

Phase-locked brain stimulation for people with Parkinson's disease

Submission date 23/04/2025	Recruitment status Recruiting	<input type="checkbox"/> Prospectively registered <input type="checkbox"/> Protocol
Registration date 23/04/2025	Overall study status Ongoing	<input type="checkbox"/> Statistical analysis plan <input type="checkbox"/> Results
Last Edited 23/04/2025	Condition category Surgery	<input type="checkbox"/> Individual participant data <input checked="" type="checkbox"/> Record updated in last year

Plain English summary of protocol

Background and study aims

Phase-locked neuromodulation uses electrical or magnetic stimulation to match the brain's natural rhythms. This method shows promise for improving treatments by precisely targeting specific brain waves. However, the accuracy of real-time phase estimation is often compromised by artifacts caused by the stimulation. Current methods either stop phase-tracking during stimulation or use special hardware, but these solutions can cause instability due to timing gaps and signal distortion. In this study, we aim to first create and test a flexible and stable system for phase-locked deep brain stimulation (PLDBS) that can deliver phase-aligned stimulation in sync with brain waves on a cycle-by-cycle basis, then we will test its safety, effectiveness in modulating certain brain waves, and the potential to influence movement.

Who can participate?

Patients aged 18 or older with DBS electrodes implanted

What does the study involve?

In this study, researchers will spend about an hour assessing which stimulation settings work best to reduce disease symptom such as bradykinesia (slow movement). Participants will do simple movement tasks like finger-tapping and maintaining posture with their eyes closed under three different conditions: standard deep brain stimulation (DBS), phase-locked DBS (PLDBS) that matches specific brain signal phases, and no stimulation.

During these tasks, researchers will record various signals from the brain and muscles to identify how different phases of brain activity affect movement. They will compare continuous DBS, no stimulation, and PLDBS using feedback from brain signals to see how effective PLDBS is. This approach helps them understand how PLDBS influences both brain activity and movement.

What are the possible benefits and risks of participating?

Involvement in the study will not affect the clinical care you receive. The research assessments and recordings that will be performed during the study are neither invasive nor harmful. The researchers do not expect harm from participating, but there is a small risk that stimulation will cause temporary tingling, cramping or slurring of speech. Should you omit your medication for

the study (not obligatory in this study) then this will only be for the morning of the study. As such you may only experience a temporary and reversible exacerbation of your symptoms, similar to forgetting a dose. The recording session may last up to two hours.

All but one of the medical devices we are using in the assessments are CE-marked. The stimulator is not CE-marked and is built at the University of Oxford. It passes all of the required safety tests and is an updated version of a similar custom-built stimulator successfully and safely used in other studies.

Where is the study run from?
University of Oxford (UK)

When is the study starting and how long is it expected to run for?
October 2020 to September 2028

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

Who is the main contact?
1. Dr Shenghong He, shenghong.he@ndcn.ox.ac.uk
2. Prof Huiling Tan, huiling.tan@ndcn.ox.ac.uk

Contact information

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Additional identifiers**EudraCT/CTIS number**

Nil known

IRAS number**ClinicalTrials.gov number**

Nil known

Secondary identifying numbers

19/SC/0550

Study information**Scientific Title**

Phase-locked deep brain stimulation for Parkinson's disease

Acronym

PLDBS-PD

Study objectives

1. Phase-locked deep brain stimulation (PLDBS) targeting different subthalamic nucleus (STN) beta phase is feasible and safe.
2. PLDBS targeting different STN beta phase modulates the stimulation evoked potentials (ERNA) in STN local field potentials (LFPs).
3. PLDBS targeting different STN beta phase leads to difference in motor behaviour.

Ethics approval required

Ethics approval required

Ethics approval(s)

Approved 26/10/2020, South Central - Oxford C Research Ethics Committee (Wellington Square, Oxford, OX3 9DU, United Kingdom; +44 2071048271; oxfordc.rec@hra.nhs.uk), ref: 19/SC/0550

Study design

Multicentre interventional study

Primary study design

Interventional

Secondary study design

Randomised cross over trial

Study setting(s)

Hospital

Study type(s)

Safety, Efficacy

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

People undergoing deep brain stimulation (DBS) surgery

Interventions

The intervention in this study comprises:

1. Brief withdrawal of the ongoing medications for PD
2. Electrical stimulation is applied unilaterally phase-locked to different phases of the neural oscillation (beta or alpha band) detected from subcortical local field potentials (LFPs) or electroencephalogram (EEGs)

For consistency, in cases with directional leads, the segmented contacts were used in ring mode. One of the two contacts in the middle is used as the stimulation contact, and an electrode patch attached to the back of the patient is used for reference. The stimulation pulses will have a biphasic pulse width of 60 microseconds, and an interphase gap of 20 microseconds, similar to those that would be used in standard clinical practice. Four different stimulation conditions will be in this study, including no DBS, continuous DBS (CDBS), PLDBS targeting two opposing phases of beta oscillations.

