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Investigating a wrist-worn device to treat tremor with electrical stimulation

Submission date
31/03/2022

Recruitment status
No longer recruiting

Registration date
14/04/2023

Overall study status
Completed

Last Edited
25/03/2024

Condition category
Nervous System Diseases

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

Plain English summary of protocol

Background and study aims
The growing global ageing population projects very significant patient growth in all conditions causing tremor. Treatments are limited and symptomatic. They do not offer long-term benefits, and their effectiveness diminishes with time. The current approach to managing tremor is through lifestyle modifications followed by drug treatment (e.g. propranolol and primidone), botulinum toxin injections (BTI) or surgery consisting of stereotactic thalamotomy or deep brain stimulation (DBS). While established, all have serious drawbacks. Drugs induce side effects and lose effectiveness. BTIs are available in specialist centres with varied results. DBS is expensive, incurs risks and side effects, and requires long-term, regular follow-up. The source of tremor is abnormal muscle activation. Electrical stimulation (ES) is therefore a logical basis for treatment; it is non-invasive, easily applicable, and requires minimal hardware. In ES, electrodes are placed above muscles to be activated and pulses are delivered, causing contractions. A range of patient testing has shown promise, but clinical translation remains negligible. This study tests a simple wearable device (band) that senses and counteracts tremor by delivering low-level imperceptible electrical stimulation (ES) to nerves in the forearm or wrist. The system has the potential to replace and/or augment current treatment options and increase quality of life for a very large patient population. The aim of this study is to determine whether this device for delivering electrical stimulation can reduce tremor severity in people with Parkinson's related tremor or essential tremor. Factors that exacerbate tremors include psychological drivers, thought at least in part to explain a significant placebo effect in tremor trials. To examine these effects, in addition to the primary outcome of tremor suppression, the trial is planned to be sham-controlled to allow direct comparison between the active and sham arms. Participants' standard of care would not be impacted by taking part in this trial.

Who can participate?
Patients aged 18 years and over who have been diagnosed with a tremor syndrome which affects their quality of life, either essential tremor or tremor related to Parkinson's disease.

What does the study involve?
This study will test the device to see if the tremor can be suppressed for a longer period. The researchers do not yet know if the device which is tuned to deliver stimulation in time with tremor (active stimulation) is better than just delivering bursts of stimulation at any time (sham

stimulation). To find out, they will compare the two methods. They will put people into two groups (the active stimulation group and the sham stimulation group) and give each group a different treatment. The results will be compared to see if one is better. To try to make sure the groups are the same to start with, each patient is put into a group by chance (randomly). Which treatment given to each individual will be decided by chance (like tossing a coin) and each individual will have a 50:50 chance of being on each treatment. This is a 'blind trial' so the participants will not know which treatment group they are in until after the trial has finished. Participants will undergo 10 stimulation sessions, each at least a day apart, measuring their tremor severity immediately before and after the intervention. After the 10-day trial intervention, two follow-up appointments will assess tremor severity on days 16 and 38 from the start of the intervention to look for longer-term effects.

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 health or safety. The electrical stimulation, either delivered with varying parameters, the active stimulation or the sham stimulation, has been shown to be imperceptible or mildly uncomfortable. There is only a small risk of this occurring and the researchers do not expect any serious complications. The research team in this study includes experienced clinicians and they will monitor individuals carefully, so they can stop any procedures if they experience any unpleasant side effects. Participants may experience a temporary improvement of tremor during the trial. Participants may feel the benefit of contributing to research into a novel treatment. The information from the study will further our understanding of the electrical treatment of tremor and contribute to the development of the treatment device.

Where is the study run from?
St George's University of London (UK)

When is the study starting and how long is it expected to run for?
March 2021 to December 2024

Who is funding the study?
National Institute for Health Research (NIHR) (UK)

Who is the main contact?
Dr Fahd Baig
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Contact information

Type(s)
Scientific

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Additional identifiers

EudraCT/CTIS number
Nil known

IRAS number
296113

ClinicalTrials.gov number
Nil known

Secondary identifying numbers
2022.0085, IRAS 296113, CPMS 54026

Study information

Scientific Title
Closed-Loop Electronic stimulation - Mechanomyogram sensor system for Passive tremor Suppression treatment (CLEMPTS)

Acronym
CLEMPTS

Study objectives
The Closed-Loop Electronic Stimulation (ES) - Mechanomyogram Sensor (MMG) System can acutely reduce tremor severity in patients with Parkinson’s disease (PD) and essential tremor (ET).

