Cortical plasticity and Intracortical inhibition in major depressive disorder using transcranial magnetic stimulation

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Ethical review	Approved WMO
Status	Recruitment stopped
Health condition type	Mood disorders and disturbances NEC
Study type	Observational non invasive

Summary

ID

NL-OMON45552

Source
ToetsingOnline

Brief title
Plasticity and inhibition in MDD

Condition

- Mood disorders and disturbances NEC

Synonym
depression, Major depressive disorder

Research involving
Human

Sponsors and support

Primary sponsor: Erasmus MC, Universitair Medisch Centrum Rotterdam
Source(s) of monetary or material Support: Ministerie van OC&W

Intervention

Keyword: Inhibition, MDD, Plasticity, TMS

Outcome measures

Primary outcome

- Intracortical inhibition as measured with the SICI paradigm: the difference in MEP amplitude induced by paired pulse stimulations with a conditioning pulse of 80% RMT and unconditioned single TMS pulses at SI1mV.

- Intracortical inhibition as measured with the CSP: the duration of the CSP after a single supratheshold TMS pulse applied at a tonically preactivated FDI muscle, averaged over 20 pulses.

- Neuronal plasticity as measured with the iTBS: mean MEP amplitude at the FDI muscle before iTBS (pre-iTBS), and at 5 time points after the iTBS procedure (0 min; 5 min; 10 min; 15 min; 20 min). The iTBS effect is determined as the mean MEP amplitude of the time points after iTBS relative to baseline values.

Secondary outcome

- Difference in HAM-D score at baseline and after 6 weeks of treatment as usual within the MDD inpatients

Study description

Background summary

The neurophysiology of MDD is complex and largely unknown. The neurotransmitter systems serotonin, norepinephrine and dopamine are thought to play a role in

classic pathophysiologic models of MDD. However, previous clinical and preclinical studies showed evidence that the Gamma-AminoButyric Acid (GABA) neurotransmitter system also is involved in the pathophysiology of MDD. GABAergic interneurons induce intracortical inhibition, which affects synaptic strengthening during long-term potentiation. To further study the role of GABAergic intracortical inhibition and cortical plasticity in the cognitive and behavioral deficits in severely depressed inpatients, a non-invasive method to study these neurophysiological processes is needed. Transcranial Magnetic Stimulation (TMS) has proven to be a very useful tool in this respect. We will use TMS to study cortical inhibition with the Short Interval Cortical Inhibition (SICI) paradigm and measuring the Cortical Silent Period (CSP). Additionally, we will use intermittent Theta-Burst Stimulation (iTBS) as TMS paradigm to induce cortical plasticity by administering intermittent bursts of pulses for two seconds long with an interburst interval of 10 seconds, and subsequently study aftereffects during a period of 20 minutes.

Study objective

The primary objective is to determine whether there is a difference in intracortical inhibition and cortical plasticity between MDD patients and unaffected controls.

Study design

Observational case-control study

Study burden and risks

The total time investment for participants will be ±3 hours, which consists for the unaffected controls of a telephone call for eligibility screening (±30 min) and a single visit to the department of Psychiatry of the Erasmus MC for the TMS measurement. For inpatients with MDD, questionnaires regarding screening will be filled in on the ward. The TMS lab is within the department of Psychiatry and easily accessible for the patients. TMS stimulations can induce a transient headache, and local pain or neck pain, which may vary from subject to subject. This is depending on individual susceptibility, and intensity and frequency of stimulation. However, these effects are negligible in terms of safety concerns (Rossi et al., 2009). The measurement will be aborted in case a participant considers the measurement painful. Additionally, the TMS protocol could theoretically induce epileptic seizures due to the high frequent stimulations during iTBS. Epilepsy was never observed as a result of iTBS in previous studies, only as a result of repetitive TMS and continuous TBS (Hong et al., 2015; Oberman et al., 2011). Nevertheless, due to the high similarity with these two TMS protocols, iTBS should be applied with caution. We will, therefore, screen participants for epilepsy risk factors using a standardized questionnaire in order to minimize the risk of an iTBS-induced epileptic

seizure. Participants will be reimbursed with ¤50 and compensated for travel and parking expenses. There are no therapeutic benefits from this study.

Contacts

Public
Erasmus MC, Universitair Medisch Centrum Rotterdam

's Gravendijkwal 230
Rotterdam 3015 CE
NL
Scientific
Erasmus MC, Universitair Medisch Centrum Rotterdam

's Gravendijkwal 230
Rotterdam 3015 CE
NL

Trial sites

Listed location countries

Netherlands

Eligibility criteria

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

Inclusion criteria

Unaffected controls:
Age: 18-85 years
Informed consent
Good health
Beck Depression Inventory * 9;Inpatients with MDD:
Age: 18-85 years
Informed consent
MDD confirmed diagnosis

Initial HAM-D score * 18
Being free of psychotropic drugs for 1 week

Exclusion criteria

Pregnancy
Use of psycho-active agents
Neurological illness influencing the motor system
Not passing the Rossi safety check-list (Rossi et al., 2009)

Study design

Design

Study type:	Observational non invasive
Intervention model:	Other
Allocation:	Non-randomized controlled trial
Masking:	Open (masking not used)
Control:	Active
Primary purpose:	Basic science

Recruitment

NL

Recruitment status:	Recruitment stopped
Start date (anticipated):	17-02-2018
Enrollment:	34
Type:	Actual

Ethics review

Approved WMO

Date:	28-02-2017
Application type:	First submission
Review commission:	METC Erasmus MC, Universitair Medisch Centrum Rotterdam (Rotterdam)

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	NL60197.078.16