The cerebral mechanisms underlying dystonic and essential tremor: a multimodal network approach

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Ethical review	Approved WMO
Status	Recruitment stopped
Health condition type	Movement disorders (incl parkinsonism)
Study type	Interventional

Summary

ID

NL-OMON45276

Source
ToetsingOnline

Brief title
Cerebral mechanisms in dystonic and essential tremor

Condition

- Movement disorders (incl parkinsonism)

Synonym
dystonia

Research involving
Human

Sponsors and support

Primary sponsor: Radboud Universitair Medisch Centrum
Source(s) of monetary or material Support: Hersenstichting

Intervention

Keyword: Dystonia, Essential tremor, Neuroscience, Tremor

Outcome measures

Primary outcome

We will use concurrent EMG-fMRI to localize and compare tremor-related activity between both groups (outcome #1) - an approach we have previously validated in Parkinson*s tremor.

Secondary outcome

Given the hypothesized role of inhibitory GABA-ergic circuits in both tremor types, we will use 3T magnetic resonance spectroscopy to compare GABA concentrations in the internal globus pallidus, cerebellum, and motor cortex between both groups (outcome #2). Also, we use a non-invasive, adaptive and controlled brain stimulation approach (transcranial alternating current stimulation; TACS) to test for the effect of inhibiting the motor cortex and cerebellum on tremor intensity (accelerometry) and, for the cerebellum, on tremor-related activity (EMG-fMRI) and (outcome #3). Previous research has shown powerful modulatory influences of TACS on both Parkinson*s tremor and ET.

Study description

Background summary

Tremor is often the presenting and most bothersome symptom of dystonia, occurring in 17-55% of patients. In patients with dystonia, tremor may involve the dystonic limb but also other body parts. Here we will define *dystonic tremor* (DT) as an umbrella term for both tremor types. There is a high risk of misdiagnosing DT, due to substantial clinical overlap with essential tremor (ET), and because disease markers are lacking. Also, there are no treatments

specifically targeting DT, so most clinicians follow a trial-and-error approach - often with unsatisfactory results. Lack of knowledge on the pathophysiology of DT hampers the development of new, mechanism-based interventions. Here we build on recent circumstantial evidence suggesting different circuit-level alterations in DT and ET. Namely, while both the basal ganglia and the cerebello-thalamic circuit may be involved in DT, the cerebellum - but not the basal ganglia - is thought to play a primary role in ET.

Study objective

We aim to identify the circuit-level cerebral mechanisms underlying DT, and separate them from those involved in ET. Furthermore, we test whether a non-invasive intervention in this circuit (applied to the motor cortex or cerebellum) can differentially impact on both tremor types. We hypothesize that DT results from an abnormal interplay between basal ganglia and the cerebello-thalamo-cortical circuit, while ET is primarily driven by abnormal cerebellar activity.

Study design

combined cross-sectional and exploratory intervention study

Intervention

The intervention involves transcranial alternating current stimulation (TACS), which is a non-invasive, non-painful way of stimulating underlying cortical brain tissue through electrodes applied to the scalp. When applied rhythmically at the frequency of cortical oscillatory activity, it can exert powerful excitatory or inhibitory (depending on the phase) effects on brain function.

Study burden and risks

The load on patients consists of the time spent on this project (2 visits), and potentially a temporary worsening of dystonic symptoms caused by withholding medication on the morning before assessments. All measurements are non-invasive, painless, and without nuclear radiation. Individual participants do not directly benefit from participation. However, we expect that this study will improve our knowledge about the cerebral mechanisms underlying DT and ET and may lead to new ways of diagnosing and perhaps treating these disorders.

Contacts

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Trial sites

Listed location countries

Netherlands

Eligibility criteria

Age
Adults (18-64 years)
Elderly (65 years and older)

Inclusion criteria

For essential tremor patients:
-Clinical diagnosis of essential tremor
-Postural tremor of both hands
-Onset of tremor before the age of 65 (to exclude pathophysiological heterogeneity caused by age-related tremor [15]);For dystonic tremor patients:
-Clinical diagnosis of dystonic tremor
-Primary focal / segmental dystonia
-Presence of postural tremor of at least one arm (which may or may not be the dystonic limb)

Exclusion criteria

-Neurological co-morbidity
-Moderate to severe head tremor (to avoid artifacts caused by extensive head motion during scanning)
-Cognitive dysfunction (clinical diagnosis of mild cognitive impairment or dementia)
-MRI or TACS contraindications

Study design

Design

Study type: Interventional

Masking:	Open (masking not used)
Control:	Uncontrolled
Primary purpose:	Basic science

Recruitment

NL

Recruitment status:	Recruitment stopped
Start date (anticipated):	20-10-2017
Enrollment:	32
Type:	Actual

Ethics review

Approved WMO

Date:	06-04-2017
Application type:	First submission
Review commission:	CMO regio Arnhem-Nijmegen (Nijmegen)

Study registrations

Followed up by the following (possibly more current) registration

No registrations found.

Other (possibly less up-to-date) registrations in this register

No registrations found.

In other registers

Register	ID
CCMO	NL60335.091.17