GABA, excitability and plasticity in the human motor cortex, an explorative study

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Ethical review	Approved WMO
Status	Recruitment stopped
Health condition type	Other condition
Study type	Interventional

Summary

ID

NL-OMON37805

Source
ToetsingOnline

Brief title
GABA in the motor cortex

Condition

- Other condition

Synonym
not applicable

Health condition

niet van toepassing

Research involving
Human

Sponsors and support

Primary sponsor: Radboud Universiteit Nijmegen
Source(s) of monetary or material Support: Radboud Universiteit Nijmegen. TOPtalent beurs (DGCN)

Intervention

Keyword: excitability, GABA, plasticity, Transcranial Magnetic Stimulation (TMS)

Outcome measures

Primary outcome

MEP and SICI amplitudes are measured using EMG, resting-state connectivity

(RSC) is indexed by analyzing rs-fMRI and GABA concentration is determined

using MR spectroscopy. The modulation of these measurements by rTMS will inform

us on the mechanistic relationship between GABA, excitability and plasticity in

the primary motor cortex.

Secondary outcome

not applicable

Study description

Background summary

GABA is an important neurotransmitter playing a pivotal inhibitory role in the human central nervous system. It is hypothesized to have a critical function in shaping the excitability and plasticity of the cortical motor system. Recently, non-invasive techniques have come available to modulate and record the GABA concentration in the human primary motor cortex. In this study, we aim to employ these techniques to investigate the relationship between GABA concentration, excitability and plasticity in the human cortical motor system.

Study objective

We aim to investigate the relation between cortical excitability, GABA concentration and plasticity in the human motor cortex. We plan to modulate the

functional integrity the primary motor cortex by using well-known repetitive transcranial magnetic stimulation (rTMS) protocols, that differentially affect the cortical excitability. We will index the GABA concentration at site of stimulation using magnetic resonance spectroscopy (MRS), and its functional connectivity coupling with other cortical regions using resting-state functional magnetic resonance imaging (rs-fMRI). The first objective of this study is to investigate the relationship between local changes in GABA concentration, excitability, and connectivity. Second, we aim to track the changes in GABA concentration, excitability and connectivity over time. This will give insight into mechanisms supporting the recovery and plasticity of the motor system following a functional perturbation. Lastly, we aspire to validate GABA spectroscopy as an objective measurement to index TBS efficacy.

Study design

The study consists of one intake session and three experimental sessions in which the excitability of the primary motor cortex will be differentially modulated by one of three off-line rTMS protocols: continuous theta-burst stimulation (cTBS: decreasing excitability), intermittent TBS (iTBS: increasing excitability), and 5 Hz stimulation (120 seconds: ineffective). The experimental sessions will take place 1 week apart of each other. Both before and after rTMS application we will record motor evoked potentials (MEP) to index cortico-spinal excitability, and determine the short-interval cortical inhibition (SICI) to index cortico-cortical excitability. Additionally, in the MR scanner we will acquire rs-fMRI and measure GABA concentration. This will be done both before rTMS application, and afterwards at three subsequent time points (at ~16 minutes, ~42 minutes, and ~63 minutes after TMS).

Intervention

During the intake session, participants will be screened and informed on the study in general and the TMS application in particular. During the following three experimental sessions, each participant will receive (in counter-balanced order) cTBS, iTBS and 5 Hz stimulation all consisting of 600 pulses during separate sessions at 80% of the active motor threshold (AMT) over the primary motor cortex.

Study burden and risks

TMS is safe and not painful. In rare cases, participants might report a (light) headache (2-4%), which can be treated easily with paracetamol. Based on incidental epileptic seizures triggered by TMS in early 90*s, safety-guidelines were established, in order to set up the maximum duration of TMS stimulation (Wassermann 1998; Anderson et al. 2006) . Updating these TMS guidelines, resulted in guidelines including safety information about repetitive TMS (e.g. TBS) (Rossi et al. 2009; Oberman et al. 2011). The protocols, intensities and

site of stimulation we chose to employ in this study are particularly well-known to be safe and pose a minimal burden and risk to the subject. The protocols all fall well within these safety TMS guidelines. (See attached appendix for the (Wassermann 1998) and (Oberman et al. 2011) guidelines and for the TMS safety report (v1.0 Augustus 2011)). Furthermore, all participants will be pre-screened for relevant medical history, epilepsy, drug abuse, head trauma, neurological or psychiatric illness, pregnancy, heart disease, cardiac pacemakers, medication pumps, tricyclic antidepressants, neuroleptics and a family history of neurological illness, psychiatric illness or epilepsy.
Because the risk associated with participation can be considered negligible and the burden can be considered minimal, we do not expect adverse events during the project.

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

healthy, right-handed partcipants (males and females). Age 18-35 years.

Exclusion criteria

Contra-indications for TMS and fMRI: drug abuse, head trauma, neurological or psychiatric illness, pregnancy, heart disease, claustrophobia, cardiac pacemakers, metal objects in the body, medication pumps, tricyclic antidepressants, neuroleptics and a familiy history of neurological illness or epilepsy.

Study design

Design

Study type: Interventional

Masking:	Single blinded (masking used)
Control:	Uncontrolled
Primary purpose:	Other

Recruitment

NL

Recruitment status:	Recruitment stopped
Start date (anticipated):	13-02-2012
Enrollment:	24
Type:	Actual

Ethics review

Approved WMO

Date:	03-02-2012
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	NL38197.091.11