ISRCTN24109245 https://doi.org/10.1186/ISRCTN24109245

Vulnerability markers in the association between cannabis and schizophrenia

Submission date
05/11/2012

Recruitment status
No longer recruiting

Registration date
19/11/2012

Overall study status
Completed

Last Edited
21/01/2019

Condition category
Mental and Behavioural Disorders

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

Plain English summary of protocol

Background and study aims
Cannabis is one of the most widely used illegal drugs across the world. It has been well documented that use of cannabis is linked to people developing mental problems, such as depression or anxiety. A major concern is that heavy use of cannabis is a leading cause of serious mental illnesses such as schizophrenia or psychosis, conditions which cause people to lose touch with reality and find it difficult to cope with day to day life. There are a huge number of chemical compounds present in cannabis, the most dominant of which are tetrahydrocannabinol (THC) and cannabidiol (CBD). It is well known that THC is the main chemical that affects the mind and can trigger psychotic behaviour. CBD however, is thought to reduce these effects and may actually counteract the effects of THC. Both THC and CBD are known to interact with specific receptors in the brain called the glutamate NMDA receptors. Mismatch negativity (MMN), an electrical signal which shows how well these receptors are working, which is often lower than it should be in people with schizophrenia. The aim of this study is to find out how TCH and CBD affect MMN in order to find out why some people can use cannabis frequently without major adverse effects, while others may develop psychosis.

Who can participate?
Adults who have been using cannabis at least 4 times a month for 3 years, and aged matched controls who have used cannabis between 5 and 20 times across their lifetime but not within 3 months prior to enrolment.

What does the study involve?
At the start of the study, all participants take an IQ test, as well as having psychological assessments designed to test how well their brains are functioning. The participants then return to the testing centre five times to be given a different substance through a vaporiser. The following five substances will be given to each participant in a random order: Tetrahydrocannabinol (THC) alone, Cannabidiol (CBD) alone (high dose), THC+ CBD (low dose), THC + CBD (high dose), and a placebo (dummy drug) which will act as a control. At each of these visits, the participants' brain activity will be recorded using Electroencephalography (EEG), which will measure the MMN.

What are the possible benefits and risks of participating?
There are no noteworthy benefits for participating in the study, other than helping to improve knowledge and understanding of the relationship between chronic cannabis use and psychosis in vulnerable individuals. Possible risks of taking part in the study include mild side effects from taking the drug, such as nausea and increased heart rate. The investigative team will carefully screen participants in order to avoid potential damaging effects such as anxiety or paranoia.
Where is the study run from?
University of Wollongong, School of Psychology (Australia)

When is the study starting and how long is it expected to run for?
November 2012 to March 2014

Who is funding the study?
National Health and Medical Research Council of Australia (NHMRC) (Australia)

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

Contact information

Type(s)
Scientific

Contact name
Dr Nadia Solowij

Contact details
School of Psychology
University of Wollongong
Wollongong
Australia
2522
+61 (02) 4221 3732
nadia@uow.edu.au

Additional identifiers

EudraCT/CTIS number

IRAS number

ClinicalTrials.gov number

Secondary identifying numbers
CT12/003

Study information

Scientific Title

Vulnerability markers in the association between cannabis and schizophrenia: a randomised controlled trial of acute cannabinoid administration

Study objectives
The acute administration of cannabinoids (THC + CBD) will modulate the amplitude of the mismatch negativity (a brain marker of glutamate receptor function) in regular cannabis users versus non-naïve controls.

Ethics approval required
Old ethics approval format

Ethics approval(s)
Joint University of Wollongong and Illawarra and Shoalhaven Local Health Network Health and Medical Human Research Ethics committee, 6 August 2012, Reference number: CT12/003

Study design
Randomised double-blind placebo-controlled crossover study

Primary study design
Interventional

Secondary study design
Randomised controlled trial

Study setting(s)
Other

Study type(s)
Treatment

Participant information sheet
Not available in web format, please use the contact details below to request a patient information sheet

Health condition(s) or problem(s) studied
Cannabis use and psychosis

Interventions
Cannabis user and non-user non-naïve control participants will receive each of the following five conditions in randomised order, administered through a vaporiser

1. Tetrahydrocannabinol (THC) alone
2. Cannabidiol (CBD) alone (high dose)
3. THC+ CBD (low dose)
4. THC + CBD (high dose)
5. Placebo

Intervention Type
Other

Phase

Not Applicable

Primary outcome measure
The effect of THC and CBD on MMN amplitude recorded immediately following drug administration

Secondary outcome measures
The effect of THC and CBD on
1. Other EEG/ERP measures including P50 and resting state EEG
2. Neuropsychological measures including CogState battery of tests
3. Psychotic-like symptoms as indicated on a visual analogue scale, the Psychotomimetic States Inventory and the Clinician Administered Dissociative States Scale.
4. The potential moderating effect of specific genetic polymorphisms on THC and CBD (alone and in combination) effects on the MMN and other EEG/ERP and neuropsychological measures.

