

# Does cannabidiol treatment lead to recovery of brain structure and function in cannabis users?

<b>Submission date</b> 13/06/2017	<b>Recruitment status</b> No longer recruiting	<input type="checkbox"/> Prospectively registered
<b>Registration date</b> 16/06/2017	<b>Overall study status</b> Completed	<input type="checkbox"/> Protocol
<b>Last Edited</b> 04/10/2022	<b>Condition category</b> Mental and Behavioural Disorders	<input type="checkbox"/> Statistical analysis plan
		<input checked="" type="checkbox"/> Results
		<input type="checkbox"/> Individual participant data

## Plain English summary of protocol

Background and study aims:

Cannabis is a widely-used illegal drug derived from the cannabis plant. Cannabidiol (CBD) is a constituent of cannabis plant matter that has gained notoriety for its supposed therapeutic, neuroprotective (protecting the nervous system) and antipsychotic properties. CBD has been shown to improve or reverse problems with cognition (mental processes) and psychotic symptoms associated with cannabis use, and preliminary evidence suggests CBD may protect against shrinking of a part of the brain called the hippocampus (which is responsible for memory), which is often seen in cannabis users. Whilst the mechanisms underlying these effects are currently unknown, there is evidence to suggest that CBD may protect against the harms associated with cannabis use and that it may do so by controlling certain pathways in the brain involving natural chemical messengers (neurotransmitters). The aim of this study is to find out whether prolonged CBD treatment in regular cannabis users has an effect on brain structure and to see if this is underpinned by changes in neurotransmitter mechanisms.

Who can participate?

Adults who have been using cannabis at least once a week for at least three years.

What does the study involve?

All participants receive capsules containing CBD to take four times a day for ten weeks. At the start of the study and ten weeks later, participants undergo brain scans to see if there have been any structural changes to the brain or changes in brain activity. Participants also answer questions via telephone about their mental health one month and three months after the end of the study.

What are the possible benefits and risks of participating?

There are no direct benefits or risk involved with participating.

Where is the study run from?

University of Wollongong (Australia)

When is study starting and how long is it expected to run for?

March 2015 to June 2018

Who is funding the study?  
Australian Research Council (Australia)

Who is the main contact?  
Professor Nadia Solowij  
nadia@uow.edu.au

## Contact information

**Type(s)**  
Scientific

**Contact name**  
Prof Nadia Solowij

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## Additional identifiers

**Protocol serial number**  
CT15/02

## Study information

**Scientific Title**  
Does cannabidiol treatment lead to recovery of brain structure and function in cannabis users? A pilot investigation

**Acronym**  
Prolonged CBD Trial

**Study objectives**  
Primary study aim:  
The aim of this study is to determine whether daily cannabidiol (CBD) administration over a 10 week period will lead to improved brain structure, function, neurochemistry and integrity (via modulation of glutamatergic and GABAergic signalling) in regular cannabis users.

Primary hypothesis:  
Prolonged CBD administration will result in larger volumes of specific hippocampal subfields

(such as CA1 and subiculum); elevated markers of hippocampal neuronal integrity (NAA); more normalised glutamate and GABA levels in the hippocampus; and increased MMN amplitude

**Secondary study aim:**

The aim of this study is to investigate the potential for CBD administration to reduce cognitive impairment, psychological symptoms and cannabis use in regular cannabis users.

**Secondary hypotheses:**

2. Prolonged CBD administration will result in the following outcomes and in turn these will be associated with the primary outcomes of Hypothesis 1: improved cognitive function; and reduced psychological symptoms
3. Prolonged CBD administration will result in reduced cannabis use

**Ethics approval required**

Old ethics approval format

**Ethics approval(s)**

Joint University of Wollongong and Illawarra and Shoalhaven Local Health District Health and Medical Human Research Ethics committee, 08/07/2015, ref: CT15/02

**Study design**

Interventional non-randomised study

**Primary study design**

Interventional

**Study type(s)**

Treatment

**Health condition(s) or problem(s) studied**

Chronic cannabis use

**Interventions**

All participants receive medical grade cannabidiol (CBD) formulated into capsules for oral administration. Each capsule contained 50mg of 99.9% pure CBD powder solved in corn oil gelatin capsules (BSPG/Trigal Pharmaceuticals, UK). Participants are instructed to take four capsules per day (100mg in the morning and 100mg in the evening, totaling 200mg daily).

