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

Submission date	Recruitment status	[_] Prospectively registered
23/04/2025	Recruiting	[_] Protocol
Registration date	**Overall study status**	[_] Statistical analysis plan
23/04/2025	Ongoing	[_] Results
Last Edited	**Condition category**	[_] Individual participant data
23/04/2025	Surgery	[X] 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
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Contact information

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Public, Scientific, Principal investigator

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Additional identifiers

Clinical Trials Information System (CTIS)
Nil known

ClinicalTrials.gov (NCT)
Nil known

Protocol serial number
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

Study type(s)
Safety, Efficacy

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 neurals 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(s)
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

Key secondary outcome(s))
Correlation between the amplitude of ERNA and behavioral outcomes assessed using Pearson correlation coefficient in different stimulation conditions.

Completion date
30/09/2028

Eligibility

Key inclusion criteria
1. Aged 18 years or older
2. Undergoing DBS treatment

Participant type(s)
Patient

Healthy volunteers allowed
No

Age group
Adult

Lower age limit
18 years

Upper age limit
90 years

Sex
All

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
United Kingdom

England

Study participating centre
University of Oxford
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Sponsor information

Organisation
University of Oxford

ROR
https://ror.org/052gg0110

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

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

Study outputs

Output type	Details	Date created	Date added	Peer reviewed?	Patient-facing?
Participant information sheet	Participant information sheet	11/11/2025	11/11/2025	No	Yes