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ENact-PD: EEG Neuro-feedback to improve motor function in Parkinson's

Submission date
09/05/2017

Recruitment status
No longer recruiting

Registration date
29/08/2017

Overall study status
Completed

Last Edited
13/02/2024

Condition category
Nervous System Diseases

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

Plain English summary of protocol

Background and study aims:
Parkinson's disease (PD) is a long-term medical condition which is caused by the gradual loss of nerve cells (neurons) in a part of the brain called the substantia nigra. These neurons are normally responsible for producing dopamine, a chemical messenger (neurotransmitter) which carries signals around the brain that help to coordinate movement. In people suffering from PD, these neurons gradually die over time, causing the level of dopamine in the brain to gradually fall. As the levels of dopamine become lower, the brain is unable to coordinate movement as effectively, causing abnormal movements such as stiffness, tremor (uncontrollable shaking) and slowness of movement (bradykinesia). This study is looking at a new method of improving movement in Parkinson's. EEG-based neurofeedback is a type of training during which people receive real-time information about their brain activity using a visual and auditory representation and learn to control their brain activity. The aim of this study is to look at the impact of neurofeedback training on movement, as well as how receptive PD patients are to this type of therapy.

Who can participate?
Adults with PD who have been on stable treatment for at least one month.

What does the study involve?
Everyone who takes part in the study is visited up to six times by a researcher, either at the University or at home. Participants take part in neurofeedback training. This involves having some sensors attached to their heads to record brain activity, which is displayed on a screen so participants can learn how to control it (e.g. how to increase brain activity and how to make it relax). Participants are asked to make some hand and arm movements and to complete some short questionnaires to find out how different levels of brain activity influence movements. For some of the visits participants are asked not to take their normal Parkinson's medications on the day of testing to see how brain training method compares to medication management of Parkinson's symptoms. The sessions take no more than 80-120 minutes in total, and include a discussion with the researcher after the neurofeedback session and as many short breaks as are needed.

What are the possible benefits and risks of participating?
Participants may find it beneficial, interesting and enjoyable to complete the tasks and questionnaires included in the study and to talk with the researcher. There are no notable risks involved with participating.

Where is the study run from?
BCUHB Movement Disorders Clinic, Llandudno General Hospital (UK)

When is study starting and how long is it expected to run for?
March 2015 to August 2018

Who is funding the study?
Betsi Cadwaladr University Health Board (UK)

Who is the main contact?
Dr John Hindle

Contact information

Type(s)
Public

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Additional identifiers

Protocol serial number
ENact-PD version 1

Study information

Scientific Title
A feasibility trial of the effects of home-based alpha frequency neurofeedback in modulating cortical activity and alleviating motor symptoms in Parkinson’s disease

Acronym
ENact-PD

Study objectives
Current hypothesis as of 04/08/2023:
Hypothesis:
EEG alpha power will be greater in Pre-test B (OFF medication) than in Pre-Test A (ON medication) and in Post-Test (OFF medication, after neurofeedback training). This finding would evidence the feasibility of home-based neurofeedback training in allowing people with PD to self-regulate brainwaves to mimic the effects of medication.

Study aim:
The aim of this study is to examine whether home-based EEG neurofeedback can be used to train PD patients to produce 'normal' pre-movement alpha ERD and, thus, replicate some of the benefits of L-dopa medication.

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Previous hypothesis:
Hypothesis:
EEG based neurofeedback will improve motor symptoms in PD over and above the effects of the medication.

Study aim:
The aim of this study is to examine whether EEG neurofeedback can be used to train PD patients

to produce “normal” pre-movement alpha ERD and, thus, replicate some of the benefits of L-dopa medication.

Ethics approval required
Old ethics approval format

Ethics approval(s)
1. Ysbyty Gwynedd, Betsi Cadwaladr University Health Board, 13/06/2016, ref: 195863
2. Wales Research Ethics Committee 4 Wrexham, 06/05/2016, ref: 16/WA/0115

Study design
Non randomised study

Primary study design
Interventional

Study type(s)
Treatment

Health condition(s) or problem(s) studied
Parkinson's Disease

Interventions
Current intervention as of 04/08/2023:
We will employ a fully within-subjects design. Each participant will receive six home visits from a researcher, with each visit separated by a minimum of 48 hours. There are two distinct phases of the experiment. The “Test” phase of the experiment comprises home visits 1, 2 and 6.

