The Role of brain area S1 in the perception of actions.
A combined TMS and fMRI study on the functional connectivity of the human mirror neuron system.

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How does the sets of brain regions of the pMNS interact to enable us to grasp so intuitively what is going on in other individuals?The present projects aims at investigating the connectivity between the brain areas identifyed as part of the human...

Ethical review	Approved WMO
Status	Pending
Health condition type	Other condition
Study type	Observational non invasive

Summary

ID

NL-OMON33685

Source
ToetsingOnline

Brief title
The role of brain area S1 in the perception of actions

Condition

- Other condition

Synonym
It is a healthy subject study.

Health condition

gezonde proefpersonen

Research involving
Human

Sponsors and support

Primary sponsor: Universitair Medisch Centrum Groningen
Source(s) of monetary or material Support: NWO 452-04-305

Intervention

Keyword: functional connectivity, mirror neuron system, S1

Outcome measures

Primary outcome

In this study we aim at shedding some light on the connections between the S1 brain area and the rest of the areas identifyed as part of the human MNS. Data collected when S1 is functioning normal and when it is disrupted is going to be analyzed by different techiques including traditional fMRI analysis tools and various methods of effective connectivity (PPI, Friston et al., 1994; DCM, Frackowiak and Friston, 2004; Granger Causality, Roebroeck, Formisano et al., 2005) to determine the pattern of connectivity and the causal effect of the target brain area in this pattern of connectivity.

Secondary outcome

n.v.t.

Study description

Background summary

Mirror Neurons (MN) were discovered in the lab of Rizzolatti and col. (for an overview see Rizzolatti and Craighero, 2004): these neurons, located in the ventral premotor cortex and the rostral inferior parietal lobe of the monkey respond while the monkey performs an action (e.g. grasping a peanut) and when

the monkey observes another individual performing a similar action - as if the monkey were in the skin of the other individual. These neurons suggest, that the brain of the monkey automatically transforms what it sees other agents do into the motor representations necessary for performing a similar action.
These findings however raised a number of important questions. (a) Does a similar system exist in the human brain? (b) What brain regions show such a mirror phenomenon? (c)Given that the function of a neuron is determined by the pattern of connections that links it to other neurons, what pattern of connectivity between brain areas make mirroring possible?

The human Mirror Neuron System
Regarding question (a), although it is not normally possible to record the activity of single neurons in humans, a number of techniques now converge to suggest that humans have indeed a mirror system similar to that of monkeys (see Rizzolatti and Craighero, 2004). Neuroimaging methods including positron emission tomography and more recently functional magnetic resonance imaging (fMRI) show that regions directly similar to those in which mirror neurons have been found in the monkey (the ventral premotor cortex and rostral posterior parietal cortex) are active both when participants perform certain actions and while they see other individuals perform similar actions (e.g. Gazzola et al., 2007).

Which Brain Areas are Involved?
Question (b) and (c) however remain a matter of controversy. In the monkey, where single cell recordings are the main method for exploring mirror neurons, an experimenter chooses where in the brain to look for mirror neurons. This has so far only been done for the ventral premotor and posterior parietal cortex. It is therefore unclear whether other brain areas have similar properties. Neuroimaging studies in humans however show that other brain areas are indeed also involved both during the observation of other people*s actions and the execution of similar actions. This data extends the original finding of mirror neurons in the monkey by suggesting that a whole network of brain regions is common to both the observation and execution of actions. This *shared circuit* involves the ventral and dorsal premotor cortex, the posteior parietal lobe, the somatosensory cortex and high level visual cortex.

Study objective

How does the sets of brain regions of the pMNS interact to enable us to grasp so intuitively what is going on in other individuals?
The present projects aims at investigating the connectivity between the brain areas identifyed as part of the human Mirror Neuron System, in particular the connections between the S1 area and the rest of the MNS. To do so two techniques are going to be used: Repetitive Transcranial Magnetic Stimulation (rTMS) is going to be used to disrupt the functioning of the targeted brain area and Functional Magnetic Resonance Imaging (fMRI) is going to be used to access the activations in the brain while the subject is observing and

executing actions. Data is going to be collected with fMRI before, immediately after the rTMS and after the effects of the rTMS have dissapeared. Data from these three sessions is going to be compared. Analysis of the data is going to include standard fMRI data analysis methods and also various methods of effective connectivity.

Study design

The study combines rTMS with fMRI to compare the activation in the brain when the S1 brain area is active and when its* function is impaired by the rTMS. In this study three scanning sessions will be recorded. During the fMRI-scan sessions subjects will observe actions and execute actions. Just before these sessions rTMS will be applied on the S1 brain area of the subjects. Two of these sessions will include sham TMS (no effect on the brain activity) and the other one will include rTMS by means of Theta Bursts stimulation (TBS), in this way the functioning of the brain area will be impaired for a short period. In all cases scanning is done immediately after the stimulation. The sham sessions serve as a control and enable the researcher to isolate the effects that are due to the rTMS stimulation and the ones due to the experimental condition. Between the fMRI sessions will be at least 24 hours.

Study burden and risks

fMRI and rTMS are both non-invasive techniques, so there is no need of special preparation of the subject. There are no risks that have been associated with the fMRI acquisition. Subjects will be exposed to a magnetic field of 3 Tesla and rapidly alternating gradients and radio frequency fields. This field is used on a routinely basis in fMRI and MRI research. No harmful side effects have been reported. On rare occasions, a peripheral nerve (abdomen) is stimulated by the changing magnet gradients. This might cause an etching feeling but it is not harmful. The data collected during the fMRI and MRI scans will be used for research purposes only. However, if severe abnormalities are noticed a specialist (radiologist or psychiatrist) will be asked for advice, upon decision of the research team. If it is confirmed by the specialist that medical treatment is needed, then the General Practitioner indicated by the subject will be notified.

The safety of the Tetha-Bursts Stimulation (TBS) has been demonstrated in recent research by Huang and col. (2005) and Di Lazzaro and col. (2005). The exclusion criteria and safety norms applied to the standard rTMS will be used as well (see Gates, 1992; Pascual-Leone et al., 1993; Wassermann eta al., 1996; Wassermann, 1998).

No harmful side effects have been reported when the international safety guidelines are followed (Wassermann, 1998). The strong magnetic fields used by both fMRI and rTMS can dislocate ferromagnetic particles inside the brain and

the eyes. In order to exclude subjects with metal particles inside their brain, subjects will be required to complete a questionnaire and only if none of the exclusion criteria is met the subject will be allowed to participate in our experiment.
No immediate benefits for the subjects are expected from their participation in this study. Results, however, will permit us to understand more fully the functioning of the human brain.

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

1. Healthy males and females
2. Older than 18 years
3. Normal vision and hearing

4. Right-handed

Exclusion criteria

1. left-handedness or ambidexterity
2. drug or alcohol abuse
3. (history of) significant medical, psychiatric or neurological conditions
4. history of head injury with loss of consciousness
5. metal in cranium
6. epilepsy or family history of epilepsy
7. cardiac pacemaker
8. infarcations
9. implanted medical pump
10. intracardiac lines
11. history of psychiatric illness
12. claustrophobia
13. (suspected) pregnancy
14. motor threshold > 69%, checked during the first session.

Study design

Design

Study type: Observational non invasive

Masking:	Open (masking not used)
Control:	Uncontrolled

Recruitment

NL

Recruitment status:	Pending
Start date (anticipated):	25-08-2008
Enrollment:	18
Type:	Anticipated

Medical products/devices used

Registration:	No

Ethics review

Approved WMO

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	NL24331.042.08