The outcome will be measured using two tasks: a cued reaching task performed on a Tablet Drawing Monitor (33 x 57 cm, Artist 22, XP-PEN, Japan) with a stylus pen, and a 20s finger-tapping task.

Assignment/Randomisation

The whole experimental session consists of sixteen 2-minute blocks. There are four blocks in each of the four tested stimulation conditions (no DBS, CDBS, PLDBS targeting two different phases) with inter-block interval of at least 2 mins with no DBS. After each block, the patient is asked to perform finger-tapping movements for 20 sec, by tapping their index fingers on their thumbs as wide and fast as possible. The order of the experimental blocks is randomised and counterbalanced across patients. To achieve this, for each patient, the first four blocks included the four stimulation conditions in randomised order, and the four conditions were repeated in reverse order in the second four blocks. The first eight blocks will be repeated again with reversed order, resulting 16 blocks and 4 blocks of each stimulation condition in total. To do so, we will Matlab function randperm to generate a random sequence from 1 to 4, e.g., 1, 3, 2, 4, which will indicate the order of the experimental conditions for the first 4 blocks to be no DBS, PLDBS_Phase1, CDBS, and PLDBS_Phase2.

Throughout these tasks, subcortical local field potentials (LFP), cortical electroencephalography (EEG), electromyography (EMG), and triaxial accelerometer signals will be recorded.

Intervention Type

Behavioural

Primary outcome measure

1. ERNA amplitude quantified from the recorded LFP signals during different stimulation conditions
2. Motor performance in reaching and finger-tapping movements assessed using the following methods during the study session:
 - 2.1. Reaction time measured using the Tablet Drawing Monitor (Artist 22, XP-PEN, Japan) by quantifying the time from Go-cue until the pen moves out of the start point during the reaching movements
 - 2.2. Velocity measured using the Tablet Drawing Monitor (Artist 22, XP-PEN, Japan) by dividing the accumulated distance by the time used during the reaching movements
 - 2.3. Root-mean-square acceleration measured using a tri-axis accelerometer during the finger-tapping movements
3. Incidence of stimulation-related adverse events (e.g., dizziness, paresthesia) monitored in different stimulation conditions throughout the study session

Secondary outcome measures

Correlation between the amplitude of ERNA and behavioral outcomes assessed using Pearson correlation coefficient in different stimulation conditions.

Overall study start date

26/10/2020

Completion date

30/09/2028

Eligibility

Key inclusion criteria

1. Aged 18 years or older
2. Undergoing DBS treatment

Participant type(s)

Patient

Age group

Adult

Lower age limit

18 Years

Upper age limit

90 Years

Sex

Both

Target number of participants

Key exclusion criteria

1. Intracranial bleeding, confusion, CSF leak or any other complication after the first stage of surgery
2. Lack of capacity to consent (judged by the clinician taking consent as not having sufficient mental capacity to understand the study and its requirements). Anyone who, in the opinion of the clinician taking consent, is unlikely to retain sufficient mental capacity for the duration of their involvement in the study.
3. Cognitive impairment/lack of capacity to perform the experimental tasks. In cases where capacity was borderline and difficult to judge subjectively, we will additionally conduct a short (10 min) quantitative assessment of cognitive function using the Mini Mental State Exam (MMSE). Patients with a score of <20 will be excluded from the study.

Date of first enrolment

01/10/2023

Date of final enrolment

30/09/2028

Locations**Countries of recruitment**

England

United Kingdom

Study participating centre**University of Oxford**

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Sponsor information**Organisation**

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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

The patient information sheet (PIS), study protocol, and consent forms are all available upon reasonable request from the study chief investigator (Dr Tan). Results of this study will be disseminated through a range of peer-reviewed scientific articles, conference presentations, and online articles.

Intention to publish date

01/09/2026

Individual participant data (IPD) sharing plan

The datasets generated and/or analysed during the current study during this study will be included in the subsequent results publication. Raw data will be anonymised and made possible for sharing. When being contacted with a request to share data generated by the study, the chief investigator will ask the requestor to provide a brief research proposal on how they wish to use the data. If the CI has doubts over the scientific validity of the proposal or the requestor's ability to analyse/interpret data correctly, this should be discussed with the requestor. The CI, Dr Huiling Tan will be in charge of ensuring that the security and confidentiality of the participants' information is maintained.

IPD sharing plan summary

Available on request, Published as a supplement to the results publication