analyses or other pre-approved purposes, via email. All participants provided informed consent. All data is de-identified.

### IPD sharing plan summary
Available on request

### Study outputs

| Output type | Details | Date created | Date added | Peer reviewed? | Patient-facing? |
|---|---|---|---|---|---|
| Results article | | 03/10/2025 | 05/11/2025 | Yes | No |
| Protocol file | | | 18/05/2020 | No | No |