Adding rTMS to exposure therapy in PTSD in a placebo-controlled design : a pilot study

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Primary Objective: To investigate treatment (sham rTMS/rTMS) differences in PTSD symptom severity, as measured with a clinician and self-rated instrument. Secondary Objective: To investigate the effect of rTMS and sham rTMS on general anxiety,...

Ethical review	Approved WMO
Status	Will not start
Health condition type	Anxiety disorders and symptoms
Study type	Interventional

Summary

ID

NL-OMON47598

Source
ToetsingOnline

Brief title
rTMS in PTSD

Condition

- Anxiety disorders and symptoms

Synonym
anxiety disorder evoked by a severe traumatic event

Research involving
Human

Sponsors and support

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

Intervention

Keyword: post-traumatic stress disorders (PTSD), repetetive transcranial magnetic stimulation (rTMS)

Outcome measures

Primary outcome

The primary outcome measures are the change in PTSD symptoms as a function of rTMS/sham rTMS add on treatment. The CAPS-5 will be assessed at pre-treatment and post treatment. The CAPS-1 will provide data on both severity and frequency of PTSD-symptoms, and presence of PTSD diagnosis. The PCL-5 is a 17-item self-report questionnaire that measures the frequency of PTSD symptoms.

Secondary outcome

The secondary outcome measures are potential changes in depressive symptoms as measured by the BDI-II as well as changes in mood as measured by the PANAS before and after each part of the intervention (ie sham or real rTMS-treatment). Dysfunctional trauma-related cognitions are measured by the Dutch version of the Posttraumatic Cognitions Inventory (PTCI; Foa, Ehlers, Clark, Tolin, & Orsillo, 1999; Van Emmerik, Schoorl, Emmelkamp, & Kamphuis, 2006; 36 items), that has good to excellent psychometric properties. In addition, it was found to be sensitive to measure changes during treatment.

Study description

Background summary

Repetitive transcranial magnetic stimulation (rTMS) is widely used both in fundamental cognitive neuroscientific studies as well as clinical applied studies investigating its potential mood stabilizing role. Recently, potential

use of rTMS has proven to be potentially promising in the treatment of post-traumatic stress disorder (PTSD), one of the most common anxiety disorders. Although the pathophysiology of PTSD remains unclear, growing evidence from functional neuroimaging studies suggest that it is consistently associated with hypoactivation of the prefrontal cortex (including medial and dorsolateral regions) and hyperactivation of deeper brain structures, such as the amygdala (Etkin et al. 2007, Hazes et al., 2012, Patel et al. 2012). The DLPFC, in particular, is involved in many complex cognitive and behavioural functions that are relevant to PTSD. An exploratory meta-analysis (Berlim et al., 2014b) suggests that active rTMS applied to the dorsolateral prefrontal cortex (DLPFC) seems to be effective and acceptable for treating PTSD.

While these results are in principle promising the complexity of the PTSD makes it necessary to combine psychotherapeutic with potential new neuromodulatory treatment options in the form of an add-on treatment. Thus far, rTMS was mainly provided to PTSD-patients who did not (yet) receive guideline psychological treatments, such as Exposure Therapy. However, an additional intervention should ideally be provided only to those patients that show no improvements after those first step treatments.

Study objective

Primary Objective:
To investigate treatment (sham rTMS/rTMS) differences in PTSD symptom severity, as measured with a clinician and self-rated instrument.

Secondary Objective:
To investigate the effect of rTMS and sham rTMS on general anxiety, comorbid depressive symptoms and mood, and posttraumatic cognitions, as assessed by clinician and self-rated instruments

Study design

The study takes place at the Department of Psychiatry and is designed as a within-patients experiment. To exclude placebo effects on the one hand but also optimize the proportionality of the sham treatment, patients will be randomized to receive in the first 2 weeks 10 real or 10 sham HF-rTMS sessions (1 sessions/day for 5 consecutive days) and in the second 2 weeks of treatment of the other condition. In between these two type of sessions and after the final treatment there will be a break of a week at the end of which patients will be reassessed in terms of symptom reduction.

Intervention

RTMS and sham treatment will be done using Magstim Rapid 2. All rTMS parameters used in the proposed study are within the range considered safe according to

the latest published safety guidelines (Rossi et al., 2009, 2011; Obermann et al., 2011) and are based on a large multi-center study (O*Reardon et al., 2007) as well as meta-analyses (see for example Schutter et al., 2009). Firstly, the resting motor threshold (rMT) will be defined in each subject as the minimal stimulation intensity evoking an MEP of * 0.05 mV in 50% of the trials in the muscle of the right thumb (M. abductor pollicis brevis). Note that rMT will be determined before every treatment/sham session. TMS will be conducted in the form of *conventional rTMS*, whereby 20 trains of 10 Hz pulses with a duration of 5 seconds and an inter-train interval of 25 seconds are applied to the right DLPFC (50 pulses per train, 1000 pulses per session).
We aim to control for placebo effects merely evoked by the regular treatment and therefore include a so-called sham condition using a sham-coil,which applies a similar electrical sensation to the skull.

Study burden and risks

Possible benefit resulting from the treatment cannot be guaranteed to participants. Transcranial magnetic stimulation (TMS) is a widely used non-invasive brain stimulation technique, based on the principle of electromagnetic induction. During stimulation the participant will likely hear the clicks of the TMS pulses and experience stimulation of nerves and muscles of the head. The most common side effect is a light transient headache (2-4% occurrence). A severe headache is uncommon (0.3-0.5% occurrence). In the current study patients will be stimulated with a protocol that falls within the safety guidelines. All participants are screened for their relevant medical history and other TMS safety aspects (e.g. presence of metal parts in the head). The study will give insight whether rTMS can become an efficient add/on therapy in PTSD, which is highly relevant given the amount of patients who do not fully respond to the current treatment options. The cross-over design is setup in such way that it minimizes the burden of a placebo-control as much as possible and improves power using a within-subject design.

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

Based on cut-off scores and in line with previous studies, we will include 20 patients with a PTSD (minimum severity score of 50 on the the Clinician-Administered PTSD Scale, CAPS-1; Blake et al., 1995). All patients will receive intensive exposure therapy as part of their standard clinical treatment at the Centre of Anxiety Disorder in Overwaal. If patients reveal a suboptimal outcome and still have a minimum severity score of 50* as measured by clinician rated and self-rating lists- they will be offered to participate in the rTMS trial if they are eligible. Their standard treatment will be continued but monitored.

Exclusion criteria

With regard to transcranial brain stimulation
* Epilepsy, convulsion or seizure (TMS)
* Serious head trauma or brain surgery
* Large or ferromagnetic metal parts in the head (except for a dental wire)
* Implanted cardiac pacemaker or neurostimulator
* Pregnancy;With regard to general experimental requirements
* History or current presence of any neurologic or psychiatric disease other than PTSD and its affective comorbid disorders (including personality disorders)

Study design

Design

Study type: Interventional

Masking:	Double blinded (masking used)
Control:	Uncontrolled
Primary purpose:	Treatment

Recruitment

NL

Recruitment status:	Will not start
Enrollment:	0
Type:	Anticipated

Ethics review

Approved WMO Date:	27-07-2017
Application type:	First submission
Review commission:	CMO regio Arnhem-Nijmegen (Nijmegen)
Approved WMO Date:	16-04-2018
Application type:	Amendment
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	NL60375.091.16