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Effect of experimental endocannabinoid modulation on brain function in individuals at high risk for psychosis

Submission date
14/07/2016

Recruitment status
No longer recruiting

Registration date
12/10/2016

Overall study status
Completed

Last Edited
08/11/2023

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
The human body has an internal system known as the endocannabinoid system which regulates processes within the body. The purpose of this study is to find out how the endocannabinoid system can affect brain function and symptoms experienced by people in an 'at-risk mental state', who may experience psychological problems or difficulties in coping with day-to-day activities. We will do this by assessing the effects of a chemical known as cannabidiol (CBD) on symptoms and brain function using Magnetic Resonance Imaging (MRI) brain scans. Cannabidiol is a cannabinoid that is extracted from the cannabis plant and is known to affect the endocannabinoid system. It is not responsible for the acute effects produced by cannabis, such as 'feeling high'. Based on published information, it appears that CBD may have certain beneficial psychological effects. We hope that in the future, the knowledge gained from this study will help in a better understanding of the causes of mental health problems and in the development of new treatments.

Who can participate?
Right-handed adults aged 18-35 who are ultra-high risk (UHR) for psychosis.

What does the study involve?
Participants are randomly allocated to one of two groups. Those in the first group are given capsules containing 600mg of cannabidiol to take once a day for 21 days. Those in the second group are given capsules containing a placebo (dummy drug) to take once a day for 21 days. At the start of the study and then again after 21 days, participants in both groups have an MRI scan of their brain and have a sample of blood taken to measure levels of endocannabinoid substances in the body.

What are the possible benefits and risks of participating?
Participants may benefit from an improvement to their mental health problems, however this is not guaranteed. There is a small risk of some mild sleepiness but otherwise no other side effects

have been reported from taking the study drug. There is a risk that some participants may feel anxious or claustrophobic during MRI scanning, and there is a small risk of some temporary, mild discomfort and bruising when having blood samples taken.

Where is the study run from?
The study is run from the Department of Psychosis Studies at the Institute of Psychiatry, Psychology and Neuroscience, King's College, London (UK)

When is the study starting and how long is it expected to run for?
April 2012 to February 2017

Who is funding the study?
Medical Research Council (UK)

Who is the main contact?
Dr Sagnik Bhattacharyya

Contact information

Type(s)
Scientific

Contact name
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Additional identifiers

EudraCT/CTIS number
Nil known

IRAS number

ClinicalTrials.gov number
Nil known

Secondary identifying numbers
16975

Study information

Scientific Title
Acute and long-term effects of endocannabinoid modulation in individuals at high risk for psychosis: an experimental study

Acronym
CANTOP

Study objectives
The aim of this study is to:
1. Investigate the precise relationship between dynamic alterations of the endocannabinoid system by administering CBD, an inverse agonist/ antagonist cannabinoid, and the functioning of the neural substrates for learning, salience and emotional processing that may underlie the psychotic and anxiety symptoms experienced by the UHR population
2. Examine whether the acute and short-term treatments of CBD are associated with an effect on plasma endocannabinoid [Anandamide, 2-Arachidonoylglycerol (2-AG), Palmitoyl-ethanolamine (PEA), Oleoyl-ethanolamine (OEA)] levels over the same time period

Ethics approval required
Old ethics approval format

Ethics approval(s)
NRES London – Camberwell St Giles Research Ethics Committee, 08/05/2013, ref: 13/LO/0243

Study design
Parallel-group double-blind randomized placebo-controlled trial

Primary study design
Interventional

Secondary study design
Randomised controlled trial

Study setting(s)
Community

Study type(s)
Other

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

Health condition(s) or problem(s) studied
Ultra high risk for psychosis

Interventions
Participants will be randomly allocated to one of the two treatment arms using a blocked randomisation list with a 1:1 allocation ratio.

Intervention arm: Participants receive oral administration of a single capsule containing 600mg of cannabidiol, to be taken once in a day in the morning for a total of 21 days.

Control arm: Participants receive oral administration of a single matched placebo capsule, to be taken once a day in the morning for 21 days.

Final follow-up assessment for all the treatment arms to be carried out on day 21 of the study which is also the final intake of the study drug.

Intervention Type
Drug

Phase
Phase I

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

Primary outcome measure
fMRI BOLD signal in the hippocampus, striatum and amygdala measured during the memory, salience and emotional (fear) processing tasks on day 1 and day 21.

Secondary outcome measures
Plasma endocannabinoid (Anandamide, 2-AG, OEA, PEA) levels measured on day 1 (110 minutes following drug administration on day 1) and day 21 (110 minutes following administration of the last dose of the drug).

Overall study start date
23/04/2012

Completion date
28/02/2017

Eligibility

Key inclusion criteria
1. Aged 18- 35 years
2. Right-handed
3. Ultra high risk (UHR) for psychosis individuals being supported by OASIS (https://www.oasislondon.com), a large clinical service for this group
4. Have positive psychotic symptoms and anxiety symptoms, as defined using the Positive and Negative syndrome scale (PANSS) and the State-Trait Anxiety Inventory (STAI)
5. Medication naïve

Participant type(s)
Patient

Age group
Adult

Lower age limit
18 Years

Upper age limit
35 Years

Sex
Both

Target number of participants
40

Total final enrolment
33

Key exclusion criteria
1. History of previous psychotic disorder or manic episode
2. Current DSM IV diagnosis of substance dependence (except cannabis dependence)
3. Neurological disorders (eg., epilepsy) or severe intercurrent illness that may put the person at risk
4. IQ of less than 70
5. Female subject who is unwilling to use two forms of contraception (one of which must be a barrier contraception), pregnant, lactating or planning pregnancy during the course of the study and 3 months from the date of the last dose and a male subject whose partner is of child-bearing potential and unwilling to use a barrier method of contraception along with their partner

Date of first enrolment
08/05/2013

Date of final enrolment
09/12/2015

Locations

Countries of recruitment
England

United Kingdom

Study participating centre
King's College, London
Institute of Psychiatry, Psychology & Neuroscience
16 De Crespigny Park
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Sponsor information

Organisation
King's College London

Sponsor details
Strand
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Sponsor type
University/education

ROR
https://ror.org/0220mzb33

Funder(s)

Funder type
Research council

Funder Name
Medical Research Council

Alternative Name(s)
Medical Research Council (United Kingdom), UK Medical Research Council, MRC

Funding Body Type
Government organisation

Funding Body Subtype
National government

Location
United Kingdom

Results and Publications

Publication and dissemination plan
Planned publication in a high-impact peer reviewed journal with intention to publish in February 2017.

Intention to publish date
28/02/2017

Individual participant data (IPD) sharing plan

IPD sharing plan summary
Available on request

Study outputs

Output type	Details	Date created	Date added	Peer reviewed?	Patient-facing?
Results article	results	01/11/2018		Yes	No
HRA research summary			28/06/2023	No	No
Protocol (other)		01/11/2018	08/11/2023	No	No
Results article		13/09/2020	08/11/2023	Yes	No