The effects of nr-TMS on the HD-EEG measurements while conducting a language test in healthy subjects.

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Ethical review	Approved WMO
Status	Recruiting
Health condition type	Nervous system neoplasms benign
Study type	Interventional

Summary

ID

NL-OMON56443

Source
ToetsingOnline

Brief title
Effects of nr-TMS on the HD-EEG

Condition

- Nervous system neoplasms benign

Synonym
Low grade glioma / Brain tumor

Research involving
Human

Sponsors and support

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

Intervention

Keyword: HD-EEG, Language, neural networks, nr-TMS

Outcome measures

Primary outcome

The primary objective is to determine whether high-density EEG (HD-EEG) measurements can identify dynamic differences in brain activity when language networks are disturbed by navigated repetitive transcranial magnetic stimulation (nr-TMS).

In the first part of the study, a baseline HD-EEG measurement will be established, this will be the measurement when no nr-TMS stimulation is performed.
In the second part of the study, the nr-TMS stimulation will be performed together with the HD-EEG measurements. We expect one of three scenarios to occur.
1. The subject is unable to name the picture, which means that the language function is disrupted.
2. The subject is able to name the picture due to the nr-TMS not stimulating any language functions.
3. The subject is able to name the picture due to the brain compensating for the nr-TMS disruption.

We will compare each of these three scenarios to the baseline using the following parameters:

- The amplitude and the latency of the wavelets in the Event Related Potentials

(ERPs)

- The power of the frequency bands in the Event Related Spectral Perturbation

(ERSP)

- The correlation between electrodes in the Functional connectivity (FC)

Hypothesis:

We expect that there will be a difference between the scenarios and the

baseline when comparing the aforementioned parameters of the HD-EEG.

Secondary outcome

not applicable

Study description

Background summary

People with a brain tumour often need brain surgery. A brain tumour may be close to areas of the brain that are responsible for speech, reading and writing. To make sure that these areas are not damaged during surgery, patients sometimes need to be awake during the operation. During the operation, the surgeon can temporarily disrupt the brain's function using small pulses of electricity, while the patient takes a speech test. This allows the surgeon to know whether the part being stimulated contains important language function. If so, the stimulated part of the brain cannot be removed. This awake brain surgery is often very exciting and tiring for patients. There are also other drawbacks to this technique, which is why it is important to have a better idea before surgery of which part of the brain is needed for speech and language and therefore cannot be removed. We hope that with better information before surgery, we will be able to reduce the time patients spend awake and perhaps even eliminate the need for surgery altogether.

One way to map the exact location of language function in the brain is to measure brain function using navigated repetitive transcranial magnetic stimulation, or Nr-TMS for short. Nr-TMS uses short magnetic pulses to

stimulate the brain. A coil containing a strong magnet is placed on the head. This magnetic field can create a small electrical current in the brain. This can temporarily disrupt the functioning of a small part of the brain. To measure these disturbances, we use a film of the brain called an electroencephalogram (EEG). We use an EEG with more electrodes than normal. Because we have more points, we can measure the brain's electrical signals more accurately. In this study, we will use the n-TMS device to disrupt speech. At the same time, we will use EEG to measure how the brain responds to this disruption. During the disruption, we will give language tests. Our ultimate goal is to perform this nr-TMS-EEG study in patients with a brain tumour before surgery. In this way, we hope to improve the outcome of the surgery.

Study objective

In this study, we will investigate what changes in brain activity when we test language function and if this can be detected on a High-Density electroencephalogram (HD-EEG). As part of this study, we will also temporarily disrupt brain activity through brain stimulation. We will use navigated repetitive transcranial magnetic stimulation (nr-TMS). During this scan, we will test the language function by asking the subject to name pictures on a screen at the same time. an MRI-scan will be made of brain of the subject.

Study design

The examination requires you to come to the hospital twice and will take up to 4 hours. The intake interview and the MRI scan will take about half an hour in total. The experiment itself will take about 3 hours.
We will do the following during the study:
- Before the first visit, you will receive an information letter along with a questionnaire with exclusion criteria. After 2 weeks, you will be called by a researcher asking if you want to participate in the study. The researcher will also go through the exclusion criteria questionnaire with you and then schedule an appointment.
- During the first visit, the researcher will have an intake interview with you. Here, the researcher will briefly explain the study again and you can ask any further questions. This will take about 15 minutes. Next, You undergo an MRI scan of your head. The MRI scan will also take about 15 minutes, of which the scanning will only take 5 minutes.
- The MRI scan will be reviewed by a neuroradiologist or neurosurgeon. If no abnormalities are found here, you will be invited to the second visit.
- During the second visit, the examination will be performed, which will take about 3 hours. Before the examination, we ask you to remove your jewellery, especially necklaces and earrings. We also ask you to put aside bank cards and any electronic devices, such as phones. The TMS device works with strong magnet which can cause damage if metals, electronic devices or bank cards are nearby.
- During the examination, you sit on a comfortable chair and are first given a

