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Investigating the effectiveness of deep brain stimulation in improving reaching movements in people with Parkinson's disease

Submission date
15/12/2022

Recruitment status
No longer recruiting

Registration date
20/12/2022

Overall study status
Completed

Last Edited
31/03/2025

Condition category
Nervous System Diseases

[_] Prospectively registered
[_] Protocol
[_] Statistical analysis plan
[X] Results
[_] Individual participant data

Plain English summary of protocol

Background and study aims
Subthalamic nucleus (STN) beta-triggered adaptive deep brain stimulation (ADBS) has been shown to provide clinical improvement compared to conventional continuous DBS (CDBS) with less energy delivered to the brain and fewer stimulation-induced side effects. However, several questions remain unanswered. First, there is a normal physiological reduction of STN beta band power just prior to and during voluntary movement. ADBS systems will therefore reduce or cease stimulation during movement in people with Parkinson’s disease (PD) and could therefore compromise motor performance compared to CDBS. Second, beta power was smoothed and estimated over a time period of 400 ms in most previous ADBS studies, but a shorter smoothing period could have the advantage of being more sensitive to changes in beta power which could enhance motor performance. In this study, we addressed these two questions by evaluating the effectiveness of STN beta-triggered ADBS using a standard 400 ms and a shorter 200 ms smoothing window during reaching movements.

Who can participate?
Patients aged 18 or older with PD with DBS electrodes implanted

What does the study involve?
This study will take place between Stage 1 and Stage 2 of your operation. If you are taking medication for PD you will be asked if you mind omitting this on the day of the study. The study can go ahead regardless, but our results might be slightly easier to interpret should you omit your medication. Should you omit your medication you can restart it the same day after the recordings.

We then tape some small electrodes and a motion-sensitive device to the skin overlying some muscles of the most affected body regions. The electrodes pick up the electrical activity from the muscles, while the device picks up physical movement. We also use a paste to place some small electrodes on your scalp and connect them to the deep brain electrodes. These record superficial and deep brain waves, respectively.

You will be asked to perform two tasks, including a reaching task performed on a Tablet Drawing Monitor with a stylus pen, and a 20s finger-tapping task. We will record a video for each of the 20-sec finger-tapping movements for later analysis. The video will only capture the tapping hand. During the task, we will test several different protocols for stimulating the deep brain electrodes. We use exactly the same parameters of stimulation that are used clinically and start by gently increasing the stimulation intensity until you begin to experience reversible side effects. We can then use a stimulation intensity that is just below this level during the rest of the study.

The whole test would take up to two hours to complete. Once we have finished, we will remove all the electrodes. That is the end of that study day, and you are then free to take your medication should you have opted to withhold it during the study.

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 PD 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?
July 2020 to December 2024

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

Type(s)
Scientific

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Additional identifiers

EudraCT/CTIS number
Nil known

IRAS number
271953

ClinicalTrials.gov number
Nil known

Secondary identifying numbers
IRAS 271953, MC_UU_00003/2 and the BRAIN Non-Clinical Post-Doctoral Fellowship (HMR04170), CPMS 45355

Study information

Scientific Title
Beta-triggered adaptive deep brain stimulation during reaching movement in Parkinson’s disease

Acronym

BetaDBSinPD

Study objectives
First, there is a normal physiological reduction of subthalamic nucleus (STN) beta band power just prior to and during voluntary movement. Adaptive deep brain stimulation (ADBS) systems will therefore reduce or cease stimulation during movement in people with Parkinson's disease (PD) and could therefore compromise motor performance compared to continuous DBS (CDBS). Second, beta power was smoothed and estimated over a time period of 400ms in most previous ADBS studies, but a shorter smoothing period could have the advantage of being more sensitive to changes in beta power which could enhance motor performance.

Ethics approval required
Old ethics approval format

Ethics approval(s)
Approved 26/10/2020, South Central - Oxford C Research Ethics Committee (Ground Floor, Temple Quay House, 2 The Square, Bristol, BS1 6PN, UK; +44(0)207 104 8379; 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)
Other

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
Parkinson's disease

Interventions
The intervention in this study comprises:
1. Brief withdrawal of the ongoing medications for PD
2. High-frequency electrical stimulation is applied unilaterally to the hemisphere contralateral to the hand performing the task.

