Accelerated intermittent Theta Burst Stimulation (aiTBS) in bipolar disorder and schizophrenia

Published: 28-04-2023
Last updated: 28-04-2025

objective is to assess feasibility, tolerability and efficacy of aiTBS in patients with bipolar depression (BPD) and negative symptoms of schizophrenia (NSS).

Ethical review	Approved WMO
Status	Recruiting
Health condition type	Schizophrenia and other psychotic disorders
Study type	Interventional

Summary

ID

NL-OMON53634

Source
ToetsingOnline

Brief title
aiTBS in bipolar disorder and schizophrenia

Condition

- Schizophrenia and other psychotic disorders

Synonym
Bipolar disorder and schizophrenia

Research involving
Human

Sponsors and support

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

Intervention

Keyword: aiTBS, Bipolar disorder, Non invasive brain stimulation, Schizophrenia

Outcome measures

Primary outcome

Primary outcomes are response (defined by 50% reduction on the HDRS, QIDS-SR , PANSS, SANS and CDSS), remission (defined by HDRS <7, QIDS-SR <5, all items on the negative scale PANSS <3, SANS <3, CDSS<6) and feasibility and tolerability measured by side-effects and drop-out rates.

Secondary outcome

To assess Heart Rate Variability (HRV) as part of parasympatic activation through dlPFC stimulation. HRV is measured through electrocardiogram (ECG).

Study description

Background summary

Repetitive Transcranial Magnetic Stimulation (rTMS) is an emerging non-invasive technique of neuromodulation. rTMS is an approved, evidence-based and safe treatment modality for major depressive disorder (MDD). Recent studies have proposed new adaptations of TMS, one adaptation being accelerated intermittent theta-burst stimulation (aiTBS). A case series of 6 patients (4 MDD and 2 BPD) found high response and remission rates following the treatment of an accelerated form of iTBS (using the Stanford Neuromodulation Therapy (SNT) protocol). Response and remission rates were 83.5% and respectively 66.7%. The treatment was found to be safe and tolerable. A-proof-of concept study in 2020 conducted by the same research group found that aiTBS using the same protocol protocol in 21 patients (19 MDD and 2 BPD) was highly effective; response and remission rates were 90.5% following the SNT protocol. The study also showed feasibility and tolerability. Following this pilot study, a double blind RCT in 2021 found that 85.7% of patients with MDD in the active STN protocol met response criteria and 78.6% met remission criteria over a 4-week follow-up period. These response and remission rates are much higher than currently approved rTMS protocols for TRD (approximately 25-65%). The question arises whether aiTBS shows efficacy in other psychiatric disorders including bipolar

depression (BPD) and negative symptoms of schizophrenia (NSS).

Study objective

objective is to assess feasibility, tolerability and efficacy of aiTBS in patients with bipolar depression (BPD) and negative symptoms of schizophrenia (NSS).

Study design

Proof-of-concept study with an open-label design. 2 groups will be included, namely patients with BPD and patients with NSS. Both groups will be treated according the aiTBS-5d-8s-50i protocol in which patients are treated for 5 consecutive days with 8 daily aiTBS with a 50 minute intersession interval. Questionnaires (HDRS, QIDS-SR, PANSS, SANS and CDSS) will be measured daily and during follow-up (2 weeks, 4 weeks, 12 weeks) to assess response.

Intervention

aiTBS according to aiTBS-5d-8s-50i protocol (5 consecutive days, 8 daily session, 10 minutes of stimulation with 50 minute interval).

Study burden and risks

the burden and risks associated with participation are considered minimal. Associated risks with stimulation are low in the studies published regarding aiTBS. The side effects of aiTBS are similar to rTMS, an already safe and tolerable treatment modality. These side effects of aiTBS are mild, short term and transient and include fatigue, some discomfort at stimulation site, neck pain, headache and dizziness. Most of these side effects occur during or shortly after the first session and tend to rapidly decrease after the first session. The most severe adverse events is induction of an epileptic seizure. Regarding aiTBS, the limited studies available (3 studies, n=56) did not report serious adverse events. In iTBS, only 1 case reported on a seizure following iTBS. In case of a seizure, the prevalence in rTMS is found to be 1 of 60000 sessions and almost nihil if a patient is free of medication or free of co-morbid neurological disorders. In iTBS, only 1 case report reported on a seizure following iTBS. To reduce risk of a seizure, participants with a higher risk (a history of epilepsy or first degree relative with epilepsy) are excluded from the study. Since aiTBS is similar to rTMS and iTBS, the same adverse events are to be expected. Therefore, the risk administering aiTBS is expected to be minimal.
A review on rTMS (Xia et al., 2008) reported the prevalence of an affective switch to hypomania/mania to be 0.84% in the active rTMS compared to 0.73% in the sham group (non-significant difference). Several case reports have described an affective switch in major depressive disorder following rTMS,

however according to recent evidence-based guidelines, there is currently no evidence to suggest rTMS is associated with an increased risk of an affective switch to hypomania or mania. A meta-analysis in 2016 (Gold et al.,) suggests that rTMS is safe in case of BPD with a very low risk of induction of an affective switch (1/106 in active group and 1/75 in sham group). 3 relevant randomized controlled trials of iTBS in patients with negative symptoms of schizophrenia, did not find a worsening in positive symptoms after iTBS.

Contacts

Public
Academisch Medisch Centrum

Meibergdreef 9
Amsterdam 1105AZ
NL
Scientific
Academisch Medisch Centrum

Meibergdreef 9
Amsterdam 1105AZ
NL

Trial sites

Listed location countries

Netherlands

Eligibility criteria

Age
Adults (18-64 years)

Inclusion criteria

- 18-65 years
- Ability to freely written informed consent
- DSM-5 diagnosis of current depressive episode in bipolar I or II disorder OR DSM-5 diagnosis of schizophrenia

- Therapy resistanve in bipolar disorder
- HDRS>16 in bipolar depression at start study
- SANS>3 on each item in schziphrenia
- Stable medication (antidepressants or antipsychotics) at least 4 weeks prior start study.

Exclusion criteria

* In BPD, (hypo) manic episode within 3 months prior start of the trial;
* In BPD, Young Mania Rating Scale (YMRS) score of >12 prior start of the trial;
* Patients with bipolar II disorder who use anti-depressant medication without anti-manic medication or patients with bipolar I disorder, not using anti-manic medication;
* Acute suicidality;
* (History of) neurological disease
* (History of) epilepsy or epilepsy in a 1st degree relative;
* Pregnancy;
* Disorder in substance abuse
* Known serious somatic health problem;
* Used recreational drugs over a period of 72 hours prior each session;
* Used alcohol within the last 24 hours prior each session;
* Specific TMS contraindications (see standard screening form, appendix 1): ICD, pacemaker, history of epileptic seizures of epilepsy in a 1st degree relative, intracranial metal implants(e.g. cochlear implant or deep brain stimulator).

Study design

Design

Study type: Interventional

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

Recruitment

NL

Recruitment status:	Recruiting
Start date (anticipated):	14-07-2023

Enrollment:	16
Type:	Actual

Medical products/devices used

Generic name:	Transcranial Magnetic Stimulator
Registration:	Yes - CE intended use

Ethics review

Approved WMO Date:	28-04-2023
Application type:	First submission
Review commission:	METC Amsterdam UMC
Approved WMO Date:	09-04-2025
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	NL83361.018.22