Participants will be on their regular medication during Pre-Test A (i.e., “ON” medication) and will refrain from taking their medication (overnight withdrawal) ahead of Pre-Test B (i.e., “OFF" medication) and Post-Test (i.e., “OFF” medication). In all visits comprising the Test phase, participants will complete assessments of PD symptomatology and perform a force production task while their cortical activity is measured. The “Training” phase of the experiment comprises home visits 3, 4 and 5. These visits are respectfully labelled as “Neurofeedback Session 1”, “Neurofeedback Session 2” and “Neurofeedback Session 3” from herein. Participants will refrain from taking their medication (overnight withdrawal) ahead of all Neurofeedback Sessions. Each neurofeedback session comprises 12 × 5 min blocks of neurofeedback training, ensuring a total of 1 hour of neurofeedback training per each session.

Session 1 (Pre-test “on” medication). To establish baseline (pre-intervention) levels of cortical activity and motor performance, participants will complete a force production task comprising 40 trials. In each trial participants will hold a bespoke handgrip dynamometer and will be asked to produce and maintain as accurately as possible a force equivalent to 10% of their maximum strength for 5 seconds (c.f., Coombes et al., 2009; Wang, Lees & Brown, 1999). We will measure their speed and accuracy at producing the contractions, and we will record cortical activity via a wireless EEG system, with electrodes positioned at Fz, Cz, C3 and C4 sites. In addition, participants will complete Motor Aspects of Experiences of Daily Living (MEDL) questionnaire, which is Part II of the Movement Disorder Society Unified Parkinson’s Disease Rating Scale (MDS-UPDRS) (Goetz et al., 2008) and their self-reported quality of life using the Parkinson’s Disease

Quality of Life Questionnaire (PDQ-8) (Jenkinson et al. 1997). They will also undertake the Motor Examination that forms Part III of the MDS-UPDRS (Goetz et al., 2008) to provide an observer-rated index of symptomatology.

Session 2 (Pre-test "off" medication). This session will be identical to the pre-test described above but will take place following the overnight withdrawal of PD medication.

Sessions 3, 4 & 5 (Neurofeedback training "off" medication). Neurofeedback training will be implemented using our bespoke Bioexplorer software protocols and a wireless EEG system (PET 4, Brainquiry) for recording EEG at frontal-central regions overlying the motor cortex (plus ocular and muscular artifacts). Participants will receive auditory feedback programmed to be (a) proportional – the pitch of a continuous tone will vary with the level of frontal-central alpha power (b) binary – the tone will change from continuous to silent when a threshold decrease in alpha power value is exceeded, and (c) shaped – the threshold for the continuous-silent transition will become progressively more extreme. Participants will be seated and holding the handgrip dynamometer (same as used in pre-test) with their dominant hand. They will be instructed to try and lower the pitch of the tone from the loudspeaker; when it falls silent they will be cued to squeeze the handgrip dynamometer. Participants will undertake 12 × 5-min bouts of neurofeedback training per session (equating to one hour of exposure to the tone per testing session). The tone will be programmed to vary in pitch based on the level of high-alpha power and silence completely when high-alpha power is decreased by 30% (neurofeedback training session 1), 55% (neurofeedback training session 2) and 80% (neurofeedback training session 3), relative to each participant's individual baseline cortical activity.

These thresholds are based on previous research documenting similar decreases in EEG power during motor preparation (Magnani et al., 2002), and from pilot testing which established that they are achievable during brief interventions. As high-alpha power is inversely related with cortical activity, the progressively more extreme thresholds are designed to encourage increased activation at the C3/C4 sites above the primary motor areas, which is characteristic of relatively autonomous and efficient motor preparation (Defebvre et al. 1994). In addition to reducing high-alpha power by the aforementioned thresholds, the system will also require <10 μV of 50-Hz activity in the signal (i.e., low impedance) and the absence of eye-blinks, as detected by an electrode paced adjacent to the eye contralateral to the dominant hand (eye-blinks were detected as >75 μV of 1- to 7-Hz activity at the eye-electrode), for the tone to silence. These control features help to ensure the signal is being regulated by cognitive processes and not contaminated by electrical, muscular or eye-blink artefacts (Ring et al., 2015).

