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Investigating the relationship between movement initiation and beta bursts in patients with Parkinson’s disease by neurofeedback training

Submission date
12/02/2020

Recruitment status
No longer recruiting

Registration date
26/02/2020

Overall study status
Completed

Last Edited
09/04/2025

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
Beta bursts (increase in certain brain signals known as beta oscillations) in specific brain circuits have been associated with rigidity and slow movement in Parkinson’s disease (PD), as well as associated with the initiation of movement in healthy subjects. The suppression of beta bursts through medication or deep brain stimulation (DBS) correlates with improvement in the symptoms of PD. In particular, the occurrence of the beta bursts just before a signal to start moving slows these movements.

In this study, we used a neurofeedback behavior task in order to investigate whether patients with Parkinson’s disease and healthy volunteers can learn to suppress beta bursts with neurofeedback training and whether the training improves performance in a subsequent movement task.

Who can participate?
Patients aged 25 – 80 with Parkinson's disease with or without DBS electrodes implanted, and adult healthy volunteers.

What does the study involve?
The participants are involved in a neurofeedback training task, in which the participants are asked to wear sensors (like a swimming cap) to monitor their brain activity. These sensors will be linked to a computer screen displaying a game. In the game, the participants will be asked to control the movement of a basketball displayed on a computer screen, which will require the suppression of the beta bursts to create the correct signal via the sensors.

After each session of the neurofeedback training, the participants are involved in a pinch task, in which the participants are instructed to produce a pinch as fast as possible in response to a cue. This will test movement initiation.

The total duration of the experiment during the first visit will be approximately 2 hours. Participants will be invited to up to two more sessions to repeat the training. This will assess if there is a learning effect of the training. The maximal interval between the additional sessions will be 2 days.

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. For patients with Parkinson's disease, involvement in the study will not affect the clinical care they receive. All recordings with patients undergoing the surgery for DBS are assisted by a local clinician.

There are no direct benefits to participants. Results from the study may, however, help in understanding the relationship between beta bursts and movement initiation, as well as to investigate the potential benefit of neurofeedback training in the treatment of PD.

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

When is the study starting and how long is it expected to run for?
May 2018 to December 2021

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

Who is the main contact?
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Contact information

Type(s)
Scientific

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Integrated Research Application System (IRAS)
220480

Protocol serial number
MR/P012272/1, MC_UU_12024/1

Study information

Scientific Title
Does NeuroFeedback Training-linked suppression of beta bursts speed up movement initiation in Parkinson’s Disease patients? Part of the NFToPD study

Acronym
NFToPD

Study objectives
Abnormally increased beta bursts in cortical-basal ganglia-thalamic circuits are associated with rigidity and bradykinesia in patients with Parkinson’s disease. Beta bursts can also be detected in the motor cortex in healthy participants, and increased beta bursts in the motor cortex have been reported to be associated with longer reaction times even in healthy motor control. We hypothesize that suppressing beta bursts in cortical-basal ganglia-thalamic circuits through neurofeedback training can improve motor performance in healthy subjects, as well as in patients with Parkinson’s disease.

Ethics approval required
Old ethics approval format

Ethics approval(s)
Approved 31/01/2018, Ethics Committee of the South Central - Oxford C Research Ethics Committee (Level 3, Block B, Whitefriars Building, Lewins Mead, Bristol BS1 2NT; nrescommittee.southcentral-oxfordc@nhs.net; +44 02071048041), ref: 18/SC/0006.

Study design
Multi-centre interventional randomized controlled study

Primary study design
Interventional

Study type(s)
Prevention

Health condition(s) or problem(s) studied
Parkinson's disease (PD)

Interventions
This study was controlled through within-subject controls, randomized to the order of intervention and non-intervention activities. An additional level of control was added through the inclusion of healthy volunteers assigned to the intervention, non-intervention, and sham-intervention arms.

The intervention involves neurofeedback training in which the participants are asked to control the movement of a basketball displayed on a computer screen which is driven by the brain activities measured in real-time, this is followed by a behavioural task to evaluate the motor performance.

The participants in this study were asked to withdraw the ongoing medications at least 6 hours before the neurofeedback training experiment by the clinical team. Then, each patient was asked to perform a neurofeedback training task targeting the beta bursts measured in each hemisphere. During the task, a basketball appeared in the top-left corner of a computer screen at the beginning of each trial. The horizontal displacement for each update was constant so that the basketball moved toward the right of the screen at a constant speed during the trial. The vertical movement of the basketball was driven by the real-time detection of beta bursts based on the bioelectrical signal recorded from the cortical-basal ganglia-thalamic circuits. If a beta burst was detected, the ball would drop by a fixed distance.

