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Repetitive Transcranial Magnetic Stimulation in Anorexia Nervosa

Submission date
08/02/2013

Recruitment status
No longer recruiting

Registration date
06/03/2013

Overall study status
Completed

Last Edited
24/03/2016

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
Anorexia Nervosa (AN) is a serious disorder with often devastating consequences. Treatment outcomes are poor with only about 3 out of 10 in remission after one year of specialist treatment. Thus there is a strong need for new treatment strategies. From several studies evidence is emerging that self regulatory ability is weakened in a range of neuropsychiatric disorders, including AN. This could be a consequence of developmental dysfunction in fronto-striatal circuits (neural pathways in brain). High frequency repetitive transcranial stimulation (rTMS) improve self regulatory control and thus symptomatology in disorders that have a fronto-striatal dysfunction, such as bulimia nervosa or obsessive compulsive disorders. The specific aims of this two part study are firstly, to conduct as study to investigate the effects of one session of repetitive transcranial magnetic stimulation (rTMS) compared to sham rTMS in reducing negative emotions and preoccupation toward food and shape. This could increase food intake by increasing self regulatory control over compensatory behaviours such as restriction. This extends our recent findings of increased self-regulatory control as expressed by reduced craving and binge eating in people with a bulimic eating disorder. Secondly, a feasibility case series study will also be conducted in which a small number of individuals with AN will be offered 20 sessions (3 days per week) of rTMS over 6 weeks in order to establish whether a longer, therapeutic delivery of rTMS improves self-regulatory control over eating.

Who can participate?
In order to be eligible to take part in the study participants must be over the age of 18, right-handed and have a current diagnosis of Anorexia Nervosa or EDNOS-anorexia type (EDNOS: Eating Disorder Not Otherwise Specified).

What does the study involve?
Participation involves having a MRI brain scan and a real or sham (placebo) rTMS session. In order to detect the effects of rTMS not all participants will receive real rTMS, that is half of the participants will receive a sham (placebo) rTMS stimulation. This will be a random allocation and participants will not be aware of which (real or sham) stimulation they receive, however will be informed upon completion of the study. Participants will also be required to complete a number

of questionnaires (assessing mood and eating habits), ratings in relation to different food types and a neuropsychological task (brain puzzle) immediately before and after the stimulation session. We will also collect saliva samples to measure cortisol (this is a stress hormone).

What are the possible benefits and risks of participating?
The most common side effect of rTMS is a mild discomfort in the scalp beneath the magnetic coil, but some people also referred to a mild headache (easily treated with simple analgesic drugs). The magnetic coil makes loud clicks during treatment that are not loud enough to harm hearing, but patients will be asked to wear earplugs as a precaution. The coil can be changed during the procedure because it may warm up. This would only be slightly above body temperature and would never cause skin or hair damage. An inbuilt safety mechanism in the machine makes it switch off automatically when it has reached 40 degrees Celsius. Although the rTMS is seen as a safe procedure, the most serious side effect reported, though very rare, is a seizure. Regarding cardiac safety of the procedure, we have observed this procedure to be safe in people with bulimic disorders. The rTMS Adult Safety Screen will be done before rTMS and a final evaluation of discomfort with the rTMS procedure will also be done with another VAS (none to extreme discomfort). In addition, a list of side effects that have been reported with rTMS as recommended by the Safety of TMS Consensus Group will be checked. There are no risks associated with the administration of the interviews, neuropsychological tests and other questionnaires or saliva collection. No specific benefit is expected besides a possible reduction in their self regulatory control over behavioural symptoms such as food restriction. Nonetheless, the latter is expected to be relatively brief in duration for individuals participating in the RCT (hours) however slightly longer for those participating in the case series (days/weeks).

Where is the study run from?
Participants will be recruited from the outpatients eating disorder service at the Maudsley hospital, and via advertisements on the b-eat (national eating disorder charity) website. The testing will be conducted at the Institute of Psychiatry, London.

When is the study starting and how long is it expected to run for?
We expect to recruit and test participants from February 2013 up until September 2014.

Who is funding the study?
Eating Disorders Unit, Institute of Psychiatry, King's College London (UK) - Departmental funds

Who is the main contact?
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Contact information

Type(s)
Scientific

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Additional identifiers

EudraCT/CTIS number

IRAS number

ClinicalTrials.gov number

Secondary identifying numbers
N/A

Study information

Scientific Title
An integrated study of (a) an experimental sham controlled randomised trial (RCT) of one session of repetitive Transcranial Magnetic Stimulation (rTMS) and (b) a 20 session feasibility case series of therapeutic rTMS in outpatients with Anorexia Nervosa (AN)

Acronym
rTMS in AN

Study objectives
Based on our previous pilot study and the ability of rTMS to stimulate underlying cortical areas, we hypothesise that; in people with AN who are presented with highly appetising food stimuli real, high-frequency neuronavigated rTMS applied to the left dorsolateral prefrontal cortex (DLPFC), compared to sham rTMS, will lead to a reduction in:
1. Wanting to restrict food intake
2. Perceived stress and negative emotions
3. Food, eating and body related preoccupations; and
4. Salivary cortisol levels

The intervention will also lead to an improvement in body/interoceptive awareness and neuropsyhological tasks. Lastly, it will lead to an increase in food intake.

