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The effect of delta-9-tetrahydrocannabivarin (THCV) on delta-9-tetrahydrocannabinol (THC)

Submission date
10/01/2013

Recruitment status
No longer recruiting

Registration date
18/03/2013

Overall study status
Completed

Last Edited
13/06/2016

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
The cannabis plant contains the molecules tetrahydrocannabinol (THC) and tetrahydrocannabivarin (THCV). It is thought that THCV prevents the psychological effects of THC. Whilst THC is an agonist (a substance that starts a chemical reaction in the body when combined with a receptor) at CB1 receptors (a type of cannabinoid receptor expressed by cells in various parts of the body), THCV is a neutral antagonist (these compete with agonists to bind to receptors but do not cause the same chemical reaction). Thus THCV can antagonise tissue responses to THC. The effects on mood and behaviour caused by pure THC in humans are well established. However, whether THCV can prevent the effects of THC in man is unknown. The theory we would like to test through a small pilot study is that pure THCV prevents the characteristic psychological and mental processing effects of intravenous (IV) THC (where THC is administered through a vein).

Who can participate?
Males between 21 and 35 and in good health, both physically and mentally, may be able to participate. It is important that participants have not suffered from mental illness, including depression or anxiety in the past. Drug or alcohol addiction rules a person out. However, participants must have taken cannabis recreationally (for enjoyment), at least once in the past and no more than 25 times.

What does the study involve?
There are two separate blocks, one block for THCV and one for the placebo (dummy treatment). Both involve four days dosing followed by a THC session. The blocks will be at least two weeks apart. The following describes what happens within a block. (Note that participants will be asked to complete two blocks, one for placebo and one for THCV). On day 1, participants will be given a tablet containing either THCV 10 mg or placebo. We then ask participants to stay at the Wellcome Clinical Research Facility for four hours, to make sure that they do not have a bad reaction to the drug. We ask them to come back to Denmark Hill on days 2, 3 and 4 for further tablets. There is no requirement to stay for monitoring as on the first day, but we ask carefully about side-effects. We will give participants a travel pass so that they do not run up any costs. A

contact number will be provided which can be accessed at any time, should there be a concern. On day 5 you will return to Denmark Hill for the experimental session - this will take place in the Wellcome Clinical Research Facility.

On day 5, participants will receive the final dose of THCV (or placebo) at the Wellcome Clinical Research Facility. Thereafter the THC will be delivered intravenously through an indwelling cannula (a fixed tube) in the forearm. It takes about 5 minutes for the effects of THC to begin. The dose is 1.25 mg. In previous studies the effects wore off after 2 hours. During this time, we will ask participants to complete a number of puzzles to test their mental processes (which take about 40 minutes), and ask them to complete questionnaires that assess mood and thoughts.

What are the possible benefits and risks of participating?
Participants will have the opportunity to take part in an interesting research project studying the effects of cannabinoid molecules under controlled, scientific conditions. The topic of cannabis and mental health is highly topical. Some people find cannabis unpleasant. Others find it relaxing and pleasurable. Some feel suspicious and paranoid. Some people become muddled and find it difficult to keep track of their thoughts. Some may feel they have special powers or a special role. Others report things seeming unreal with different perceptions of time and feeling high or anxious. The effects wear off after 1-2 hours. If a participant has a bad reaction to the drug they will be able to stop at any time. The study doctor will provide reassurance until the experience subsides, and rescue drugs (lorazepam tablets) will be made available.

Where is the study run from?
The Denmark Hill Campus of King's College London (Wellcome Clinical Research Facility, Kings College Hospital, UK).

When is the study starting and how long is it expected to run for?
The study will begin in February 2013 and run for approximately one year.

Who is funding the study?
The study is departmentally funded, which includes an unrestricted grant to the principal investigator from GW Pharmaceuticals.

Who is the main contact?
Dr Paul Morrison
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Contact information

Type(s)
Scientific

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Additional identifiers

EudraCT/CTIS number

IRAS number

ClinicalTrials.gov number

Secondary identifying numbers
CSA/11/032

Study information

Scientific Title
The effect of delta-9-tetrahydrocannabivarin (THCV) on delta-9-tetrahydrocannabinol (THC): a randomised double-blind crossover study

Acronym
ToTS

Study objectives
ToTS: Tetrahydrocannabivarin on Tetrahydrocannabinol Study

The hypothesis is that pure delta-9-tetrahydrocannabivarin (THCV) inhibits the characteristic psychological and cognitive effects of intravenous (IV) delta-9-tetrahydrocannabinol (THC).

Ethics approval required
Old ethics approval format

Ethics approval(s)
NRES Committee London - Camden & Islington, 24/10/2011, ref: 11/LO/1537

Study design
Randomised double-blind crossover study

Primary study design
Interventional

Secondary study design
Randomised cross over trial

Study setting(s)
Other

Study type(s)
Other

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 elicited psychopathology and cognitive impairment

Interventions
Delta-9-tetrahydrocannabivarin (THCV) 10 mg per day for 5 days or matched placebo.

Intervention Type
Drug

Phase
Not Applicable

Drug/device/biological/vaccine name(s)
Delta-9-tetrahydrocannabivarin

Primary outcome measure
Scores on the following cognitive tasks:
1. The Hopkins Verbal Learning Task
2. Digit-span
3. The time estimation task

Psychotic symptoms:
1. The Community Assessment of Psychic Experiences (CAPE) scale
2. The Self Assessment Module (SAM) scale

Measures will be taken at baseline, post THCV/placebo and post THC over the course of 5 days

Secondary outcome measures
Scores on the following scales of psychopathology:
1. The Mood Adjective Check List
2. Becks Anxiety Inventory
3. Visual Analogue Scales
4. The State Social Paranoia Scale

Measures will be taken at baseline, post THCV/placebo and post THC over the course of 5 days

Overall study start date
01/03/2013

Completion date
01/03/2014

Eligibility

Key inclusion criteria
Healthy male volunteers aged 21-35 who have used cannabis not more than 25 times

Participant type(s)
Healthy volunteer

Age group
Adult

Sex
Male

Target number of participants
10

Key exclusion criteria
1. History (or family history) of mental illness (including any psychotic disorder, depression /anxiety)
2. Major physical illness,
3. Previous treatment with psychotropic medicines and drug/alcohol addiction

Date of first enrolment
01/03/2013

Date of final enrolment
01/03/2014

Locations

Countries of recruitment
England

United Kingdom

Study participating centre
King's College London
London
United Kingdom
SE5 8AF

Sponsor information

Organisation
King's College London (UK)

Sponsor details
SLAM/IoP R&D Office
De Crespigny Park

Denmark Hill
London
England
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Sponsor type
University/education

Website
http://www.kcl.ac.uk/iop/research/office/index.aspx

ROR
https://ror.org/0220mzb33

Funder(s)

Funder type
Industry

Funder Name
GW Pharmaceuticals (UK) - departmental funds via an unrestricted grant to the principal investigator

Results and Publications

Publication and dissemination plan
Not provided at time of registration

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	01/02/2016		Yes	No