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The effects of transcranial cerebellar electrical stimulation on symptoms in Friedreich ataxia

Submission date
10/01/2023

Recruitment status
No longer recruiting

Registration date
16/01/2023

Overall study status
Completed

Last Edited
30/05/2023

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
The cerebellum modulates a wide range of motor and cognitive behaviours thanks to reciprocal connections between the cerebellum and the brain cortex. The main cerebellar output structure is the dentate nucleus (DN) that targets the brain cortex through the dentato-thalamo-cortical tract (DTC). Friedreich ataxia (FRDA) is the most common autosomal recessive ataxia and is hallmarked by DN progressive atrophy and associated DTC impairment. Patients display progressive cerebellar ataxia and a wide spectrum of cognitive impairments whose severity progresses in parallel to motor symptoms severity, suggesting a common core pathophysiology. Cerebellar transcranial direct current stimulation (ctDCS) is a non-invasive technique that may improve DTC functioning. ctDCS has shown efficacy in improving motor and cognitive performances in degenerative ataxia of mixed origins but its mechanisms are poorly characterized. This study aims to understand the relationship between the DTC, brain functional architecture and clinical phenotype in FRDA and assess the potential efficacy of ctDCS to alleviate FRDA symptoms.

Who can participate?
Patients with FRDA

What does the study involve?
Patients in the study will have anodal ctDCS or sham stimulation applied for 20 minutes a day for five consecutive days. At the beginning and end of the stimulation period, subjects will undergo clinical and brain functional imaging assessment with functional magnetic resonance imaging (fMRI).

What are the possible benefits and risks of participating?
Benefits to participating will be the potential clinical improvement in ataxic motor symptoms, finger tapping accuracy, cognitive performances as well as modulation of brain resting state functional connectivity. In the current state of knowledge, we believe that, if the subject has no contraindications to MRI, examinations performed by MRI do not involve any risk or danger for participants. Similarly, transcranial stimulation of the cerebellum is a process that has already been studied and the protocol for performing the stimulation is now well known. Rarely reported side effects do occur during stimulation and consist of a metallic taste and an itching or

tingling sensation under the electrodes. To remedy these effects there are sugary drinks and menthol pastilles available. For tingling, cool compresses are available.

Where is the study run from?
HUB-Erasme Hospital, Free University of Brussels (HUB-Hôpital Erasme, Université Libre de Bruxelles) (Belgium)

When is the study starting and how long is it expected to run for?
June 2021 to November 2022

Who is funding the study?
1. Friedreich's Ataxia Research Alliance (USA)
2. Belgian National Fund for Scientific Research (Belgium)
3. Erasmus Fund for Medical Research (Belgium)

Who is the main contact?
Prof Gilles Naeije, gilles.naeije@erasme.ulb.ac.be (Belgium)

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Additional identifiers

Protocol serial number
P2021/347

Study information

Scientific Title
Dentato-thalamo-cortical tracts in Friedreich ataxia: impact of its modulation on Friedreich ataxia symptoms and brain functional architecture

Acronym
FRDA_ctDCS

Study objectives
Anodal cerebellar transcranial direct current stimulation (ctDCS) will improve motor and cognitive symptoms in Friedreich ataxia by restoring cerebellar cortical inhibition

Ethics approval required
Old ethics approval format

Ethics approval(s)
Approved 23/08/2021, Ethics Committee Hôpital Erasme (Ethics Committee Erasme HUB-Hôpital Erasme, 808, route de Lennik, 1070 Anderlecht, Belgium; +32 (0)2 555 37 07; comite.ethique@erasme.ulb.ac.be), ref: B4062021000183

Study design
Prospective interventional randomized sham-controlled trial

Primary study design
Interventional

Study type(s)
Treatment

Health condition(s) or problem(s) studied

Friedreich ataxia

Interventions
The function Randperm (2) in the Matlab program will be used to allocate the subjects either to the intervention first and the sham intervention second or the other way around. Participating Friedreich's ataxia patients will be included in a randomized cross-over sham-controlled study where anodal cerebellar transcranial direct current stimulation (ctDCS)/sham stimulation will be applied for 20 minutes a day for five consecutive days. At the beginning and end of the stimulation period, subjects will undergo clinical and brain functional imaging assessment with functional magnetic resonance imaging (fMRI).

Intervention Type
Device

Phase
Not Applicable

Drug/device/biological/vaccine name(s)
ctDCS

Primary outcome(s)
1. Impairments in cerebellar ataxia measured using the Scale for the Assessment and Rating of Ataxia (SARA) before and after intervention
2. Assessment of cerebellar ataxia measured using the Composite Cerebellar Functional Severity Score (CCFS) before and after intervention
3. Cerebellar cognitive affective syndrome measured using the Cerebellar Cognitive Affective Score (CCAS) before and after intervention

Key secondary outcome(s))
Somatosensory cortices evoked response to a tactile oddball paradigm measured using functional magnetic resonance imaging (fMRI) before and after intervention

Completion date
01/11/2022

Eligibility

Key inclusion criteria
Clinically confirmed Friedreich ataxia

Participant type(s)
Patient

Healthy volunteers allowed
No

Age group
Mixed

Sex

All

Total final enrolment
24

Key exclusion criteria
Other comorbid neurological diseases

Date of first enrolment
01/09/2021

Date of final enrolment
01/06/2022

Locations

Countries of recruitment
Belgium

Study participating centre
HUB-Hôpital Erasme, Université Libre de Bruxelles
808, route de Lennik
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Sponsor information

Organisation
HUB-Hôpital Erasme, Université Libre de Bruxelles

Funder(s)

Funder type
Research organisation

Funder Name
Friedreich's Ataxia Research Alliance

Alternative Name(s)
FA Research Alliance, Friedreichs Ataxia Research Alliance Fara, FARA

Funding Body Type
Government organisation

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

Location
United States of America

Funder Name
Fonds De La Recherche Scientifique - FNRS

Alternative Name(s)
Fund for Scientific Research (F.R.S.–FNRS), F.R.S. - FNRS, Fund for Scientific Research - FNRS, Belgian National Fund for Scientific Research, FNRS

Funding Body Type
Government organisation

Funding Body Subtype
Local government

Location
Belgium

Funder Name
Fonds Erasme

Alternative Name(s)
Erasmus Fund, Erasmus Fund for Medical Research, The Erasmus Fund, Fonds Erasme pour la Recherche Médicale, Le Fonds Erasme

Funding Body Type
Government organisation

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

Location
Belgium

Results and Publications

Individual participant data (IPD) sharing plan

Datasets generated during and /or analysed during the current study will be available upon request from gilles.naeije@erasme.ulb.ac.be. The data shared upon request will be patients' characteristics, behavioural scores (SARA, CCAS, CCFS) and fMRI raw files, at group and subject levels.

IPD sharing plan summary

Available on request

Study outputs

Output type	Details	Date created	Date added	Peer reviewed?	Patient-facing?
Basic results			30/05/2023	No	No
Participant information sheet	English		16/01/2023	No	Yes
Participant information sheet	French, parent and patients aged 14-17 version 2.0	17/08/2021	16/01/2023	No	Yes
Participant information sheet	French, patients version 2.0	17/08/2021	16/01/2023	No	Yes
Participant information sheet	French, patients aged 14-17 version 1.0	17/02/2015	16/01/2023	No	Yes