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Deep brain stimulation for addiction

Submission date	Recruitment status	[ ] Prospectively registered
09/07/2024	Recruiting	[ ] Protocol
Registration date	**Overall study status**	[ ] Statistical analysis plan
01/08/2024	Ongoing	[ ] Results
Last Edited	**Condition category**	[ ] Individual participant data
14/11/2024	Mental and Behavioural Disorders	[X] Record updated in last year

Plain English summary of protocol

Background and study aims
Alcohol and opioid addiction are major public health issues with significant personal and social costs and risks of physical and mental illness and early death. The disorders are associated with high relapse rates with many remaining refractory (not responding) to conventional therapies. Deep brain stimulation (DBS) acts like a brain pacemaker to normalise abnormal brain activity. It is effective for severe Parkinson's disease and other neurological disorders and for obsessive-compulsive disorder. DBS has been approved for use in tremor since 2002. More than a quarter of a million people worldwide have DBS devices implanted. A small randomised controlled trial and at least four pilot studies suggest both safety and potential effectiveness in alcohol and opioid use disorders. This study aims to use DBS to treat refractory alcohol and opioid addiction. Addictions can be considered an imbalance of excessive acceleration and lack of braking. DBS will stimulate the nucleus accumbens involved in the drive of motivation and reward for addictions and the ventral internal capsule white matter tracts involved in braking and decision-making to balance function.

Who can participate?
Adults (aged 18-60 years) with alcohol or opioid use disorder of at least 5 years duration, with at least three relapses, and who have failed conventional therapies

What does the study involve?
This is a 10-month study. DBS involves a neurosurgical procedure under general anaesthesia. The participant will stay in hospital for 7 to 10 days. The participant will be followed to optimise stimulation for 6 months then enter a 4-month randomised cross-over trial. They will also take part in brain recording studies to understand the disorder and to help optimise treatment. The DBS team will continue to follow the participant for as long as they have the device in place.

What are the benefits and risks of participating?
Severe untreated chronic addiction that is not responding to the usual treatments is at high risk of comorbid medical illness and early death. DBS has been approved since 2002 and has been shown to be relatively safe and effective in other neurological disorders and obsessive-compulsive disorder. More than a quarter million individuals have undergone DBS for other disorders. Specific to addictions, a small randomized controlled trial and several pilot studies also has shown DBS to be relatively safe and potentially effective. The risks of the neurosurgery can include infection, bleeding and seizure. The neurosurgical team are highly experienced

functional neurosurgeons with the lead neurosurgeon having completed more than 500 DBS surgeries. Risks of stimulation include hypomania which can be managed by changing stimulation parameters.

Where is the study run from?
1. Cambridge University Hospital, University of Cambridge (UK)
2. Kings College Hospital, Kings College London (UK)

When is the study starting and how long is it expected to run?
January 2018 to January 2026

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

Who is the main contact?
1. Prof. Valerie Voon, vv247@cam.ac.uk
2. Dr David Okai

Study website
https://brain-pacer.com

Contact information

Type(s)
Public, Scientific, Principal Investigator

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Additional identifiers

EudraCT/CTIS number
Nil known

IRAS number
316169

ClinicalTrials.gov number
Nil known

Secondary identifying numbers
IRAS 316169, CPMS 56678

Study information

Scientific Title
Deep brain stimulation for disorders of addiction: mechanisms and a pilot blinded randomized cross-over placebo-controlled trial

Acronym
Brain-Pacer

Study objectives
Deep brain stimulation of the nucleus accumbens and ventral internal capsule is more effective than sham stimulation on alcohol and opioid use outcomes in alcohol and opioid use disorder.