Ethics approval required
Old ethics approval format

Ethics approval(s)
Approved 17/11/2022, London - Stanmore Research Ethics Committee (Health Research Authority, Skipton House, 80 London Road, London, SE1 6LH, UK; +44 (0)207 104 8387, +44 (0) 207 104 8263; stanmore.rec@hra.nhs.uk), REC ref: 22/LO/0689

Study design
Randomized sham-controlled single-blinded parallel-arm study

Primary study design
Interventional

Secondary study design
Randomised parallel trial

Study setting(s)
Hospital

Study type(s)
Treatment

Participant information sheet
Not available in web format, please use the contact details to request a participant information sheet

Health condition(s) or problem(s) studied
Parkinson's disease-related tremor and essential tremor

Interventions
The trial is designed to determine whether the investigational device reduces tremor severity compared with sham electrical stimulation (ES) as measured by an accelerometer. The intervention has been shown in preliminary studies to reduce tremor for in the acute phase, the effects potentially lasting for up to 24 hours. The primary outcome is to assess the acute reduction in tremor. Further exploratory secondary endpoints include assessing for sustained effects and the neurophysiological effects of repeated stimulation.

The researchers will recruit 20 participants: 10 with essential tremor and 10 with Parkinson’s disease-related tremor.

Following device development, a trial will take place with 20 patients. Participants will be randomised to the active or sham ES sessions using simple block randomisation. Patients will undergo 10 ES sessions, each at least a day apart, measuring the tremor severity immediately before and after the intervention. After the 10-day trial intervention, two follow-up appointments will assess tremor severity at days 16 and 38 from the start of the intervention to look for longer-term effects.

Intervention Type
Device

Phase
Phase II

Drug/device/biological/vaccine name(s)
Not provided at time of registration

Primary outcome measure
Tremor severity measured by an accelerometer immediately before and after each of the 10 active or sham ES sessions

Secondary outcome measures
1. Patient-reported acute tremor suppression (measured using the Patient Global Impression of Change scale) and clinician-rated reduction in upper limb tremor (measured using relevant sub-scores of FahnTolosaMarin Clinical Rating Scale for Tremor (FTM) and clinician global impression of change scale) measured immediately before and after each of the 10 ES sessions
2. Induced neuroplasticity assessed using functional MRI or transcranial magnetic stimulation at

baseline and at the end of the study
3. Side effects of stimulation and any adverse reactions recorded at any time during the study
4. Tremor measured with a wrist-worn wearable ambulatory monitor for 24 hours comparing before and after stimulation, measured before starting the intervention and at selected visits

Overall study start date
01/03/2021

Completion date
31/12/2024

Eligibility

Key inclusion criteria
1. Adults aged over 18 years
2. Diagnosed with essential tremor or Parkinson's related tremor by a neurologist with expertise in movement disorders
3. Functional disability due to tremor reported by patient or clinician
4. Willing and able to give informed consent

Participant type(s)
Patient

Age group
Adult

Lower age limit
18 Years

Sex
Both

Target number of participants
20

Key exclusion criteria
1. Cognitive impairment (judged by the clinician on the care team or in the research team as a participant not having sufficient mental capacity to understand the study and its requirements). This includes anyone who, in the opinion of clinicians on the care team or clinicians in the research team, is unlikely to retain sufficient mental capacity for the duration of their involvement in the study.
2. Subject has a severe medical or psychiatric illness that would interfere with completing initial and follow-up assessments
3. Participation in concurrent research which involves a novel therapeutic IMP or device
4. Although the device is not expected to interfere with pregnancy, women who are pregnant would not be eligible to take part
5. Active treatment with an implantable stimulation device (such as a cardiac pacemaker or deep brain stimulation implantable programmable generator)
6. Allergies to neoprene, mylar, electrode hydrogel or medical tape

Date of first enrolment
20/04/2023

Date of final enrolment
31/12/2023

Locations

Countries of recruitment
England

United Kingdom

Study participating centre
St George Healthcare NHS Trust
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Sponsor information

Organisation
St George’s University Hospitals NHS Foundation Trust

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Sponsor type
Hospital/treatment centre

Website
https://www.stgeorges.nhs.uk/

ROR

https://ror.org/039zedc16

Funder(s)

Funder type
Government

Funder Name
National Institute for Health Research

Alternative Name(s)
National Institute for Health Research, NIHR Research, NIHRresearch, NIHR - National Institute for Health Research, NIHR (The National Institute for Health and Care Research), NIHR

Funding Body Type
Government organisation

Funding Body Subtype
National government

Location
United Kingdom

Results and Publications

Publication and dissemination plan
After the main publication or after 180 days from the trial end date any investigator or group of investigators may prepare further publications. In order to ensure that the sponsor will be able to make comments and suggestions where pertinent, material for public dissemination will be submitted to the sponsor for review at least 60 days prior to submission for publication, public dissemination, or review by a publication committee. The sponsor's reasonable comments shall be reflected. All publications related to the trial shall credit the chief and co-investigators as co-authors where this would be in accordance with normal academic practice and shall acknowledge the sponsor and the funders.

Intention to publish date
01/05/2025

Individual participant data (IPD) sharing plan
The data-sharing plans for the current study are unknown and will be made available at a later date

IPD sharing plan summary
Data sharing statement to be made available at a later date

Study outputs

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