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How brain functioning affects the results of transcranial magnetic stimulation treatment

Submission date	Recruitment status	[X] Prospectively registered
22/08/2025	Recruiting	[ ] Protocol
Registration date	**Overall study status**	[ ] Statistical analysis plan
28/08/2025	Ongoing	[ ] Results
Last Edited	**Condition category**	[ ] Individual participant data
09/09/2025	Mental and Behavioural Disorders	[X] Record updated in last year

Plain English summary of protocol

Background and study aims
The symptoms of depression can be complex and vary widely between people. If you're depressed, you may feel sad, hopeless and lose interest in things you used to enjoy. Transcranial magnetic stimulation (TMS) is a noninvasive procedure that uses magnetic fields to stimulate nerve cells in the brain to improve symptoms of depression. TMS is typically used when medication hasn't been effective.
This study aims to test whether a new TMS protocol, including individual imaging-based targeting, improves outcomes in depression.

Who can participate?
Patients aged 18 to 67 years referred to the Helsinki University Central Hospital for rTMS for major depressive disorder (MDD)

What does the study involve?
The study involves a 2-hour visit to Aalto University Advanced Magnetic Imaging Centre for magnetic resonance imaging (MRI). This is followed by a 1-2-hour meeting including definition of dose and possible targets for the treatment. A nurse uses a randomized list to select the protocol, and the participants and the researchers who evaluate the outcome will not know the method. TMS is delivered five times a week for up to 20 sessions and combined with brief cognitive tasks and questionnaires.

What are the possible benefits and risks of participating?
Possible benefits of the study include improved outcomes of rTMS treatment and risks resemble those of usual TMS treatment, including uncomfortable stimulation site sensations and a small risk of seizure.

Where is the study run from?
Helsinki University Central Hospital Department of Psychiatry (Finland)

When is the study starting and how long is it expected to run for?
January 2023 to May 2028

Who is funding the study?
1. Research Council of Finland
2. Finnish government funding for health care research
3. Helsinki and Uusimaa Hospital District

Who is the main contact?
Dr Tuukka Raij, tuukka.raij@hus.fi

Contact information

Type(s)
Public, Scientific, Principal Investigator

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Additional identifiers

EudraCT/CTIS number
Nil known

IRAS number

ClinicalTrials.gov number
Nil known

Secondary identifying numbers
7111

Study information

Scientific Title
Effect of cognition and target model optimization on outcome of Helsinki individual transcranial magnetic stimulation treatment

Acronym
HIT3

Study objectives
New protocol results in better outcome than regular transcranial magnetic stimulation (TMS)

Ethics approval required
Ethics approval required

Ethics approval(s)
Approved 25/06/2025, HUS regional medical research ethics committee (HUS Keskuskirjaamo, Helsinki, PO Box 200, Finland; +358 (0)403594618; eettiset.toimikunnat@hus.fi), ref: HUS/12135/2022

Study design
Interventional double-blind randomized controlled trial

Primary study design
Interventional

Secondary study design
Randomised parallel trial

Study setting(s)
Hospital

Study type(s)
Treatment, Efficacy

Participant information sheet
Not available in web format, please use the contact details to request a participant information sheet

Health condition(s) or problem(s) studied
Major depressive disorder, resistant to at least two antidepressants

Interventions
Participants are randomized 1:1 to receive transcranial magnetic theta burst stimulation with:
1. Regular theta burst protocol
2. New protocol including individually planned targeting

Each group is further divided 1:1 to a cognitive priming task or no task.

The research nurse who delivers treatment uses balanced lists for randomization, while researchers who evaluate the outcome and the patient remain blind to the treatment arm. Theta burst stimuli are delivered at 120% (or nearest tolerated) of motor threshold five times a week for 20 days.

Intervention Type
Device

Pharmaceutical study type(s)
Not Applicable

Phase
Phase III

Drug/device/biological/vaccine name(s)
Transcranial magnetic stimulation

Primary outcome measure
Severity of depression measured using the Montgomery Åsberg Depression Rating Scale (MADRS) rated before and within 2 weeks after treatment

Secondary outcome measures
1. Functioning measured using the Social and Occupational Functioning Scale (SOFAS) before and within 2 weeks after treatment
2. Severity of depression measured using the self-evaluated Patient health questionnaire (PHQ-9) before and within 2 weeks after treatment and 6 weeks after treatment
3. Remission defined as MADRS <11 within 2 weeks after treatment
4. Response defined as MADRS within 2 weeks after treatment >50 % less than MADRS before treatment

Overall study start date
01/01/2023

Completion date
31/05/2028

Eligibility

Key inclusion criteria
1. Diagnosis of major depressive disorder (DSM-IV) as the principal diagnosis with Patient Health Questionnaire-9 score >14
2. Inability to tolerate antidepressant medication or unresponsiveness to minimum of 2 months trial with adequate dose of antidepressant
3. No change in antidepressive medication in 4 weeks prior to treatment

Participant type(s)
Patient

Age group
Adult

Lower age limit
18 Years

Upper age limit
67 Years

Sex
Both

Target number of participants

Independent data monitoring group conducts interim analysis at n = 40 with stopping rules p <0.005 or a new power calculation suggesting power <80 % to detect group difference with p <0.048 with n = 80

Key exclusion criteria
1. Previous rTMS treatment
2. Borderline personality features exceeding 7 points in McLean Screening Instrument for Borderline Personality Disorder, or other somatic or psychiatric conditions that likely interfere with recovery from depression with TMS (an unstable medical illness, substantial neurological illness, chronic pain, psychotic disorder or current psychotic symptoms, substance abuse or dependency within last 3 months, >2 mg lorazepine equivalents benzodiazepine use daily or any anticonvulsant, or lifetime history of non-response to an adequate course - i.e., a minimum of eight treatments - of electroconvulsive therapy)
3. Patients with safety risks including active suicidality, pregnancy, magnetic metal or leads in the upper body, or history of seizures

Date of first enrolment
15/09/2025

Date of final enrolment
31/12/2027

Locations

Countries of recruitment
Finland

Study participating centre
Helsinki University Central Hospital Department of Psychiatry
Valskarinkatu 12
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Finland
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Sponsor information

Organisation
Hospital District of Helsinki and Uusimaa

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Sponsor type
Hospital/treatment centre

Website
https://www.helsinki.fi/fi/laaketieteellinen-tiedekunta/tutkimus/tieteenalat/psykiatrian-osasto

ROR
https://ror.org/020cpqb94

Funder(s)

Funder type
Government

Funder Name
Research Council of Finland

Alternative Name(s)
Suomen Akatemia, Finlands Akademi, Academy of Finland, AKA

Funding Body Type
Government organisation

Funding Body Subtype
Universities (academic only)

Location
Finland

Funder Name
Helsinki and Uusimaa Hospital District

Funder Name
Government of Finland

Results and Publications

Publication and dissemination plan
Planned publication in a peer-reviewed journal

Intention to publish date
31/12/2028

Individual participant data (IPD) sharing plan
The datasets generated during and/or analysed during the current study are not expected to be made available due to the need to protect privacy of the participants.

IPD sharing plan summary
Not expected to be made available