The roles of occipital and parietal regions in visual awareness: A Transcranial Magnetic Stimulation study

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

Summary

ID

NL-OMON33292

Source
ToetsingOnline

Brief title
TMS for visual awareness

Condition

- Other condition

Synonym
nvt

Health condition

niet van toepassing

Research involving
Human

Sponsors and support

Primary sponsor: Radboud Universiteit Nijmegen
Source(s) of monetary or material Support: Ministerie van OC&W

Intervention

Keyword: consciousness, subjective awareness, TMS, visual perception

Outcome measures

Primary outcome

The effect of TMS on the three stimulation sites in the main experiment will be assessed using a visual task performed in an fMRI scanner. We will test whether stimulation to V1, PPC, and vertex differentially affected subjects* visibility ratings. We predict that V1 stimulation will lead to decrease in visibility ratings for gratings presented anywhere in the visual field, while PPC stimulation will only affect the visibility of gratings in the contralateral visual field. Vertex stimulation is not expected to have any effects on visibility ratings. Further, we predict that the changes in visibility rating will be mediated by changes in the activation patterns in the prefrontal cortex and will test for that in the fMRI part of the experiment.

Secondary outcome

The effectiveness of TMS stimulation will be assessed in a pilot experiment. We will test whether stimulation to V1, PPC, and vertex differentially affected subjects* visibility ratings. Again, we predict that V1 stimulation will lead to decrease in visibility ratings for gratings presented anywhere in the visual field, while PPC stimulation will only affect the visibility of gratings in the contralateral visual field. Vertex stimulation is not expected to have any

effects on visibility ratings. In the pilot experiment we will only collect

behavioural data in order to assess the effectiveness of TMS.

Study description

Background summary

In everyday perception, people rarely distinguish between the objective and subjective aspects of their percepts. The silent assumption is that everything that meets the eye is consciously seen and creates activations in the brain that are strong enough to influence thinking and behaviour. However, the past hundred years of psychophysics research has convincingly demonstrated that this is not the case. More recently, a wealth of fMRI and TMS studies have investigated the neural bases of the objective and subjective aspects of perception.
A particularly striking example of the dissociation between subjective awareness and objective processing of visual stimulation is the condition called *blindsight.* Blindsight refers to the phenomenon that, after a lesion to the primary visual cortex, a subject can exhibit above-chance performance in detecting or discriminating visual stimuli in a forced-choice setting, despite the lack of acknowledged consciousness of the stimuli. In some instances, blindsight subjects can perform at an impressively high level of accuracy (higher than 80%) in the forced-choice task, even when the subjects believe that they are guessing.
A related phenomenon, which involves dissociation between objective processing and subjective visibility, is the condition known as *visual neglect.* Damage to the posterior parietal cortex (PPC) results in attentional deficits that concern stimuli presented in the contralesional space. Further, it has been shown that when neglect patients claim not to see a stimulus in the contralesional visual field, they still perform higher than chance on forced-choice tasks. Unfortunately, despite their tremendous importance for understanding the various aspects of visual processing, cases of blindsight and visual neglect are very rare. Recently, Boyer et al. (2005) and Nyffeler et al. (2008) succeeded in inducing blindsight-like and neglect-like conditions, respectively, in normal subjects using TMS. Such studies allow researchers to explore the above discussed conditions without the complications of worrying about side effects of natural lesions.

Study objective

In the present study we will attempt to produce blindsight-like and neglect-like conditions in normal subjects using theta burst stimulation (TBS) and then explore how visual processing proceeds using fMRI. More specifically,

our hypotheses are:
1) TBS to the primary visual cortex V1 will result in a blindsight-like condition characterized by a significant decrease in subjective awareness of visual stimuli but relatively unaffected ability to perform visual tasks.
2) TBS to PPC will result in a neglect-like condition characterized by a significant decrease in subjects* ability to subjectively experience stimuli presented in their contralateral visual field.

Study design

The study is designed as a crossover experiment with healthy adult volunteers.

In the pilot experiment, we will use 40-second continuous theta-burst stimulation (cTBS). The study will investigate the role of V1 and PPC in visual perception. Stimulation of both regions will be compared to vertex stimulation. We expect that stimulation of both V1 and PPC will results in significantly lower visibility ratings when compared to vertex. Further, we expect that the effect will be global for V1 but will be localized to the contralateral visual field in the case of PPC stimulation.
Subjects will first receive 40 seconds of cTBS and then do a visual task. The visual task will consist of discriminating between different orientations of low-contrast gratings, and rating the visibility of those gratings. We will stimulate healthy participants with cTBS in a within subjects-design. Subjects will come for a total of three sessions - one for each of the three targets regions: V1, PPC, and vertex.
Prior to the experiment, participants are informed about the study in detail and about the possible risks. They are screened using a questionnaire to ensure their eligibility for participation. In the first session of the pilot experiment, participants receive practice with the behavioural task. Afterwards, we will establish subjects* active motor threshold (aMT) as determined using TMS pulses. The aMT is defined as the lowest TMS intensity needed to evoke a reproducible and measurable (with electromyography) muscle twitch in the first dorsal interosseus of the right hand (Rossini et al. 1994). The aMT provides an indication of the excitability of a participant*s brain and will be used to determine the stimulation intensity in the later TMS sessions. We will also acquire an anatomical image of the participant's brain to aid placement of the TMS coil.
In sessions 2-4 participants receive 40 seconds of triplets of 50 Hz pulses in a 5 Hz rhythm at 80% of the participant*s aMT to V1, PPC and vertex respectively. The placement of the coil will be guided an anatomical MRI scan of the individual subject. The stimulation locations will be determined using the BrainSight TMS-MRI co-registration system. This system allows to navigate the TMS coil in relation to the individual anatomical MRI in real-time with millimetre accuracy. Sessions 1, 2, and 3 are spaced at least 7 days apart and will be counterbalanced across subjects.

