

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

<b>Submission date</b> 14/07/2016	<b>Recruitment status</b> No longer recruiting	<input type="checkbox"/> Prospectively registered
<b>Registration date</b> 12/10/2016	<b>Overall study status</b> Completed	<input checked="" type="checkbox"/> Protocol
<b>Last Edited</b> 08/11/2023	<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

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**

Dr Sagnik Bhattacharyya

**Contact details**

Department of Psychosis Studies

Box PO67

Institute of Psychiatry, Psychology and Neuroscience

King's College London

De Crespigny Park

London

United Kingdom

SE5 8AF

## Additional identifiers

**Clinical Trials Information System (CTIS)**

Nil known

**ClinicalTrials.gov (NCT)**

Nil known

**Protocol serial number**

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), Palmitoylethanolamine (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

## Study type(s)

Other

## 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(s)**

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.

**Key secondary outcome(s)**

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).

**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

**Healthy volunteers allowed**

No

**Age group**

Adult

**Lower age limit**

18 years

**Upper age limit**

35 years

**Sex**

All

**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**

United Kingdom

England

**Study participating centre****King's College, London**

Institute of Psychiatry, Psychology & Neuroscience

16 De Crespigny Park

London

United Kingdom

SE5 8AF

## Sponsor information

**Organisation**

King's College London

**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, Medical Research Committee and Advisory Council, MRC

**Funding Body Type**

Government organisation

**Funding Body Subtype**

National government

**Location**

United Kingdom

## Results and Publications

**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?
<a href="#">Results article</a>	results	01/11/2018		Yes	No
<a href="#">Results article</a>		13/09/2020	08/11/2023	Yes	No
<a href="#">HRA research summary</a>			28/06/2023	No	No
<a href="#">Protocol (other)</a>		01/11/2018	08/11/2023	No	No