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Transcranial Magnetic Stimulation (TMS) treatment study in auditory verbal hallucinations

Submission date
29/01/2012

Recruitment status
No longer recruiting

Registration date
10/02/2012

Overall study status
Completed

Last Edited
04/09/2014

Condition category
Mental and Behavioural Disorders

[ ] Prospectively registered
[ ] Protocol
[ ] Statistical analysis plan
[X] Results
[ ] Individual participant data

Plain English summary of protocol

Background and study aims
Auditory hallucinations are a common and often stressful symptom of psychiatric patients. About a third of patients do not respond to common drug treatments. In these patients, repetitive transcranial magnetic stimulation (rTMS) has been demonstrated as an effective therapy. The aims of this study are to improve the currently existing TMS treatment by evaluating the effects of the new theta burst protocol. The duration of effects is an important issue when establishing a new therapy. The theta burst protocol has shown longer lasting after effects as compared to previously used TMS protocols. We also aim to investigate the effects of TMS on cerebral blood flow. So far, it is not entirely clear why and how TMS works. We want to investigate the neuronal activity in language-related brain areas before and after TMS treatment with magnetic resonance imaging techniques.

Who can participate?
Patients with schizophrenia or schizoaffective disorder, suffering from medication-resistant auditory verbal hallucinations.

What does the study involve?
Participants will be randomly allocated to undergo a two-week treatment with TMS or a control treatment. Two magnetic resonance sessions and several psychopathology assessments have to be conducted.

What are the possible benefits and risks of participating?
Several studies of transcranial magnetic stimulation therapy for auditory hallucinations have shown significant positive effects. The patients included in the study suffer from medication resistant auditory hallucinations, a symptom that is often stressful and reduces quality of life. One possible benefit is a reduction of auditory hallucinations in the active treatment groups. 20-25% of patients have minor headaches at the beginning of the treatment period. In rare cases epileptic seizures have been reported. To minimize the risk of seizures several electroencephalography measurements will be conducted before and throughout the study. The study will be interrupted if we detect signs of elevated risk of seizures.

Where is the study run from?
The study takes place in the University Hospital of Psychiatry (Switzerland).

When is study starting and how long is it expected to run for?
Patients will be enrolled in the study from December 2008 to December 2012.

Who is funding the study?
Swiss National Fund (Switzerland).

Who is the main contact?
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Contact information

Type(s)
Scientific

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Study information

Scientific Title
Transcranial Magnetic Stimulation (TMS) treatment study in auditory verbal hallucinations: a randomised controlled trial

Study objectives
1. Theta-burst TMS is superior to previously used repetitive transcranial magnetic stimulation (rTMS) protocols concerning onset, extent and duration of reduction of auditory verbal hallucinations.
2. TMS effects are due to a reduction of neuronal activity in language related regions as measured by arterial spin labeling.

Ethics approval required
Old ethics approval format

Ethics approval(s)

Bern Cantonal Ethics Committee (Kantonale Ethikkommission Bern), 08/12/2008, ref:EK 112/08

Primary study design
Interventional

Study design
Randomized controlled trial

Study type(s)
Treatment

Health condition(s) or problem(s) studied
Schizophrenia or schizoaffective disorder, medication resistant auditory hallucinations

Interventions
1. Theta Burst transcranial magnetic stimulation (TBS group)
2. 1Hz transcranial magnetic stimulation and
3. Control group (treatment as usual)

A custom TMS stimulator (MagPro R 100, Medtronic Functional Diagnostics, Skovlunde, Denmark) is used to generate repetitive biphasic magnetic pulses. Magnetic pulses are delivered with a figure-8-coil (Magnetic Coil Transducer MC-B70, Medtronic). During the experiment, rTMS pulse intensity is adjusted to 90% of the motor threshold. Patients will be randomly assigned to receive a 1 Hz or theta burst (TBS) TMS protocol. In both treatment groups, the target area is stimulated for 10 consecutive days. Stimulation at 1 Hz was applied once a day, 4min on day 1, 8min on day 2 and 16min from day 3-10.

In the TBS group, each burst contains 3 pulses at 30 Hz, repeated with an interburst interval of 100 ms. TBS is applied in double trains with a 15 min intertrain interval. On the first 3 days, 2 double trains of TBS will be applied, whereas on days 310, 1 double TBS train was applied. Safety protocols are in accordance with international safety standards of rTMS experimentation.

The control group is receiving treatment as usual.

Magnetic resonance imaging and psychopathological ratings are performed one day before the start and on the last day of the study

Intervention Type
Other

Phase
Not Applicable

Primary outcome(s)
1. Psychopathology rates:
1.1. Positive and negative symtpom scale
1.2. Psychotic Symptom Rating Scales (PSYRATS)
1.3. Auditory hallucination rating scale
2. Cerebral blood flow as measured by magnetic resonance arterial spin labeling

Key secondary outcome(s)

1. Comparison of conventionally used 10-20 EEG coil placement approach with a frameless steretactic neuronavigation system to functionally defined (fMRI) target area
2. TMS effects on electroencephalography measures
3. Assessment of side effects

Completion date
31/12/2012

Eligibility

Key inclusion criteria
1. Diagnosis of schizophrenia or schizoaffective disorder according to ICD-10
2. Medication-resistant auditory verbal hallucinations
3. 1865-years of age, and right-handed
4. Therapy refractoriness is defined as non response to at least 2 antipsychotic treatments in common dosages, each administered for at least 8 weeks

Participant type(s)
Patient

Healthy volunteers allowed
No

Age group
Adult

Lower age limit
18 Years

Sex
All

Key exclusion criteria
1. History of epileptic seizures
2. Signs of elevated neuronal activity by electroencephalography (EEG)
3. Magnetic resonance (MR) contraindications, and
4. Medical disorders other than schizophrenia or schizoaffective disorder

Date of first enrolment
15/12/2008

Date of final enrolment
31/12/2012

Locations

Countries of recruitment
Switzerland

Study participating centre
University Hospital of Psychiatry
Bern
Switzerland
3000

Sponsor information

Organisation
Swiss National Fund (Switzerland)

ROR
https://ror.org/00yjd3n13

Funder(s)

Funder type
Government

Funder Name
Swiss National Fund (Switzerland) (ref 59077)

Results and Publications

Individual participant data (IPD) sharing plan

IPD sharing plan summary
Not provided at time of registration

Study outputs

Output type	Details	Date created	Date added	Peer reviewed?	Patient-facing?
Results article	results	15/03/2013		Yes	No