Repetitive Transcranial Magnetic Stimulation (rTMS) in youth with obsessive compulsive disorder (OCD) and/or Gilles de la Tourette syndrome (GTS): A feasibility study

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Primary Objective: To explore the acceptability and feasibility of rTMS added to exposure with response prevention and/or medication as an intervention in youth with OCD and/or GTS. Secondary Objective(s): - To explore the effects of added rTMS on...

Ethical review	Approved WMO
Status	Pending
Health condition type	Psychiatric disorders NEC
Study type	Interventional

Summary

ID

NL-OMON57012

Source
ToetsingOnline

Brief title
rTMS for OCD and/or GTS in youth

Condition

- Psychiatric disorders NEC

Synonym
Gilles de la Tourette syndrome (GTS, Obsessive-compulsive disorder (OCD)

Research involving
Human

Sponsors and support

Primary sponsor: Amsterdam UMC
Source(s) of monetary or material Support: Levvel Amsterdam (overeenkomst toekenning t.b.v. onderzoek tussen Levvel en AMC Medicial Research B.V.),Stichting BWRCJ;een vermogenstichting met als doel middelen ter beschikking te stellen de hulpverlening aan jeugdigden.

Intervention

Keyword: adolescent, obsessive-compulsive disorder, tourette syndrome, transcranial magnetic stimulation

Outcome measures

Primary outcome

Feasibility of rTMS added to treatment-as-usual, conceptualized as the

practical and personal preferences and obstacles for performing the rTMS,

possible side effects and drop-out rates (qualitative interview & experiences

of researchers).

Secondary outcome

- Symptoms of OCD (obsessive-compulsive behavior score & CY-BOCS)

- Symptoms of GTS (tic behavior score & YGTSS)

Other study parameters

- Clinical impression of outcome (CGI)

- Session results (SRS/ORS)

- Symptoms of anxiety (SCARED)

- Symptoms of depression (CDI-2)

Study description

Background summary

Obsessive-compulsive disorder (OCD) is a serious psychiatric condition, characterized by uncontrolled and recurring thoughts (obsessions), repetitive behaviors (compulsions) or both. The lifetime prevalence of OCD is around 2-3%. In about 45% of patients with OCD the symptoms already begin before the age of 18, and in 65% of all patients before the age of 25. OCD causes a lot of stress and dysfunction in all forms of activities, and has negative impact on the psychosocial development of patients and their families.
Current evidence-based treatment options include psychotherapy (cognitive behavioral therapy; CBT) and antidepressant medication (such as selective serotonin reuptake inhibitors (SSRIs) and tricyclic antidepressants (TCAs)). In current guidelines it*s recommended to first start CBT, and, if lack of efficacy, add pharmacological treatment. Previous studies showed better efficacy of these forms of treatment than placebo. Still, there is a group of patients who doesn*t respond (enough) to CBT (whether or not in combination with medication). Furthermore, medication itself is not always tolerated due to side effects, or not wanted by the patient itself (and/or parents).

Gilles de la Tourette Syndrome (GTS) is a neurodevelopmental movement disorder characterized by repetitive movements and vocalizations called tics. The worldwide prevalence in children and adolescents is 0.77 - 1%. Also GTS is known to negatively affect quality of life, not only at home, but also in school and with friends and family. Treatment options for children with GTS are limited. Two forms of behavioral therapy, habit reversal training (HRT) and exposure and response prevention (ERP), are used. Different kinds of medication, for example aripiprazole, can also be used, but carry a side effect burden as well. Both forms of treatment have similarly results on the reduction of tics. In about one third of the patients the symptom reduction is less than 50% to even minimal.

Repetitive transcranial magnetic stimulation (rTMS) is a noninvasive neuromodulatory technique that uses fluctuating extracranial magnetic fields to generate cortical currents that focally stimulate the cerebral parenchyma by depolarizing the neural cell membrane, leading to changes in the brain circuits involved in psychiatric disorders. A coil is therefore placed on the patients head. The efficacy of rTMS depends on multiple aspects, such as the location of the target area (the dorsolateral prefrontal cortex is commonly used), and the frequency that is been used (low-frequency versus high frequency). The total number of needed sessions is not yet clear, with variating frequencies per week and different durations in total weeks. Daily treatment for several weeks although has shown its effect in several psychopathologies, such as depression. In previous studies the possible side effects have been investigated and seem to be minimal. Seizure is the most severe side effect of

rTMS, but had a very low incidence of occurring and seems to hardly only affect patients with predisposing factors (on which can be screened on forehand).

The number and range of neuropsychiatric disorders that are treated by rTMS is growing in the last years. In adults it has already been shown that rTMS is effective for symptom reduction of OCD symptoms. Some small studies have also suggested improvement of tic severity after use of rTMS in GTS. The research on children and adolescents is limited. We therefore would like to perform a feasibility study in youth aged 12 - 18 years with ODC and/or GTS, receiving rTMS as add-on therapy next to their treatment-as-usual (TAU).

Study objective

Primary Objective:
To explore the acceptability and feasibility of rTMS added to exposure with response prevention and/or medication as an intervention in youth with OCD and/or GTS.

