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# The Oxford study of calcium channel antagonism, cognition, mood instability and sleep

**Submission date**
17/05/2018

**Recruitment status**
No longer recruiting

**Registration date**
08/06/2018

**Overall study status**
Completed

**Last Edited**
05/07/2022

**Condition category**
Mental and Behavioural Disorders

[ ] Prospectively registered
[X] Protocol
[ ] Statistical analysis plan
[ ] Results
[ ] Individual participant data
[ ] Record updated in last year

## Plain English summary of protocol

Background and study aims
Everyone has times when we feel happy or 'high', and other times when we feel low. For some people these ups and downs are more dramatic and can interfere with day-to-day activities. This degree of 'mood instability' may or may not be part of a psychiatric diagnosis such as bipolar disorder. Researchers are trying to understand more about mood instability and its origins in the brain so that they can better identify and treat disorders in which mood instability occurs. A group of molecules called calcium channels help regulate the activity of brain cells and so influence how the brain works and how people feel and behave. To explore the role of calcium channels in brain function, this study tests what happens when these channels are blocked using the drug nicardipine. This drug is commonly used to treat high blood pressure (because calcium channels are involved in this as well), but its effects on brain and behaviour have not been properly tested. The aim of this study is to find out what beneficial (or harmful) effects nicardipine produces on variability of mood and cognition (thought processes), sleep, brain activity (measured using two kinds of brain scan), and calcium actions in blood cells.

Who can participate?
Healthy men and women aged 18-35 with a history of mood instability

What does the study involve?
Participants undergo an assessment at the study site in Oxford, completing a range of questionnaires and tasks and providing a blood sample. Participating women take a pregnancy test. The researchers also explain a range of tests and ratings which participants are asked to complete every day, carried out using an iPad and some other devices they are given to take home. After two weeks the participants return for two brain scans, some further tests, and are randomly allocated to be given a supply of either nicardipine or placebo (dummy) capsules. Participants take the capsules twice a day for two weeks, during which time they continue all the same tests and ratings as before. On the final day of the study (day 28), participants return for repeat brain scans, blood tests, and a repeat of some tasks from the first visit. They are also 'debriefed' and any remaining questions they have are answered.

What are the possible benefits and risks of participating?
Participating will help researchers learn more about mood instability and how calcium channels are involved in it. The results will help show if calcium channel blocking drugs may be of value in patients with disorders of mood, cognition or sleep. If the results are positive, they will encourage development of new drugs of this type which could be more effective and better tolerated than the existing ones. Participants are reimbursed for their involvement and reasonable travel expenses are paid. They may get side effects from the medication, but these are expected to be mild and participants can withdraw from the study at any time if they are bothered by them, or for any other reason.

Where is the study run from?
NIHR Clinical Research Facility at the Warneford Hospital in Oxford (UK)

When is the study starting and how long is it expected to run for?
October 2017 to September 2020

Who is funding the study?
1. Wellcome Trust (UK)
2. NIHR Oxford Health Biomedical Research Centre (UK)

Who is the main contact?
Prof. Paul Harrison

### Study website
https://www.psych.ox.ac.uk/getinvolved/oxcams

# Contact information

### Type(s)
Public

### Contact name
Prof Paul Harrison

### Contact details
Department of Psychiatry
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# Additional identifiers

### EudraCT/CTIS number

### IRAS number
213212

### ClinicalTrials.gov number

### Secondary identifying numbers
IRAS 213212

# Study information

### Scientific Title
The Oxford study of calcium channel antagonism, cognition, mood instability and sleep

### Acronym
OxCaMS

### Study objectives
What are the effects of L-type calcium channel (LTCC) antagonism on the brain and brain function? This exploratory experimental medicine study will examine how LTCC antagonism affects cognition, behaviour, mood instability, sleep, and neural activity (as measured by functional MRI and magnetoencephalography [MEG]), in healthy volunteers selected for mood instability.

Based upon current genetic, biochemical and electrophysiological data about the roles of LTCCs, the trialists hypothesise that LTCC antagonism will reduce variability in mood and cognitive performance, modulate sleep parameters, and impact on neural circuit and oscillatory activity.

### Ethics approval required
Old ethics approval format

### Ethics approval(s)
NHS South Central Oxford C Research Ethics Committee, ref: 17/SC/0029, IRAS 213212

### Study design
Interventional randomised double-blind placebo-controlled single-centre experimental medicine study

### Primary study design
Interventional

### Secondary study design
Randomised controlled trial

### Study setting(s)
Hospital

### Study type(s)
Treatment

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

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

Mood instability, which is a feature of bipolar disorder and other psychiatric disorders including borderline personality disorder, but can also occur in the absence of any diagnosis

## Interventions
The intervention is nicardipine or placebo. The design is as follows. There is a 14-day run-in phase (when participants undergo functional brain imaging and complete repeated assessments of mood, cognition, activity and sleep). On day 15, participants are randomised, double-blind, to nicardipine (Cardene) sustained release (SR), 30 mg oral capsule twice a day, or matched placebo, for another 14 days. During this period, all assessments and scans are repeated, with participants and investigators remaining blind to treatment allocation.