'cap' (a bathing cap with holes) with electrodes on your head. These electrodes are filled with a paste and record the brain video. The skin under the holes will be scratched a little to make the brain video as good as possible. This can be slightly uncomfortable, but not painful.
- When this cap is connected, we will show you pictures on a screen and ask you to name them as quickly as possible in a sentence. For example; if the picture shows a cat, you say: "This is a cat". If a dog is shown: "This is a dog" and so on.
- Next, an instrument with reflective balls will be attached to the EEG cap. This is needed for the navigation device. The examiner will also prepare the TMS device for the further examination, during which you will be asked to sit relaxed and still.
- Before the stimulation starts, the intensity of the stimulation will be determined. During this determination, an attempt will be made to induce muscle movements in the hand with the TMS device. You will not notice anything, except that involuntary muscle movements may feel a little strange.
- When everything is ready, you will again be asked to name pictures that you see on a screen. During this second part of the examination, we will switch on the TMS device, which will emit magnetic pulses during the measurement. These magnetic pulses may cause you to have difficulty naming the pictures you see, but this effect only lasts a few seconds. These magnetic pulses do not hurt. Sometimes some muscles in the face may tighten, which can be bothersome. If so, we can stimulate in a different way that makes this less present.
- After a number of naming pictures and stimulation with the TMS device, the measurement is finished and you are able to leave the hospital on your own.

Intervention

Participants will receive nr-TMS pulses, the effect of which will be measured using HD-EEG. these pulses will be administered on the left fronto-temporal region of the brain. Stimulation will take place for 1 second at a frequency of 5 Hz at an intensity of 100% of the resting Motor Threshold (rMT). This is followed by a 3-second rest period. This amount, frequency, and intensity of the TMS pulses falls published safety standards are (Rossi et al., 2009, Clin Neurophysiol).

Study burden and risks

MRI
There are no known risks associated with having an MRI scan. You may find it uncomfortable to lie still for a long time during the scan. Lying in the scanner may also make you feel claustrophobic. However, you should be aware that unexpected abnormalities may be found on the MRI scan. If this is the case, your doctor will be informed.

EEG

There are no known risks associated with having an EEG. You may feel uncomfortable if you have to wear the EEG cap for a long time or if the paste remains in your hair after the examination.

TMS

The risk of nr-TMS can be considered negligible to minimal. You may hear the TMS pulse, which sounds like a loud clicking sound. The TMS device may cause the muscles around your face to contract. This may feel uncomfortable, but will only last a short time. If it becomes too uncomfortable, you can tell us at any time and the session can be adjusted or stopped. You may experience mild, short-term side effects during stimulation. The most common side effects are neck pain/discomfort (±40%), localised scalp discomfort (±39%), tension headache during and immediately after stimulation (±28%) and dizziness. Rarely, seizures have been reported in nr-TMS studies in patients (e.g. with epilepsy) or in studies using particularly intense (non-standard) stimulation. The most serious - but very rare - side effect of nr-TMS is the occurrence of a single seizure. This occurs in 0.08 per 1000 sessions and the chance is virtually zero if you do not have epilepsy or any other neurological condition. For this reason, a neurologist or neurosurgeon will be present at the trial or in a nearby trial unit to provide appropriate assistance. In addition, a KNF lab technician (student) will often be present at the trial. To minimise these risks, you will be given a full pre-test screening. See Appendix D for a full list of contraindications to nr-TMS.
On one occasion, superficial burns were also described as a result of the TMS stimulator overheating. There is a temperature-protection system in our equipment: every 4 seconds the temperature of the stimulator is measured and if it exceeds 40°C, the TMS device is automatically switched off. This risk is present in all TMS treatments.

Computer program for displaying images and timing TMS.

To ensure that the images are displayed at exactly the same time as the TMS pulses are delivered, we use a computer program. This programme was developed and tested at the UMCG. Because this computer program is new, it carries possible risks. The program may crash, a cable may break, or the stimulation values may be entered incorrectly. This can cause you to perhaps get more TMS pulses that you are meant to. However, there is a safeguard in the system that ensures the pulses are always within safe stimulation norms. At least two researchers are present during each measurement to minimise the risk of negative consequences for you. This is because the stimulator can be removed directly from the head by one examiner and, in addition, the person standing by the computer can also directly ensure that the computer, i.e. the TMS equipment, is switched off. In addition, there is a large stop button on the TMS device itself through which the equipment can be switched off.

Contacts

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Trial sites

Listed location countries

Netherlands

Eligibility criteria

Age
Adults (18-64 years)

Inclusion criteria

- Between 18 and 40 years of age.
- Signed and dated informed consent prior to any study-related procedures.
- Native Dutch speaker.
- Normal vision or corrected to normal vision with contact lenses.

Exclusion criteria

- History of seizures.
- Family history of epilepsy.
- History of unexplained spells or loss of consciousness.
- History of stroke.
- History of head injury.

- History of head surgery.
- Brain-related neurological illness.
- Presence of metal objects in the head.
- Presence of implanted medical devices such as pacemakers or medical pumps.
- Pregnancy.
- (History of) psychiatric disorder.
- Claustrophobia.
- Glasses (contact lenses are allowed)
- False teeth that are connected via a magnetic click system
- Age over 40 years or under 18 years.
- Drinking more than 2 units of alcohol the night before participation.
- Participation in TMS research the day before the experiment.
- Feeling tired and/or not sleeping well the night before participation.

Study design

Design

Study type: Interventional

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

Recruitment

NL

Recruitment status:	Recruiting
Start date (anticipated):	29-01-2024
Enrollment:	10
Type:	Actual

Ethics review

Approved WMO

Date:	18-12-2023
Application type:	First submission
Review commission:	METC Universitair Medisch Centrum Groningen (Groningen)

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	NL84797.042.23