Session 6 (Post-test "off" medication). Session 6 will be identical to Session 2 described above (i. e., participants perform the grip force task without the neurofeedback tone), thereby allowing us to establish the effectiveness of the neurofeedback intervention.

All of the training sessions described below will take place in the participant's own home early in the day to reduce the length of time of being off medication. The research team have experience of such off-medication studies at home and have found it to be acceptable to participants.

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Previous intervention:
The study will employ a fully within-subject design with Session (1, 2, 3, 4, 5, 6) as the repeated-measures factor. This design will allow us to assess: the effects of PD medication on motor function (comparison of session 1 and session 2); the effects of neurofeedback training on motor function (comparison of session 2 and session 6); and a comparison of the relative effects

of medication versus neurofeedback training (comparison of effect sizes generated above). The sessions, which will take place on separate days, are described below:

Session 1 (Pre-test "on" medication). To establish baseline (pre-intervention) levels of motor performance, participants will complete a force production task comprising 40 trials. In each trial participants will hold a bespoke handgrip dynamometer and will be asked to produce and maintain as accurately as possible a force equivalent to 10% of their maximum strength for 5 seconds (c.f., Coombes et al., 2009; Wang, Lees & Brown, 1999). A selection of additional tests of motor function commonly adopted in the PD literature will also be assessed including movement latency and velocity (Montgomery et al, 1991), maximum grip force (Benice et al, 2007) and the motor subscale of the MDS-UPDRS (Goetz et al, 2008). Participants will be "on" their prescribed PD medication during the first pre-test session. A self-report measure of symptoms will also be obtained and will ask participants how often they have experienced given symptoms over the previous week. In total there are 37 symptoms which will be asked about. This questionnaire is modified from Hobson et al (1999) quality of life questionnaire in PD.

Session 2 (Pre-test "off" medication). This session will be identical to the pre-test described above but will take place following the overnight withdrawal of PD medication. The pre and post-test sessions (i.e., sessions 1, 2 & 6) will take place in the research laboratories of Bangor University or in patient homes as to the preference of the patient. The subsequent training sessions and the post-test session described below will also take place following overnight withdrawal from medication. All of the training sessions described below will take place in the participant's own home early in the day to reduce the length of time of being off medication. The research team have experience of such off medication studies at home and have found it to be acceptable to participants.
As a 'within subject' comparison study, internal consistency will be ensured with each respective participant tested, consistently, within the same environment, as is their preference (e.g. home or laboratory). This will allow us to observe within subject comparisons and crucially, individual changes pre and post intervention.

Sessions 3, 4 & 5 (Neurofeedback training "off" medication). Neurofeedback training will be implemented using our bespoke Bioexplorer software protocols and a wireless EEG system (PET 4, Brainquiry) for recording EEG at frontal-central regions overlying the motor cortex (plus ocular and muscular artifacts). Participants will receive auditory feedback programmed to be (a) proportional – the pitch of a continuous tone will vary with the level of frontal-central alpha power (b) binary – the tone will change from continuous to silent when a threshold decrease in alpha power value is exceeded, and (c) shaped – the threshold for the continuous-silent transition will become progressively more extreme. Participants will be seated and holding the handgrip dynamometer (same as used in pre-test) with their dominant hand. They will be instructed to try and lower the pitch of the tone from the loudspeaker; when it falls silent they will be cued to squeeze the handgrip dynamometer at a force equivalent to 10% of their maximum for 5 seconds. Participants will undertake 12 × 5 minute bouts of neurofeedback training per session (equating to one hour of exposure to the tone per testing session). The threshold level for the change from continuous to silent will be adjusted every testing session, starting with a sustained 1 second reduction in pre-movement alpha power, and ending with a sustained 3 second reduction in pre-movement alpha power (note: these durations may be modified based on pilot testing). This shaping of feedback increases the likelihood that participants emit the desired pattern of alpha power de-synchronisation.

Session 6 (Post-test "off" medication). Session 6 will be identical to Session 2 described above (i. e., participants perform the grip force task without the neurofeedback tone), thereby allowing us to establish the effectiveness of the neurofeedback intervention.