Secondary Objective(s):
- To explore the effects of added rTMS on symptoms of OCD and GTS.
- To explore the safety (including side-effects and/or complications) of added rTMS.
- To prepare a larger trial into the effectiveness of rTMS on symptoms OCD and GTS, based on the results of this acceptability and feasibility study, and the willingness to participate and time to include all patients in this feasibility study.

Study design

This study will combine a qualitative study design and a randomized multiple baseline single-case experimental design (SCED). The qualitative data from interviews will be used to explore the acceptability and feasibility of rTMS.

Intervention

The patients will be treated with a low frequency 1 Hz rTMS protocol on the (pre)supplementary motor area (SMA). rTMS treatment will be given for 20 times, once a day, 5 days/week, for 4 weeks. We will use several questionnaires (C-YBOCS, YGTSS) every 5th rTMS session, and more questionnaires (SCARED, CDI-2, EQ-5D-Y) and qualitative interviews pre- and post treatment.

Study burden and risks

The total duration of this feasibility study is 12 weeks. After informed consent, a baseline phase of 2, 3 or 4 weeks will follow. After this, a total of 20 rTMS sessions will take place on working days for 4 weeks. After the last

rTMS session, there is a follow-up phase of 4 weeks. Participating patients are already in the clinical (day) clinic of Levvel Amsterdam. Each session includes 5 minutes of preparation, 25 minutes of stimulation, for a total of 40 minutes per session. During the entire research period (maximum 12 weeks), a daily (on weekdays) short assessment by the participant takes place, with a total of 120 minutes for 12 weeks. Psychometry is administered every fifth rTMS session, with a total of 30 minutes for all questionnaires. The first baseline session lasts (maximum) 1:30 hours, due to measurements and technical procedures, psychometry, ECG and vital functions. The last two measurement moments (T5 at the end of the 20th rTMS session, and T6 4 weeks after the last rTMS session) last (maximum) 1:15 hours and 1:30 hours, respectively.
Questionnaires are also discussed with parents at three times (at the start, at the end of rTMS and at the end of the entire study), lasting 0:45 - 1:00 hours. During the entire research period (maximum 12 weeks), parents are also asked to complete a daily short assessment via a digital application, lasting a total of 120 minutes.

The time burden for the participant is estimated at approximately 24 hours. The time burden for the parent is estimated at a maximum of 5 hours.

The risks associated with rTMS are very low, as in previous studies rTMS is shown as safe and non-invasive. Most common side-effects in adults are neckpain/discomfort (±40%), local discomfort of the scalp (±39%), tension headaches during and after stimulation (±28%) and dizziness. The discomfort and pain mainly occur during the first sessions, and become less as the number of treatments progresses. In earlier studies in children similar side-effects are seen. Headache (±11,5%) and local discomfort of the scalp (2,5 - 12%) most common, and less frequently fatigue and dizziness, which also disappear after stopping rTMS.
The most severe, but extremely rare, side-effect is a seizure. The prevalence is 0.08 of 1000 sessions and almost nihil when patients are medication free or do not have a co-morbid neuro-logical disorder.

Contacts

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Trial sites

Listed location countries

Netherlands

Eligibility criteria

Age
Adolescents (12-15 years)
Adolescents (16-17 years)

Inclusion criteria

1. Age 12 to 18 years old;
2. Diagnosed with Obsessive-Compulsive Disorder (OCD) and/or Gilles de la Tourette Syndrome (GTS); based on a semi-structured interview such as the Structural Clinical Interview for DSM 5 Childhood Disorders (SCID 5 Junior).
3. Nonresponse (defined as <30% response on symptoms measured by the Child-Yale Brown Obsessive Compulsive Scale (C-YBOCS) or the Yale Global Tic Severity Scale (YGTSS) after treatment (mostly CBT and/or medication);
4. In case of receiving pharmacological treatment have a stable dosage for at least 10 weeks before start of the trial, and no alternations in dosage during the study.

Exclusion criteria

1. Intracerebral metal implants (e.g. cochlear implant, brain stimulator);
2. (History of) epilepsy or epilepsy in a first degree relative;
3. Any other neurological disorder with seizure risk;
4. Acute suicidal ideations;
5. Bipolar disorder;
6. Current disorder in substance abuse;
7. Any known other serious somatic health problem;
8. Pregnancy.

rTMS contraindications

1. History of epileptic seizures or epilepsy in a first degree relative;
2. Cochlear implants;
3. Implanted neurostimulators;
4. Cardiac demand pacemakers;
5. Implanted defibrillator.

Study design

Design

Study type: Interventional

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

Recruitment

NL

Recruitment status:	Pending
Start date (anticipated):	01-05-2024
Enrollment:	8
Type:	Anticipated

Medical products/devices used

Generic name:	repetitive transcranial magnetic stimulation
Registration:	Yes - CE intended use

Ethics review

Approved WMO Date:	06-09-2024
Application type:	First submission
Review commission:	METC Amsterdam UMC
Approved WMO Date:	22-01-2025
Application type:	Amendment

Review commission: METC Amsterdam UMC

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	NL86507.018.24