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 has a fixed frequency of 130Hz, a biphasic pulse width of 60 microseconds, and an interphase gap of 20 microseconds,

similar to those that would be used in clinical. Four different stimulation conditions were considered in this study, including no DBS, continuous DBS (CDBS), adaptive DBS with the stimulator controlled by the beta amplitude estimated in real-time using a 200-ms smoothing window (ADBS-200), and adaptive DBS with a 400-ms smoothing window (ADBS-400). The protocol involved 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 eight blocks of 15 trials of reaching movements, with an inter-trial interval of 4-5 sec (randomised). There are two blocks in each of the four tested stimulation conditions (no DBS, CDBS, ADBS-200, ADBS-400; details in next section). 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.

For each participant, the randomisation was applied to four different stimulation conditions including no DBS, CDBS, ADBS-200, and ADBS-400. To do so, we used Matlab function randperm to generate a random sequence from 1 to 4, e.g., 1, 3, 2, 4, indicates the order of the experimental conditions to be no DBS, ADBS-200, CDBS, and ADBS-400. Once this is done, we repeat all four conditions in inverse order (4, 2, 3, 1), e.g., (ADBS-400, CDBS, ADBS-200, no DBS). In this way, the experimental conditions are randomised and counterbalanced across patients.

Intervention Type
Mixed

Primary outcome measure
1. Motor performance in reaching and finger-tapping movements assessed using the following methods during the study session:
1.1. 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
1.2. 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
1.3 Root-mean-square acceleration measured using a tri-axis accelerometer during the finger-tapping movements
2. Resting tremor severity measured using an accelerometer during the finger-tapping movements
3. Stimulation on time compared across different stimulation conditions during the reaching and finger-tapping tasks. The stimulation on/off time will be recorded automatically by the C++ program

Secondary outcome measures
1. Modulations in subthalamic nucleus brain oscillations by movement and different stimulation protocols measured from the recorded bipolar LFP signals during the reaching movements during the study session
2. Association between changes in brain oscillations and belabour measured using linear mixed effect modelling during the reaching movements during the study session

Overall study start date

01/07/2020

Completion date
31/12/2024

Eligibility

Key inclusion criteria
Patients aged 18 years old and over with Parkinson's disease and deep brain stimulation electrodes implanted

Participant type(s)
Patient

Age group
Adult

Lower age limit
18 Years

Sex
Both

Target number of participants
25

Key exclusion criteria
1. Cognitive impairment (judged by the clinician taking consent as not having the sufficient mental capacity to understand the study and its requirements). This is including anyone who, in the opinion of the clinician taking consent is unlikely to retain the sufficient mental capacity for the duration of their involvement in the study.
2. Severe motor impairment (judged by the clinician taking consent as not having the sufficient motor capacity to perform the motor task in the study)
3. Patients unwilling to briefly withdraw the ongoing medications
4. Severe visual impairment

Date of first enrolment
01/01/2021

Date of final enrolment
31/12/2024

Locations

Countries of recruitment
England

United Kingdom

Study participating centre
University of Oxford
Nuffield Department of Clinical NeurosciencesLevel 6
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Sponsor information

Organisation
University of Oxford

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Sponsor type
University/education

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

ROR
https://ror.org/052gg0110

Funder(s)

Funder type
Government

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

Funder Name
the BRAIN Non-Clinical Post-Doctoral Fellowship

Results and Publications

Publication and dissemination plan
1. Planned publication in a high-impact peer-reviewed journal
2. Conference presentations
3. Online articles

Intention to publish date
31/12/2022

Individual participant data (IPD) sharing plan
The data and codes will be shared on the data-sharing platform of the MRC Brain Network Dynamics Unit: https://data.mrc.ox.ac.uk/mrcbndu/data-sets/search.

1. The name and email address of the investigator/body who should be contacted for access to the datasets: Prof Huiling Tan, huiling.tan@ndcn.ox.ac.uk
2. The type of data that will be shared: The de-identified research data including the recorded electrophysiological data, behavioural data, hand videos, and the code for analyzing these data
3. Dates of availability: Once the study results are officially published in peer-reviewed journals
4. Whether consent from participants was required and obtained: Yes, consent forms from the participants were obtained before conducting any part of the experiment
5. Comments on data anonymization: All personal information that could identify the participant will be removed or changed before the information is shared with other researchers or results are made public.
6. No further ethical or legal restrictions or additional comments

IPD sharing plan summary
Stored in publicly available repository

Study outputs

Output type	Details	Date created	Date added	Peer reviewed?	Patient-facing?
HRA research summary			20/09/2023	No	No
Results article		11/07/2023	31/03/2025	Yes	No