Participants are clinically and cognitively assessed and EEG and MRI measured obtained at baseline and after 10 weeks of daily CBD administration. They are also followed up by brief telephone assessment one month and three months after the end of the trial.

**Intervention Type**

Drug

**Phase**

Phase II

**Drug/device/biological/vaccine name(s)**

Cannabidiol.

### **Primary outcome(s)**

1. Hippocampal volumetrics (whole hippocampus as well as subfields (e.g. CA1 and subiculum) is assessed by magnetic resonance imaging (MRI) using high resolution T1 weighted images at baseline and following 10 weeks of CBD administration
2. Markers of hippocampal neuronal integrity (NAA), as well as glutamate and GABA levels in the hippocampus, are measured using magnetic resonance spectroscopy (MRS) at baseline and following 10 weeks of CBD administration
3. MMN amplitude is recorded via electroencephalography (EEG) at baseline and following 10 weeks of CBD administration

### **Key secondary outcome(s)**

1. Other EEG and fMRI measures including P50 and resting state EEG/fMRI measured at baseline and following 10 weeks of CBD administration
2. Neuropsychological measures, assessed utilising the Rey Auditory Verbal Learning Test (RAVLT), and the Cambridge Neuropsychological Test Automated Battery (CANTAB) and CogState test batteries at baseline and following 10 weeks of CBD administration
4. Psychological symptomatology, as assessed by the Beck Depression Inventory (BDI); State-Trait Anxiety Index (STAI-I and II); Profile of Mood States (POMS); Community Assessment of Psychic Experiences (CAPE); Schizotypal Personality Questionnaire (SPQ); and Cannabis Experiences Questionnaire (CEQ) at baseline and following 10 weeks of CBD administration.
5. Substance use measures, utilising Timeline Follow Back; Cannabis Withdrawal Scale (CWS), Severity of Dependence Scale; and the Alcohol Use Disorder Identification Test (AUDIT) at baseline and following 10 weeks of CBD administration.
6. Levels of CBD and THC metabolites and neurotransmitter markers in blood and urine weekly throughout the 10 week trial

### **Completion date**

30/06/2018

## **Eligibility**

### **Key inclusion criteria**

1. Cannabis use at least once per week for a minimum of three years
2. Between 18 and 55 years of age

### **Participant type(s)**

Healthy volunteer

### **Healthy volunteers allowed**

No

### **Age group**

Adult

### **Lower age limit**

18 years

### **Sex**

All

## **Key exclusion criteria**

1. Current regular (more than once per month) use of substances other than cannabis, aside from alcohol and tobacco
2. Consumption of more than 28 standard drinks of alcohol per week
3. A history of regular illicit drug use (more than weekly) or dependence on or treatment seeking for any substance other than cannabis
4. Any neurological or psychiatric disorders (assessed by the MINI International Psychiatric Interview Plus)
5. Pregnancy or lack of contraception use for female cannabis users
6. Contraindications for EEG or MRI (e.g. epilepsy, metal implants, claustrophobia)

## **Date of first enrolment**

08/07/2015

## **Date of final enrolment**

10/06/2016

## **Locations**

### **Countries of recruitment**

Australia

### **Study participating centre**

#### **University of Wollongong**

School of Psychology and Illawarra Health and Medical Research Institute  
Northfields Avenue  
Wollongong  
Australia  
2522

### **Study participating centre**

#### **Liverpool Cancer Therapy Centre and Ingham Institute**

Liverpool Hospital (MRI scanner facility)  
Campbell Street  
Liverpool  
Australia  
NSW 2170

## **Sponsor information**

### **Organisation**

University of Wollongong

ROR

<https://ror.org/00jtmb277>

## Funder(s)

### Funder type

Government

### Funder Name

Australian Research Council

### Alternative Name(s)

arc\_gov\_au, The Australian Research Council, Australian Government Australian Research Council (ARC), ARC

### Funding Body Type

Government organisation

### Funding Body Subtype

Other non-profit organizations

### Location

Australia

## Results and Publications

### Individual participant data (IPD) sharing plan

The current data sharing plans for the current study are unknown and will be made available at a later date.

### IPD sharing plan summary

Not provided at time of registration

### Study outputs

Output type	Details	Date created	Date added	Peer reviewed?	Patient-facing?
<a href="#">Results article</a>		01/03/2018	04/10/2022	Yes	No
<a href="#">Results article</a>		01/03/2018	04/10/2022	Yes	No