Ethics approval required
Old ethics approval format

Ethics approval(s)
NRES Committee London - City & East, 02/11/2012, ref: 12/LO/1525

Study design
Randomised parallel-group double-blind study

Primary study design
Interventional

Secondary study design
Randomised parallel trial

Study setting(s)
Hospital

Study type(s)
Treatment

Participant information sheet
Not available in web format, please use the contact details below to request a patient information sheet

Health condition(s) or problem(s) studied
Anorexia nervosa

Interventions
In the RCT, 64 participants will be randomised to receive real or sham rTMS in a parallel group double blind design. Ten participants from the RCT will do the feasibility study of 20 sessions of real rTMS 3 x week.

Repetitive Transcranial Magnetic Stimulation (rTMS) consists of a coil that is held by the researcher over the head of the participant which delivers pulses of magnetic field with a preselected frequency (10Hz in this study) and strength (determined individually as 110% of the motor threshhold). An individuals motor threshold will be determined by finding the minimum stimulus output to evoke 5 out of 10 motor evoked potentials greater than 50 microvolts. The target site for stimulation, the left DLPFC will be located using the brain scans acquired earlier in the day from the structural MRI. Neuronavigation software called Brainsight will be used to locate the area from the scan uploaded. After defining the exact area for stimulation, participants will be given 20 trains of 5 seconds (1000 pulses) with rest intervals of 55 seconds. This protocol is similar to those used in other studies and are within those recommended for safe use.

The sham rTMS makes the same noise but does not deliver any magnetic field. For the case series study, rTMS will be applied in 20 separate sessions, using the same parameters as the RCT.

Intervention Type
Procedure/Surgery

Primary outcome measure
The specific aim of both the RCT and the case series is to investigate the effects of repetitive transcranial magnetic stimulation (rTMS) on preoccupation with food, eating, weight and shape in people with Anorexia Nervosa (AN). The primary outcome measures used to asses this are Visual Analogue Scale (VAS) measuring levels of stress, anxiety, urge restrict, urge exercise, feeling fullness and feeling fat. In addition, the Depression Anxiety Stress Scale (DASS) and Eating Disorders Examination Questionnaire (EDE-Q) will be primary outcome measures in the feasibility case series study.

Secondary outcome measures
The secondary aims of the RCT is to investigate the effects of rTMS on a) performance in neuropsychological tasks, b) stress levels as measured by cortisol (a stress hormone that can be measured in saliva). In addition, we will investigate the acceptability and tolerability of rTMS in people with AN. The secondary outcome measures used to asses these are a computerised delayed discounting task, salivettes which collect saliva samples when chewed and VAS which asses tolerance and acceptability of rTMS.

Overall study start date
01/02/2013

Completion date
01/12/2014

Eligibility

Key inclusion criteria
1. Male and female participants who are aged 18 to 40
2. Body mass index (BMI) between 14 and 18.5 kg/m2
3. Current Diagnostic and Statistical Manual of Mental Disorders, 4th Edition (DSMIV) diagnosis of AN Restricting type (ANR), AN Binge/purging type (ANBP) or EDNOS anorexia type (EDNOSAN) (EDNOS: Eating Disorder Not Otherwise Specified)

Participant type(s)
Patient

Age group
Adult

Lower age limit
18 Years

Sex
Both

Target number of participants
64 (RCT) and 10 (Feasibility Study)

Key exclusion criteria
1. Having a history of head or eye injury
2. Having a history of a neurological disease including previous seizures of any kind
3. Having metallic implants in the head
4. Being dominantly left-handed
5. Being on a dose of any psychotropic medication that has not been stable for at least 14 days prior to participation in the study
6. Taking antipsychotic medication
7. Taking anticonvulsive medication
8. Being pregnant
9. Smoking more than 10 cigarettes /day
10. Having a current other major psychiatric disorder (e.g. major depressive disorder, substance

dependence, schizophrenia or bipolar disorder) needing treatment in its own right
11. Severe abnormalities in their blood test during the month prior to the study
12. An rTMS safety questionnaire will also be administered and if considered not safe to deliver rTMS, people will subsequently be excluded on this basis

Date of first enrolment
01/02/2013

Date of final enrolment
01/09/2014

Locations

Countries of recruitment
England

United Kingdom

Study participating centre
Institute of Psychiatry
London
United Kingdom
SE58AF

Sponsor information

Organisation
King's College London (UK)

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Sponsor type
University/education

Website

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ROR
https://ror.org/0220mzb33

Funder(s)

Funder type
University/education

Funder Name
King’s College London

Alternative Name(s)
Collegium Regale Londiniense, King's, KCL

Funding Body Type
Government organisation

Funding Body Subtype
Universities (academic only)

Location
United Kingdom

Results and Publications

Publication and dissemination plan
Not provided at time of registration

Intention to publish date

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	23/03/2016		Yes	No