## Intervention Type
Drug

## Phase
Not Applicable

## Drug/device/biological/vaccine name(s)
Nicardipine

## Primary outcome measure
1. Cognitive variability, measured at varying time points and evaluated using a range of cognitive tasks, comprising:
1.1. The N-Back task of working memory (baseline and study endpoint)
1.2. The Stop-Signal task (baseline and study endpoint)
1.3. The theory of visual attention (TVA) (baseline and study endpoint)
1.4. The emotional test battery (ETB) (baseline and study endpoint)
1.5. 'Wheel of fortune' (daily over the 4-week study period)
1.6. Whack-A-T (daily over the 4-week study period)
1.7. Fractals (daily over the 4-week study period)

## Secondary outcome measures
1. Blood oxygen level dependent signal during rest and during cognitive testing (fMRI); induced and evoked field activity (MEG); measured pre- and post- randomisation to nicardipine/placebo, on study days 14 and 28 respectively
2. Activity monitored by Geneactiv watch (daily over the 4-week study period)
2.1. Actigraphy data from a maximum of two wearable units, allowing analysis of indices of:
2.1.1. Frequency and amplitude of movements during daytime activity
2.1.2. Categorisation of activity types
2.1.3. Duration, timing, and quality of sleep
2.2. Sleep quality indicator questionnaire, measured at baseline and post-randomisation to nicardipine/placebo
3. Leucocyte calcium channel expression and calcium signalling, measured using qPCR quantification of calcium channel subunit transcripts and Fura dye imaging of calcium fluxes, at baseline and study endpoint
4. Heart rate (R-R interval) variability, measured by ePatch fitted at baseline visit for 72 hours, and again three days after commencing nicardipine/placebo for a further 72 hours
5. Mood instability as defined using root mean square of the successive differences (RMSSD), measured by twice daily PANAS questionnaire over the 4-week study period

### Overall study start date
01/10/2017

### Completion date
30/09/2020

# Eligibility

### Key inclusion criteria
Healthy volunteers with score of ≥7 on the Mood Disorder Questionnaire (MDQ) with evidence of associated functional impairment:
1. Willing and able to given informed consent to participate in the study
2. Male or female
3. Aged 18 – 35
4. Significant mood instability (defined as a score of ≥7 on the Mood Disorder Questionnaire) causing at least mild dysfunction
5. No indication that urgent psychiatric treatment is required
6. Pre-treatment tests including renal, cardiac and liver function acceptable for the initiation of treatment with nicardipine
7. Willing and able to comply with the study requirements
8. Willing to allow his/her General Practitioner, if appropriate, to be notified of his/her participation in the study

### Participant type(s)
Healthy volunteer

### Age group
Adult

### Lower age limit
18 Years

### Sex
Both

### Target number of participants
40

### Total final enrolment
32

### Key exclusion criteria
1. Contraindication(s) to nicardipine (as documented in the Summary of Product Characteristics for Cardene SR)
2. History of or current axis I mental disorder if, in the opinion of the investigator, it will compromise safety or affect data quality
3. Regular psychotropic drug use within the last 12 weeks. Recent ‘as required’ use of psychotropic medication may be permitted at the investigators' discretion, if it will not compromise safety or affect data quality
4. Currently taking any other medication or herbal extracts that would affect study results or

safety (e.g. St. John's Wort)
5. Participant judged to be at significant immediate risk of suicide/self-harm
6. Clinically significant alcohol use or substance misuse
7. Requiring urgent treatment for an acute mood episode
8. Female and pregnant, lactating or planning a pregnancy during the course of the study
9. Female of child-bearing potential not willing to use effective contraception
10. Participation in a research study involving an investigational medicinal product in the previous 12 weeks
11. Individuals who are intolerant of or unwilling to take lactose or gelatine
12. Participants who have a pacemaker, non-MR-compatible metal implant, or any other contraindication for MR or MEG brain scanning will be excluded from the corresponding brain scanning element(s) of the study
13. Individuals who are not willing to consume gelatine (due to drug and placebo capsules being made of gelatine)

### Date of first enrolment
19/12/2017

### Date of final enrolment
31/10/2019

## Locations

### Countries of recruitment
England

United Kingdom

### Study participating centre
**NIHR Oxford cognitive health Clinical Research Facility**
Warneford Hospital
Warneford Lane
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United Kingdom
OX3 7JX

## Sponsor information

### Organisation
University of Oxford

### Sponsor details
c/o Heather House
Head of Clinical Trials and Research Governance
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**Sponsor type**
University/education

**Website**
https://researchsupport.admin.ox.ac.uk/ctrg

**ROR**
https://ror.org/052gg0110

# Funder(s)

**Funder type**
Charity

**Funder Name**
Wellcome Trust

**Alternative Name(s)**

**Funding Body Type**
Private sector organisation

**Funding Body Subtype**
International organizations

**Location**
United Kingdom

**Funder Name**
NIHR Oxford Health Biomedical Research Centre

# Results and Publications

## Publication and dissemination plan

The protocol for this study has been prepared for publication in an open access journal. The trialists intend to publish all results of OxCAMS in journals. All publications will be open access. Brief summaries of the findings will be posted on Departmental and BRC websites.

## Intention to publish date

31/12/2022

## Individual participant data (IPD) sharing plan

Participant level data is being held on a secure server and, at the end of the study, data will be made available to applicants on submission of an appropriate analysis plan to the Principal Investigator, subject to ethical approval.

## IPD sharing plan summary

Available on request

## Study outputs

| Output type | Details | Date created | Date added | Peer reviewed? | Patient-facing? |
|---|---|---|---|---|---|
| Protocol article | protocol in : | 12/02/2019 | | Yes | No |
| HRA research summary | | | 28/06/2023 | No | No |