Ethics approval required
Ethics approval required

Ethics approval(s)
Approved 30/06/2023, Yorkshire and the Humber: Sheffield Research Ethics Committee (NHS Blood and Transplant Blood Donor Centre Holland Drive, Newcastle, NE2 4NQ, United Kingdom; +44 (0)207 104 8282; sheffield.rec@hra.nhs.uk), ref: 23/YH/0110

Study design
Multicenter interventional double-blind randomized controlled crossover trial

Primary study design
Interventional

Secondary study design
Randomised cross over trial

Study setting(s)
Hospital, University/medical school/dental school

Study type(s)
Treatment

Participant information sheet
See study outputs table

Health condition(s) or problem(s) studied
Alcohol and opioid use disorder

Interventions
Following neurosurgical implantation, deep brain stimulation (DBS) will be delivered at chronic high frequency (~130 hz; 2-4 V) in the nucleus accumbens and ventral internal capsule. The stimulation protocol parameters will be optimized over the 6-month open-label stimulation optimization period. At postoperative month 6, participants will undergo a single-blind randomized cross-over controlled trial (order randomized) of four arms: dual stimulation, single stimulation and sham with each arm, lasting for 1 month.

Intervention Type
Device

Pharmaceutical study type(s)
Not Applicable

Phase
Phase II

Drug/device/biological/vaccine name(s)
Deep brain stimulation

Primary outcome measure
Alcohol and opioid use is measured using Timeline Followback during randomised control cross-over trial at baseline and months 1, 2, 3 and 4

Secondary outcome measures
Alcohol and opioid use is measured using Timeline Followback during open-label stimulation optimisation at baseline and months 1, 2, 3, 4, 5, 6

Overall study start date
01/01/2018

Completion date

31/01/2026

Eligibility

Key inclusion criteria
1. Diagnosis of treatment-refractory opioid use disorder (OUD) or alcohol use disorder (AUD) (DSM-5 diagnosis)
2. Comorbid nicotine dependence, other psychoactive use disorder permissible as long as OUD or AUD is the primary diagnosis
3. At least 5 years duration
4. 3+ failed abstinence attempts
5. Failed psychotherapy and standard pharmacotherapy
6. Age 18 to 60 years old
7. MRI compatible
8. Capable of informed consent

Participant type(s)
Patient

Age group
Adult

Lower age limit
18 Years

Upper age limit
60 Years

Sex
Both

Target number of participants
12

Key exclusion criteria
1. Deep brain stimulation or neurosurgical contraindication (e.g. unable to tolerate general anaesthesia, risk of bleeding)
2. History of repeated falls
3. Other major psychiatric (e.g. schizophrenia, bipolar disorder or severe major depression) or neurologic disorder
4. Major head injury
5. Marked cognitive impairment or cortical atrophy

Date of first enrolment
31/08/2023

Date of final enrolment
31/08/2025

Locations

Countries of recruitment
England

United Kingdom

Study participating centre
Cambridge University Hospitals NHS Foundation Trust
Cambridge Biomedical Campus
Hills Road
Cambridge
United Kingdom
CB2 0QQ

Study participating centre
Kings College London, IoPPN
16 De Crespigny Park
London
United Kingdom
SE5 8AB

Study participating centre
Humber Teaching NHS Foundation Trust
Trust HQ, Block A, Ground Floor
Beverley Road
Willerby Hill
Hull
United Kingdom
HU10 6FE

Study participating centre
Turning Point
Suffolk Recovery Network
Sanderson House
17-19 Museum Street
Ipswich
United Kingdom
IP1 1HE

Sponsor information

Organisation
Cambridge University Hospitals NHS Foundation Trust

Sponsor details
Hills Road
Cambridge
England
United Kingdom
CB2 0QQ
+44 (0)1223 217418
cuh.research@nhs.net

Sponsor type
Hospital/treatment centre

Website
http://www.cuh.org.uk/

ROR
https://ror.org/04v54gj93

Organisation
University of Cambridge

Sponsor details
Hills Road
Cambridge
England
United Kingdom
CB2 0QQ
+44 (0)1223 217418
cuh.research@nhs.net

Sponsor type
University/education

Website
http://www.cam.ac.uk/

ROR
https://ror.org/013meh722

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
Publication plans will include publication of the clinical trial data and mechanistic physiological studies.

Intention to publish date
31/08/2026

Individual participant data (IPD) sharing plan
The datasets generated during and/or analysed during the current study will be available upon request following publication from Prof. Valerie Voon (vv247@cam.ac.uk).

IPD sharing plan summary
Available on request

Study outputs

Output type	Details	Date created	Date added	Peer reviewed?	Patient-facing?
Participant information sheet	version 2.01	12/01/2024	11/07/2024	No	Yes