The main experiment will be similar to the pilot experiment but will involve

fMRI scanning. Subjects will first receive 40 seconds of cTBS and then do a visual task while being scanned in an fMRI scanner. As in the pilot experiment, the visual task will consist of discriminating between different orientations of low-contrast gratings, and rating the visibility of those gratings. We will collect data in the fMRI scanner for up to one hour, excluding the time needed for acquisition of structural images. We will stimulate healthy participants with cTBS in a within subjects-design. Subjects will come for a total of four sessions.
Prior to the experiment, participants are informed about the study in detail and are informed about the risks, and they are screened using a questionnaire to ensure their eligibility for participation. In the first session, subjects will receive practice with the behavioural task. The aMT is established (see above for details) and an anatomical image of the participant's brain is acquired to aid placement of the TMS coil. Sessions 2-4 will mimic sessions 1, 2, and 3 from the pilot experiment. Subjects will receive cTBS to either V1, PPC, or vertex with the intensity and placement of stimulation chosen as above. The only difference is that subjects will do the visual task after the stimulation in the MRI scanner rather than in front of a computer.
Sessions 2, 3, and 4 are spaced at least 7 days apart and will be counterbalanced across subjects.

Intervention

We will use 40-second continuous theta-burst stimulation (cTBS). cTBS refers to a simulation paradigm in which participants receive brief trains of pulses of 50 Hz in a 5 Hz (the theta frequency) rhythm. Compared to the more traditional 1Hz repetitive TMS (rTMS), cTBS can be applied at lower thresholds (80% of the motor threshold), the duration of stimulation is much shorter (20-50 seconds), and the effect is more consistent and lasts longer than the effect of rTMS. Traditionally cTBS was predominantly applied to motor regions (cf. Huang et al. 2005, Vallesi et al. 2007; Classen & Stefan 2007), but recent studies showed an effect of cTBS on V1 (Franca et al., 2006), PPC, and vertex (Hilgetag et al. 2001; Nyffeler et al., 2008). Thus, cTBS has already been tested and found safe as a method of stimulating all the regions that we will target in the present study.

Study burden and risks

When TMS was first developed, several studies have applied stimulation for long periods of time, at high intensities, with high-frequency (> 5 Hz). Using these high-intensity high-frequency stimulation resulted in several occasions in an epileptic phase in the subject (without long-term damage). This resulted in strict safety regulations for the use of combinations of stimulus strength, duration, and frequency. Since these regulations have been in place, there have been no epileptic fits in healthy subjects in studies abiding by there

guidelines. We use these guidelines in the proposed study. Therefore, it is in principle possible that rTMS causes an epileptic fit, but the risk of this happening is very small in healthy subjects, unless subjects are stimulated for prolonged periods of time at frequencies 10-25 hz at high stimulation intensities. TBS is a recent development in TMS research. Instead of a continuous stimulation frequency with isochronous intervals TBS uses short trains of pulses that are repeated at 5 Hz. TBS uses less pulses than rTMS and lower intensities, while the effects are of the same magitude as for rTMS. Since its introduction, TBS has been used in a high number of studies. In our study we will use TBS and all volunteers will be screened using a questionnaire. We know of no cases in which TBS has caused an epileptic fit in a healthy volunteer.

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

Right-handed individuals, with normal or corrected-to-normal vision and no history of neurological or psychological disorders are included.

Exclusion criteria

- Pacemaker
- Metal parts in head or mouth
- History of brain surgery
- History of epilepsy or first-grade family member with epilepsy
- Psychological or neurological disorder
- Pregnancy

Study design

Design

Study type:	Interventional
Intervention model:	Crossover
Masking:	Open (masking not used)
Control:	Uncontrolled

Recruitment

NL

Recruitment status:	Recruiting
Start date (anticipated):	01-07-2009
Enrollment:	60
Type:	Actual

Medical products/devices used

Registration:	No

Ethics review

Approved WMO Date:	29-05-2009
Application type:	First submission
Review commission:	CMO regio Arnhem-Nijmegen (Nijmegen)

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	NL26942.091.09