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A randomized clinical trial through combined therapy in patients with mild cognitive impairment

Submission date
30/08/2023

Recruitment status
No longer recruiting

Registration date
15/09/2023

Overall study status
Completed

Last Edited
26/02/2024

Condition category
Mental and Behavioural Disorders

[ ] Prospectively registered
[X] Protocol
[ ] Statistical analysis plan
[ ] Results
[ ] Individual participant data
[ ] Record updated in last year

Plain English summary of protocol

Background and study aims
Mild Cognitive Impairment (MCI) represents an early stage of specific forms of dementia and provides an opportunity for interventions to delay functional decline and improve overall quality of life. This study investigates the effectiveness of cognitive training and transcranial alternating current stimulation (tACS) intervention in enhancing working memory among individuals diagnosed with mild cognitive impairment.

Who can participate?
People between 60 and 75 years old with MCI

What does the study involve?
Participants will be randomly assigned to one of two groups. One group will receive cognitive training and transcranial alternating current stimulation (tACS), while the other will receive sham stimulation. Both groups will undergo a 12-session intervention program, with sessions held twice weekly over 6 weeks. The primary goal of the intervention is to enhance working memory, a critical cognitive function essential for executive tasks and long-term memory. Throughout the study, the researchers will measure brain activity and evaluate working memory function. These assessments will occur before, immediately after, and 3 months after the intervention to assess its effectiveness.

What are the possible benefits and risks of participating?
Participation in this study offers the potential benefit of improved working memory, which can significantly enhance the quality of life for individuals with MCI. However, it's important to note that the intervention's effectiveness is still being researched. Participants undergoing tACS may experience mild discomfort or tingling sensations on the scalp during the stimulation sessions, but these sensations are typically short-lived and not associated with serious risks.

Where is the study run from?
1. Universidad de Valparaíso (Chile)
2. Universidad del Desarrollo (Chile)

When is the study starting and how long is it expected to run for?
January 2019 to December 2024

Who is funding the study?
1. National Research and Development Agency (ANID) (Chile)
2. Universidad del Desarrollo (Chile)

Who is the main contact?
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Contact information

Type(s)
Principal Investigator

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Additional identifiers

EudraCT/CTIS number
Nil known

IRAS number

ClinicalTrials.gov number
NCT05291208

Secondary identifying numbers
SA19I0118

Study information

Scientific Title
Evaluation of a cognitive training therapy based on cerebral oscillations stimulation in patients with mild cognitive impairment through a randomized clinical trial

Study objectives
HA1: Users with Mild Cognitive Impairment participating in the Combined Cognitive Training Program (CCTP) show a pre-post intervention increase in prefrontal theta oscillatory activity, which will be greater than the increase observed in those users participating in the Traditional Cognitive Training Program (TCTP).

H01: The pre-post intervention increase in prefrontal theta oscillatory activity for users with MCI participating in the CCTP will be similar to the pre-post intervention increase in prefrontal theta oscillatory activity for users with MCI participating in the TCTP.

HA2: The increase in prefrontal theta oscillatory activity generated by the Combined Cognitive Training Program (CCTP) is reflected in a post-intervention increase in cognitive performance for users with Mild Cognitive Impairment compared to their pre-intervention cognitive performance.

H02: The increase in prefrontal theta oscillatory activity generated by the Combined Cognitive Training Program (CCTP) is not reflected in a post-intervention increase in cognitive performance for users with Mild Cognitive Impairment compared to their pre-intervention cognitive performance.

Ethics approval required
Ethics approval required

Ethics approval(s)
Approved 30/10/2019, Comité Etico - Científico Clínica Alemana/Universidad del Desarrollo (Avenida Las Condes #12461, Torre 3, 2° piso, Las Condes, Santiago, 7590943, Chile; +56 (0)562 3279157; ceccasudd@udd.cl), ref: 2019-083

Study design
Single-center interventional double-blinded randomized controlled trial

Primary study design
Interventional

Secondary study design
Randomised controlled trial

Study setting(s)
University/medical school/dental school

Study type(s)
Treatment

Participant information sheet
See study outputs table

Health condition(s) or problem(s) studied
Mild Cognitive Impairment (MCI)

Interventions

This is a phase II randomized, double-blind clinical trial with a 3-month follow-up period. The study aims to enroll 62 participants diagnosed with Mild Cognitive Impairment (MCI) aged over 60 years, residing in Valparaíso, Chile.

