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Investigating the possibility and benefit of closed-loop deep brain stimulation by detecting the voluntary movement and postural tremor on patients with tremor

Submission date
12/02/2020

Recruitment status
Suspended

Registration date
14/02/2020

Overall study status
Completed

Last Edited
23/04/2020

Condition category
Nervous System Diseases

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

Plain English summary of protocol

Background and study aims

Lots of patients suffer from tremor which predominantly occurs during voluntary movement and /or while maintaining a certain posture. For example, Essential tremor (ET), a progressive neurological disorder that causes involuntary and rhythmic shaking, is one of the most common movement disorders. Dystonia tremor is another condition in which tremor is typically intermittent (stops and starts). Continuous deep brain stimulation (DBS) is an approved and effective therapy for both ET or Dystonia tremor. However, due to disease progression or the brain becoming used to stimulation, many patients lose the benefit of DBS over time. In these circumstances, an increased stimulation intensity is usually required in order to maintain the beneficial effect. Increased stimulation intensity can be associated with side effects including unpleasant sensations, slurred speech and unsteadiness walking. A promising innovative DBS treatment, known as closed-loop or adaptive DBS, aims to only deliver stimulation when necessary, and so, reduce these side effects, save on battery power, and prolong the time for which DBS provides benefit to patients.

In this study, the researchers will evaluate if the closed-loop DBS system is effective in reducing tremor, saves energy in comparison to traditional continuous DBS, and could be used to predict the onset of tremors so DBS can be switched on in advance for improved patient outcomes.

Who can participate?
Patients aged 25 to 80 with essential tremor or dystonia tremor undergoing DBS for the treatment of the symptoms.

What does the study involve?
The patients will be asked to perform some self-paced movements of everyday life, meanwhile,

the researchers will either switch off the DBS, switch on the DBS continuously, or set the DBS to a novel setting (adaptive/closed-loop). The total duration of the experiment will be approximately 3 hours.

What are the possible benefits and risks of participating?
The assessments and recordings that will be performed during the study are neither invasive nor harmful. They do not pose any risk to the health or safety of the participants. The risk to participants is minimal. Involvement in the study will not affect the clinical care the patients receive. All recordings with patients are assisted by a local clinician. There are no direct benefits to participants. Results from the study may, however, help in developing an innovative treatment for tremor.

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

When is the study starting and how long is it expected to run for?
December 2018 to January 2022

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

Who is the main contact?
1. Dr Shenghong He
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Contact information

Type(s)
Scientific

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Additional identifiers

EudraCT/CTIS number
Nil known

IRAS number
249989

ClinicalTrials.gov number
Nil known

Secondary identifying numbers
MR/P012272/1, MC_UU_12024/1, IRAS 249989

Study information

Scientific Title
Closed-loop Deep Brain Stimulation for Tremor: CDBSoT

Acronym
CDBSoT

Study objectives
Patients with essential tremor or dystonia tremor suffer from tremor predominantly during voluntary movements and when they are trying to maintain a posture. This study aims to test whether we can detect movements and the presence of tremor based on the signals recorded from electrodes implanted in the brain and whether we can use this decoded information to switch on and off the Deep Brain Stimulation (DBS) so that the brain is stimulated only when necessary.

Ethics approval required
Old ethics approval format

Ethics approval(s)
Approved 23/10/2018, Ethics Committee of the South Central - Oxford B Research Ethics Committee (Level 3, Block B, Whitefriars Building, Lewins Mead, Bristol BS1 2NT; +44 02071048058; nrescommittee.southcentral-oxfordb@nhs.net), ref: 18/SC/0436

Study design
Multicentre interventional study

Primary study design
Interventional

Secondary study design
Non randomised study

Study setting(s)
Hospital

Study type(s)
Diagnostic

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
Essential Tremor (ET) or Dystonia tremor in which tremor mainly affect voluntary movement or while maintaining postures

Interventions
The researchers will assess which stimulation parameters have the best effect to suppress tremor. This procedure is part of the normal clinical procedure and will take approximately 1 hour.

The participants will be asked to do some simple movement tasks, such as gripping a device that measures the force generated, during standard clinical deep brain stimulation (DBS) and with stimulation turned off. Meanwhile, the thalamic local field potentials (LFP), EEG, EMG, and accelerometer signals will be recorded. This procedure is for the researchers to prepare the models for movement or postural tremor decoding and will take approximately 1 hour.

Participants will be asked to perform some voluntary movements and/or maintaining some specific postures to evoke tremor. These will be self-paced movements typically seen in everyday life, such as drawing, reaching and picking up a cup, or holding a book. They will then receive continuous DBS, adaptive DBS or no DBS during these movements or postures. Adaptive DBS (also known as ‘closed loop DBS’) responds to the detection of movements and tremor. This procedure is for testing the performance of the adaptive DBS and will take approximately 1 hour.

In this study, the control conditions include continuous DBS and when the stimulation turned off, therefore provides within-subject control. The effect of adaptive DBS is evaluated in terms of decoding performance (accuracy, sensitivity, and false-positive rate), saved energy compared to continuous DBS, and tremor suppression.

Intervention Type
Behavioural

Primary outcome measure
1. Voluntary movement and postural tremor decoding performance assessed through recorded LFPs and accelerometer signals at baseline, 1h, and 2h.
2. Effectiveness and efficiency of the proposed adaptive DBS assessed by the energy saved compared to continuous DBS and the suppression of tremor compared with when the DBS is turned off measured using accelerometer and patient's self-report at baseline, 1h, and 2h.

Secondary outcome measures
1. Different feature contributions for voluntary movement and posture tremor decoding assessed through recorded LFPs and accelerometer signals at baseline, 1h, and 2h.
2. The possibility for predicting the onsets of voluntary movement and postural tremor using LFPs, thus the DBS can be switched on in advance assessed by recorded LFPs and accelerometer signals at baseline, 1h, and 2h.
3. Possibilities of movement/tremor decoding on different contacts using the anatomy information of the DBS electrodes for the patients at baseline, 1h, and 2h.

Overall study start date
01/12/2018

Completion date
31/01/2022

Eligibility

Key inclusion criteria
1. Aged 25 to 80 years
2. Diagnosis of essential tremor or dystonia tremor
3. Undergoing DBS for tremor symptoms

Participant type(s)
Patient

Age group
Adult

Sex
Both

Target number of participants
10 - ET with DBS electrodes implanted

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
01/12/2018

Date of final enrolment
31/08/2021

Locations

Countries of recruitment
England

United Kingdom

Study participating centre
University of Oxford
Nuffield Department of Clinical Neurosciences
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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
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

Funder Name
Rosetrees Trust

Alternative Name(s)
Teresa Rosenbaum Golden Charitable Trust, Rosetrees

Funding Body Type
Private sector organisation

Funding Body Subtype
Trusts, charities, foundations (both public and private)

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

31/08/2021

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

Study outputs

Output type	Details	Date created	Date added	Peer reviewed?	Patient-facing?
HRA research summary			28/06/2023	No	No