Overall study start date
12/11/2012

Completion date
31/03/2014

Eligibility

Key inclusion criteria
Cannabis user group
1. Cannabis use for at least 3 years, and at least 4 times a month.
2. All participants must be between 18 and 55 years of age.

Control group
1. Cannabis use at least 5 times but less than 20 times in total across lifetime; and for those participants only having used 5-10 times, they must have used at least once in the last 2 years; while for those participants having used between 10 and 20 times, the most recent exposure must not have been more than 10 years ago. No cannabis use in the past 3 months.
2. All participants must be between 18 and 55 years of age.

Participant type(s)
Patient

Age group
Adult

Lower age limit
18 Years

Sex
Both

Target number of participants
40

Key exclusion criteria
Cannabis user group
1. Daily cannabis use, or use of any illicit substance more than once a month for a period of six months
2. Head injury resulting in trauma to the brain, prolonged unconsciousness or concussion or required surgery, prolonged hospitalisation or rehabilitation
3. Medical diagnosis that would interfere with EEG testing (epilepsy, stroke, brain tumour, HIV positive, Hepatitis B or C, meningitis, encephalitis, MS, microcephaly), or a medical diagnosis contraindicated for cannabis exposure (e.g. asthma, cardiovascular disease, untreated hypertension).
4. Co-ingestion / concurrent use of medicines or drugs which will interfere with testing or are contraindicated for cannabis exposure (e.g. antipsychotics, antidepressants, benzodiazepines, amphetamines, opioids, alcohol).
5. A Body Mass Index (BMI) of less than 18 kg/m2 or more than 28 kg/m2.
6. A history of anaemia
7. Pregnancy
8. A current diagnosis of a psychotic disorder, or a score of 50 or more on the Community Assessment of Psychic Experiences. A first degree family member with psychotic diagnosis.
9. Use of any illicit substance (other than cannabis) in the 14 days prior to testing.
10. Meets DSM-IV criteria for dependence on alcohol or drugs other than cannabis; history of treatment for substance use problems other than cannabis.

Control group
1. Use of any illicit substance more than once a month for a period of six months.
2. Head injury resulting in trauma to the brain, prolonged unconsciousness or concussion or required surgery, prolonged hospitalisation or rehabilitation.
3. Medical diagnosis that would interfere with EEG testing (epilepsy, stroke, brain tumour, HIV positive, Hepatitis B or C, meningitis, encephalitis, MS, microcephaly), or a medical diagnosis contraindicated for cannabis exposure (e.g. asthma, cardiovascular disease, untreated hypertension).
4. Co-ingestion /concurrent use of medicines or drugs which will interfere with testing or are contraindicated for cannabis exposure (e.g. antipsychotics, antidepressants, benzodiazepines, amphetamines, opioids, alcohol).
5. A body Mass Index (BMI) of less than 18 kg/m2 or more than 28 kg/m2.
6. A history of anaemia.
7. Pregnancy
8. A current diagnosis of a psychotic disorder, or a score of 50 or more on the Community Assessment of Psychic Experiences.
9. A first degree family member with psychotic diagnosis. Use of any illicit substance (other than cannabis) in the 14 days prior to testing.
10. Meets DSM-IV criteria for dependence on alcohol or drugs or a history of treatment for substance use problems.

Date of first enrolment
12/11/2012

Date of final enrolment
31/03/2014

Locations

Countries of recruitment
Australia

Study participating centre
School of Psychology
Wollongong
Australia
2522

Sponsor information

Organisation
University of Wollongong (Australia)

Sponsor details
Northfields Avenue
Wollongong
Australia
2522

Sponsor type
University/education

ROR
https://ror.org/00jtmb277

Funder(s)

Funder type
Research council

Funder Name
National Health and Medical Research Council of Australia (NHMRC) (Australia) Project Grant ID: 1007593

Results and Publications

Publication and dissemination plan

Intention to publish date

Individual participant data (IPD) sharing plan

IPD sharing plan summary

Not provided at time of registration

Study outputs

Output type	Details	Date created	Date added	Peer reviewed?	Patient-facing?
Results article	results	16/10/2014		Yes	No
Results article	results	01/02/2019		Yes	No