Each participant completed four 'Training' blocks and four 'No Training' blocks on each recording day, with 10 trials in each block. In the 'Training' trials, the participants were instructed to keep the basketball floating at the top of the screen by preventing it from dropping, which will require the suppression of the beta bursts. In the 'No Training' trials, the participants were instructed to simply pay attention to the movement of the ball displayed on the screen. After each trial, the participants were instructed to perform a thumb of finger pinch movement as fast as possible in response to a Go cue to generate a force overshooting a predefined force level.

The control in this study included within-subject 'No Training' condition, and the involvement of healthy subjects. For the 'No Training' condition, the participant was asked to simply pay

attention to the movement of the ball displayed on the screen without trying to suppress the beta bursts. Thus we can compare the presence of the beta bursts between 'Training' and 'No Training' conditions within-subject.

For the healthy subjects, in addition to the 'No Training' condition, we included a 'Sham Feedback' group, in which the beta bursts triggering the movement of the basketball was quantified based on the replay of the bioelectrical signal recorded from other participants, in order to investigate whether the effect was associated with 'Real Feedback' rather than other underlying factors in the task.

The order of the blocks in 'Training' and 'No Training' conditions, and the order of the experiments for left and right hemispheres were randomized for each participant. The healthy participants were pseudo-randomly assigned to the 'Sham Feedback' group or the 'Real Feedback' group. The existence of a 'Sham Feedback' group was blinded to all participants. Both the participants and the experimenter who gave instructions and conducted the recordings were blinded about the group each participant was assigned to, resulting in a double-blind sham-controlled design.

The total duration of the experiment during the first visit will be approximately 2 hours. Participants will be invited to up to two more sessions to repeat the training. This will assess if there is a learning effect of the training. The maximal interval between the additional sessions will be 2 days.

Intervention Type
Behavioural

Primary outcome(s)
1. Self-modulation of the targeted neural signal by the participants with neurofeedback training. This will be assessed by bioelectrical signals recorded during the neurofeedback training experiment at 2h. This will include the beta burst characteristic, average beta power, and coherence between the STN and cortex derived from the recording of local field potentials (LFPs) and electroencephalography (EEG) in cortical-basal ganglia-thalamic circuits such as sub-thalamic nucleus (STN) or sensorimotor cortex (C3 or C4).
2. Changes in motor performance associated with the neurofeedback training measured by reaction time and peak movement velocity derived from the original measurements such as the generated force in the pinch task at 2h

Key secondary outcome(s))
1. Neurofeedback control performance over the duration of the study measured through recorded data from the neurofeedback training task at 2h
2. How other symptoms related to Parkinson's disease change with neurofeedback training. This will be assessed through records from the neurofeedback training, measurements from the motor task, the intensity of tremor recorded using a 3D accelerometer, the Unified Parkinson's Disease Rating Scale (UPDRS) score and patient notes whether on or off medication at 2h.
3. The potential effect of the neurofeedback training in the DBS patients measured by the anatomy information of the DBS electrodes at 2h for the DBS patients. The researchers can investigate the correlations between the primary and secondary outcome measurements, to better understand the potential effect of the neurofeedback training.
4. The learning effect of repeated neurofeedback training at 2h, 2 days, and 4 days.

Completion date

31/12/2021

Eligibility

Key inclusion criteria
1. Aged 25 to 80 years
2. Falls into one of the three categories:
a. Diagnosis of Parkinson's disease with DBS electrodes implanted
b. Diagnosis of Parkinson's disease without DBS electrodes implanted
c. No diagnosis of Parkinson's disease, healthy volunteer

Participant type(s)
Mixed

Healthy volunteers allowed
No

Age group
Adult

Sex
All

Key exclusion criteria
1. Cognitive impairment (judged by the clinician taking consent as not having sufficient mental capacity to understand the study and its requirements). Including 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.
2. Severe motor impairment (judged by the clinician taking consent as not having sufficient motor capacity to perform the motor task in the study).
3. Unwilling to briefly withdraw the ongoing medications.
4. Severe visual impairment

Date of first enrolment
01/08/2018

Date of final enrolment
21/05/2021

Locations

Countries of recruitment
United Kingdom

England

Study participating centre

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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, Medical Research Committee and Advisory Council, MRC

Funding Body Type
Government organisation

Funding Body Subtype
National government

Location
United Kingdom

Funder Name
Rosetrees Trust

Alternative Name(s)

Rosetrees, Teresa Rosenbaum Golden Charitable Trust

Funding Body Type
Private sector organisation

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

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

Study outputs

Output type	Details	Date created	Date added	Peer reviewed?	Patient-facing?
Results article		13/05/2020	09/04/2025	Yes	No
Results article		18/11/2020	09/04/2025	Yes	No
HRA research summary			28/06/2023	No	No
Other publications	pilot study	01/03/2019		Yes	No