T-mult: exploring the impact of TMS induced virtual lesions on the multimodal brain network and cognition

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To explore the effect of reversible virtual lesions on cognitive functioning in the domain of executive functioning and on network organization / to define local network resilience and the interplay between local resilience and global network...

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

Summary

ID

NL-OMON53939

Source
ToetsingOnline

Brief title
T-mult

Condition

- Other condition
- Neurological disorders NEC

Synonym
not applicable

Health condition

cognitief functioneren

Research involving
Human

Sponsors and support

Primary sponsor: Vrije Universiteit Medisch Centrum
Source(s) of monetary or material Support: Vidi 198.015

Intervention

Keyword: cognition, connectome, multilayer, TMS

Outcome measures

Primary outcome

The primary effect of rTMS will be assessed through the change in performance on a neuropsychological test measuring executive functioning in the domain of executive functioning pre- and post-intervention.

Secondary outcome

Secondarily, changes in network organization will be characterised by (multimodal) neuroimaging pre- and post-treatment. Pre-treatment imaging will include magnetoencephalography (MEG), diffusion MRI (dMRI), task-based functional MRI (tbfMRI), and resting state fMRI (rsfMRI); post-treatment imaging will include only tbfMRI.

Study description

Background summary

Lesional brain disease, such as glioma or MS, is usually progressive. Patients often suffer from cognitive decline, mainly in the domain of executive functioning, impacting not only their quality of life but also that of their caregivers. However, the impact of lesions is seemingly unpredictable: some patients may show relative stability of cognitive functioning despite the occurrence of severely progressive lesions, while others decline rapidly after only minor disease progression. To study the individualized impact of new lesions on the brain network and on cognition, reversible *virtual lesions* can be induced in healthy subjects by perturbing parts of the brain through

low-frequency repetitive transcranial magnetic stimulation (rTMS). The idea is that lesions occurring in areas that are strong local (but not global) hubs pre-TMS, are associated with greater cognitive decline and greater global network deviation post-TMS.

Study objective

To explore the effect of reversible virtual lesions on cognitive functioning in the domain of executive functioning and on network organization / to define local network resilience and the interplay between local resilience and global network deviation.

Study design

Experimental study using single-session rTMS (versus sham). Healthy volunteers will be randomly assigned to either an intervention or a control group, with pre- and post-neuroimaging and cognitive testing.

Intervention

50 will undergo a single session of inhibitory rTMS to the dorsolateral prefrontal cortex (DLPFC); 50 will be active controls (through use of a sham coil).

Study burden and risks

Participants will visit the outpatients* clinic where they will first undergo neuroimaging, cognitive assessment, and TMS motor threshold testing; subsequently, participants will undergo either inhibitory rTMS or sham rTMS, after which they will undergo task fMRI and simultaneous cognitive assessment. Inhibitory rTMS is a non-invasive, well-tolerated technique to infer virtual lesions. Possible side effects include transient headache (moderate risk), and syncope, transient hearing changes, transient unintended cognitive/neuropsychological effects, and seizure (all low risk; note that risk of seizure in healthy controls in combination with low-frequency stimulation is negligible). Overall, risk to participants is considered to be low, particularly if exclusion criteria are adhered to. Lesional brain disease has a significant impact not only on the patients suffering from it and their caregivers but also on society, and obtaining a better understanding of the effect of new lesions on the brain network and cognition could help inform future studies into such diseases and might provide a first step towards intervention/treatment. Therefore, in our view, there is negligible risk associated with the participation of healthy, motivated volunteers, whereas the potential value of this study is significant.

Contacts

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Trial sites

Listed location countries

Netherlands

Eligibility criteria

Age
Adults (18-64 years)

Inclusion criteria

* Age between 20 and 65 years old
* Native Dutch speaker
* Able to provide written informed consent.

Exclusion criteria

* Current diagnosis of neurological or psychiatric disease (including traumatic head injury)
* Current and regular use of centrally acting drugs (recreational or prescribed, including analgesics), including use of alcohol ~8 hours prior to an appointment
* Presence of any contraindications for MRI, MEG, or TMS (including

resting-motor threshold >75% of maximum stimulator output or no useful motor-evoked potential elicitable)
* Previous rTMS treatment.

Study design

Design

Study type:	Interventional
Intervention model:	Parallel
Allocation:	Randomized controlled trial
Masking:	Single blinded (masking used)
Control:	Placebo
Primary purpose:	Other

Recruitment

NL

Recruitment status:	Recruiting
Start date (anticipated):	31-05-2023
Enrollment:	100
Type:	Actual

Ethics review

Approved WMO

Date:	25-01-2023
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	NL82268.029.22