

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

Submission date 10/01/2023	Recruitment status No longer recruiting	<input type="checkbox"/> Prospectively registered <input type="checkbox"/> Protocol
Registration date 16/01/2023	Overall study status Completed	<input type="checkbox"/> Statistical analysis plan <input checked="" type="checkbox"/> Results
Last Edited 30/05/2023	Condition category Nervous System Diseases	<input type="checkbox"/> 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)

Contact information

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Additional identifiers

EudraCT/CTIS number

Nil known

IRAS number**ClinicalTrials.gov number**

Nil known

Secondary identifying numbers

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

Secondary study design

Randomised cross over trial

Study setting(s)

Hospital

Study type(s)

Treatment

Participant information sheet

See study outputs table

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 measure

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

Secondary outcome measures

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

Overall study start date

01/06/2021

Completion date

01/11/2022

Eligibility

Key inclusion criteria

Clinically confirmed Friedreich ataxia

Participant type(s)

Patient

Age group

Mixed

Sex

Both

Target number of participants

25

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

Anderlecht

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Sponsor information

Organisation

HUB-Hôpital Erasme, Université Libre de Bruxelles

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Sponsor type

Hospital/treatment centre

Website

<http://www.ulb.ac.be/>

Funder(s)**Funder type**

Research organisation

Funder Name

Friedreich's Ataxia Research Alliance

Alternative Name(s)

FA Research Alliance, 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)

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, Fonds Erasme pour la Recherche Médicale

Funding Body Type

Government organisation

Funding Body Subtype

Trusts, charities, foundations (both public and private)

Location

Belgium

Results and Publications

Publication and dissemination plan

Planned publication in a high-impact peer-reviewed journal

Intention to publish date

01/02/2023

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?
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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
Basic results			30/05/2023	No	No