Participants will be randomized using the stratified randomization method, whose strata will be age (<75 years and >=75 years), schooling (6 to 12 years and > 12 years), and sex (male and female). After stratification, simple randomization will be used. Each participant will have the same probability of being assigned to either of the two intervention groups. To achieve this objective, the randomization process will be conducted utilizing the Faculty of Medicine Redcap system at Clinica Alemana-Universidad del Desarrollo. This system will allocate each participant to one of the two intervention groups. The person responsible for generating the random assignment sequence list will be unaware of the people who recruit and evaluate the participants. This generated sequence will be blind until the interventions are assigned.

Participants will undergo an intervention that combines 12 cognitive training sessions with non-invasive brain stimulation, specifically transcranial Alternating Current Stimulation (tACS). Participants will receive either active tACS or sham stimulation in eight sessions, depending on their assigned intervention group. Each session will have an approximate duration of 1 hour and will occur twice a week over 6 weeks.

tACS will be applied in sessions 3, 4, 5, 6, 7, 8, 9, and 11 with two 3 x 1 arrays of electrodes. The central stimulation electrodes will be positioned in F3 and CP3 (10-20 system). The AC stimulation will be 1 mA from the baseline to the stimulation peak. The stimulation will have a gamma sine waveform (80 Hz) over the positive phase of the theta oscillation (between 4 and 8 Hz, adjusted by each subject based on prior EEG recording, Reinhart et al., 2019) with impedances always under 10 kOhm.

Intervention Type
Mixed

Primary outcome measure
Prefrontal theta oscillation activity is measured using electrophysiological changes underlying the working memory process at baseline, 13 and 20 weeks

Secondary outcome measures
1. Working Memory Index is measured using WAIS-IV Digit Retention subtest at baseline, 13 and 20 weeks
2. Working memory and the capacity for cognitive flexibility are measured using Trail Making Test B (TMT-B) at baseline, 13 and 20 weeks

Overall study start date
05/01/2019

Completion date
30/12/2024

Eligibility

Key inclusion criteria
1. Age equal to or greater than 60 years
2. Presence of Mild Cognitive Impairment, according to the diagnostic criteria established in

Petersen et al. (2014)
3. Have six or more years of complete schooling (presence of reading and writing)

Participant type(s)
Patient

Age group
Senior

Lower age limit
60 Years

Upper age limit
75 Years

Sex
Both

Target number of participants
54

Key exclusion criteria
1. The previous diagnosis of other neurodegenerative diseases
2. Attending another cognitive training program
3. History of Epilepsy or current presence of epileptic seizures
4. Presence of psychiatric diseases
5. Presence of a relevant depressive picture (GDS >=2)
6. History of important neurological alterations such as the history of stroke, transient ischemic attack, cranial brain trauma
7. Important alterations of communication

Date of first enrolment
26/01/2022

Date of final enrolment
21/09/2024

Locations

Countries of recruitment
Chile

Study participating centre
Centro de Investigación del Desarrollo en Cognición y Lenguaje
Angamos 655 7-09 R2, Reñaca
Viña del Mar
Chile
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Study participating centre
Social Neuroscience and Neuromodulation Laboratory (neuroCICS)
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Sponsor information

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Universidad del Desarrollo

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University/education

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ROR
https://ror.org/05y33vv83

Funder(s)

Funder type
Government

Funder Name
Agencia Nacional de Investigación y Desarrollo

Alternative Name(s)
Agencia Nacional de Investigación y Desarrollo de Chile, National Agency for Research and Development, Government of Chile, Chilean National Agency for Research and Development, Agencia Nacional de Investigación y Desarrollo de Chile (ANID), ANID

Funding Body Type
Government organisation

Funding Body Subtype
National government

Location
Chile

Funder Name
Universidad del Desarrollo

Results and Publications

Publication and dissemination plan
The results of the study will be presented at national and international congresses and seminars and published in relevant scientific journals.

Intention to publish date
30/03/2025

Individual participant data (IPD) sharing plan
The datasets generated during and analyzed in the current study will be stored in a publicly available repository at OSF.io: https://osf.io/xh7tr/ (DOI: 10.17605/OSF.IO/XH7TR). The datasets include behavioral and electroencephalographic anonymised data for each participant. Each participant provided their informed consent for their data to be shared anonymously for future analyses or studies. All the date will become available once the primary clinical trial results are published.

IPD sharing plan summary
Stored in publicly available repository

Study outputs

Output type	Details	Date created	Date added	Peer reviewed?	Patient-facing?
Protocol article		23/02/2024	26/02/2024	Yes	No