Intervention Type
Other

Primary outcome(s)
Current primary outcome measure as of 04/08/2023:
Cortical activity is measured using an EEG at each session (session 1 pre-test “on” medication; session 2 pre-test “off” medication; sessions 3, 4 and 5 neurofeedback training “off” medication, and session 6 post-test “off” medication). The EEG will involve 4 active electrodes (Brainquiry) mounted in a nylon cap and placed at C3, Cz, C4 and Fz sites in accordance with the international 10-20 electrode system.

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Previous primary outcome measures:
1. Cortical activity is measured using an EEG at each session (session 1 pre-test “on” medication; session 2 pre-test “off” medication; sessions 3, 4 and 5 neurofeedback training “off” medication, and session 6 post-test “off” medication). The EEG will involve 4 active electrodes (Brainquiry) mounted in a nylon cap and placed at C3, Cz, C4 and Fz sites in accordance with the international 10-20 electrode system
2. Grip force accuracy during each squeeze will be measured continuously using strain gauges mounted in a handgrip dynamometer, interfaced with a data acquisition system (Power 1401) and laptop running Spike2 software at sessions 1, 2 and 6
3. Motor ability will be measured using the newer MDS-UPDRS Parkinson’s motor score and motor quality of life section at sessions 1, 2 and 6
4. Movement onset delay and velocity will be measured using pre- and post-intervention using a simple reaching task at sessions 1, 2 and 6

Key secondary outcome(s))
Current secondary outcome measures as of 04/08/2023:
1. Grip force accuracy and the time taken to initiate movement will be recorded during each squeeze will be measured continuously using strain gauges mounted in a handgrip dynamometer, interfaced with a data acquisition system
2. Observed-rated symptomology. This will be assessed during the test phase via scores on the MDS-UPDRS (Goetz et al., 2008) Part III Motor Examination.
3. Self-reported symptomology. This will be assessed during the test phase via scores on the MDS-UPDRS (Goetz et al., 2008) Part II Motor Aspects of Experiences of Daily Living (MEDL) questionnaire, on the Parkinson’s Disease Quality of Life Questionnaire (PDQ-8) (Jenkinson et al. 1997).
4. Participant acceptability will be measured via a short interview about the participants’ subjective experience of home-based neurofeedback training

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Previous secondary outcome measure:
Participant acceptability will be measured using a simple short questionnaire asking about the participants’ subjective experience of the procedure at session 6.

Completion date
30/08/2018

Eligibility

Key inclusion criteria
1. Idiopathic PD diagnosed using the UK Brain Bank Diagnostic Criteria
2. Hoehn and Yahr stage 1-3 (Hoehn and Yahr, 1967; Bhidayasiri and Tarsy, 2012)
3. On stable treatment for the last one month and no planned changes over the period of the study
4. Ability to give informed consent
5. Aged 18 years and over

Participant type(s)
Patient

Healthy volunteers allowed
No

Age group
Adult

Lower age limit
18 years

Sex
All

Total final enrolment
16

Key exclusion criteria
1. Clinical diagnosis of dementia
2. Active psychosis, clinically significant depression or behavioural disturbance
3. Presence of another neurological condition
4. Active adjustment of medication during the predicted study period
5. Inability to give informed consent

Date of first enrolment
16/02/2018

Date of final enrolment
30/07/2018

Locations

Countries of recruitment
United Kingdom

Wales

Study participating centre
BCUHB Movement Disorders Clinic
Llandudno General Hospital

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Sponsor information

Organisation
Betsi Cadwaladr University Health Board

ROR
https://ror.org/03awsb125

Funder(s)

Funder type
Hospital/treatment centre

Funder Name
Betsi Cadwaladr University Health Board

Results and Publications

Individual participant data (IPD) sharing plan
The datasets generated during the current study will be available upon reasonable request from Dr Andy Cooke (a.m.cooke@bangor.ac.uk).

IPD sharing plan summary
Available on request

Study outputs

Output type	Details	Date created	Date added	Peer reviewed?	Patient-facing?
Abstract results	Presented at the International Association of Gerontology and Geriatrics - European Region Congress (https://iagger2019.se/program/scientific-program/ presentation PO.S:141)	23/05/2019	01/09/2023	No	No
Basic results			29/06/2020	No	No
HRA research summary			28/06/2023	No	No