Transcranial magnetic stimulation (TMS) to slow down cognitive decline in Alzheimer*s disease (AD): TMSLA - a monocentric randomized controlled trial.

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Ethical review	Approved WMO
Status	Pending
Health condition type	Other condition
Study type	Interventional

Summary

ID

NL-OMON57241

Source
ToetsingOnline

Brief title
TMSLA

Condition

- Other condition

Synonym
Alzheimer's disease, dementia

Health condition

neurodegeneratieve aandoeningen, dementie

Research involving

Human

Sponsors and support

Primary sponsor: Amsterdam UMC
Source(s) of monetary or material Support: subsidie Hersenstichting en Alzheimer Nederland

Intervention

Keyword: Alzheimer's disease, CSF biomarkers, MEG, TMS

Outcome measures

Primary outcome

The primary outcome will be the pre-to-post difference in clinical dementia rating, as measured with the clinical dementia rating - sum of boxes scale (CDR-SB), in the real rTMS condition compared to the sham condition.

Secondary outcome

Secondary outcome measures include additional cognitive and clinical rating scales, neuropsychological assessment batteries, magnetoencephalography, and cerebrospinal fluid biomarkers.

Study description

Background summary

New amyloid-targeting drugs for Alzheimer's disease (AD) offer minimal or unclear efficacy and often cause adverse events, highlighting the need for new therapies. In recent years, repetitive transcranial magnetic stimulation (rTMS) has shown increasing success. A recent randomized, double-blind, sham-controlled, phase 2 trial by Koch et al. (2022) {Koch, 2022 #10} demonstrated promising results from a 24-week rTMS treatment protocol targeting the precuneus. This brain region is considered a main hub of the human brain connectome and a prominent area of AD pathology. The results showed stable cognitive performance and increased brain activity in the treatment group, whereas the sham group worsened. We aim to conduct a replication study and

further investigate the working mechanism of precuneus-rTMS in AD to gain a better understanding.

Study objective

The main objective is to replicate the results of the recent successful efficacy study on precuneus rTMS in AD by Koch et al. (2022). Secondary objectives include investigating what functional brain activity/network changes underlie the effects of rTMS and whether differences in cognitive performance are reflected in cerebrospinal fluid AD biomarker levels.

Study design

A monocentric, 2-arm, randomized, double-blind, sham-controlled, phase 2 trial over 24 weeks with a 6-month follow-up to confirm the effectiveness of precuneus rTMS in individuals with mild AD.

Intervention

32 sessions of 20 Hz rTMS over the precuneus: a 2-week intensive phase with daily (5x/week) rTMS, followed by a 22-week maintenance phase with weekly rTMS.

Study burden and risks

rTMS is a form of non-invasive brain stimulation and is proven to be safe and generally tolerable, with sometimes mild side effects including transient headache and scalp sensations. The risk of inducing an epileptic seizure remains negligible. The main burden for both groups is the number of hospital visits due to the extensive treatment protocol of 32 sessions. Benefits for the treatment group include a possible temporary improvement and/or stabilizing effect on cognitive decline. By participating, both groups help the field gain knowledge about AD and potential new treatment options.

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

- Biomarker-supported Alzheimer*s disease (Abnormal CSF p-tau/Aβ42 ratio of > 0.023 or Amyloid PET positive).
- Between 50 and 85 years old.
- Clinical dementia rating (CDR) score of 0.5 or 1 {Morris, 1993 #80}.
- Mini-mental state examination (MMSE) score between 18 and 26.
- Presence of a caregiver.

Exclusion criteria

- Medical history of other neurodegenerative diseases, stroke, or epilepsy.
- Severe psychiatric dysregulation, hampering successful study participation and leading to possible cognitive impairment. Eligibility for participation will be based on clinical evaluation by an expert neurologist and/or psychiatrist.
- Extensive cerebrovascular damage on MRI classified as Fazekas level 2 or 3. Patients with abnormalities classified as Fazekas level 3 are excluded {Fazekas F Fau - Chawluk, #115}. For Fazekas level 2, patient*s eligibility for participation will be evaluated by an expert neurologist.
- Presence of metal in the head or cranial/thoracic implants, including cochlear implants.
- Cholinesterase inhibitors with unstable d osage in the last 2 months.
- Extreme claustrophobia or metallic objects in or on the body, preventing MRI and MEG examination.

- Previous rTMS treatment (for blinding reasons).

Study design

Design

Study phase:	2
Study type:	Interventional
Intervention model:	Parallel
Allocation:	Randomized controlled trial
Masking:	Double blinded (masking used)
Control:	Placebo
Primary purpose:	Treatment

Recruitment

NL

Recruitment status:	Pending
Start date (anticipated):	01-01-2025
Enrollment:	62
Type:	Anticipated

Medical products/devices used

Generic name:	Magstim Transcranial Magnetic Stimulation
Registration:	Yes - CE intended use

Ethics review

Approved WMO

Date:	08-01-2025
Application type:	First submission
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	NL87473.018.24