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Using brain imaging to evaluate the effects of anxiety medication in patients with social anxiety disorder

Submission date
26/02/2014

Recruitment status
No longer recruiting

Registration date
17/03/2014

Overall study status
Completed

Last Edited
17/10/2017

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
Serotonin is identified as one of the causes and treatments of anxiety disorders like social anxiety disorder. A group of drugs called selective serotonin reuptake inhibitors (SSRIs) is often recommended as first treatment for this condition. However, it is not known how SSRIs work and SSRIs have rarely been studied in neuroimaging studies. The aims of this study are to examine changes in brain activation patterns, brain connectivity, brain structure and neural responses in participants taking SSRIs for social anxiety disorder.

Who can participate?
Men and women between 18-65 years old, suffering from social anxiety disorder

What does the study involve?
All participants undergo brain scanning before and after a nine week treatment period. During some of these scans, participants are exposed to emotionally relevant tasks, like viewing slides of faces with different emotional expressions, while their brain activity is being recorded with fMRI (functional magnetic resonance imaging). Other scans involve measurements of the serotonin and dopamine transporter proteins of the brain using PET (positron emission tomography). These brain scans are then repeated after drug treatment with either SSRIs or a dummy drug for social anxiety disorder (called placebo). Participants are randomly allocated to one of these two treatments. After the drug treatment period, and after brain scanning, all participants are offered additional treatment with cognitive behaviour therapy (CBT). This is a 9 week structured form of psychotherapy focusing on thoughts and behaviours that are problematic for people suffering from social anxiety disorder.

What are the possible benefits and risks of participating?
Benefits include free treatment of a potentially serious anxiety condition. Participants also receive a small sum of money (approximately 380 USD). The risks involved are minimal, with the benefits far outweighing the risks. During PET scans, participants are exposed to radioactive material, but in low doses that do not affect normal bodily functions. Pregnant or breastfeeding women will not be included. There are also safety issues regarding MRI/fMRI scans, i.e.

individuals who have metallic materials within the body may not be allowed to participate. Also individuals who have heart pacemakers or have underwent surgery of the heart or head may not participate. There may be unwanted side effects such as nausea or diminished libido from the study drugs, although previous research indicates that they are generally well tolerated.

Where is the study run from?
Uppsala University (Sweden)

When is the study starting and how long is it expected to run for?
It is expected that the study will start in mid-March 2014 (recruitment, initial neuroimaging, treatment) for the 24 participants while the remaining 24 participants will be assessed and treated during the autumn of 2014. A one year follow-up (with questionnaires) will be conducted. The study is expected to be completed by December 2015.

Who is funding the study?
Funding has been provided by the Swedish Council of Health, Working Life and Welfare; the Swedish Foundation for Humanities and Social Sciences; and the Swedish Research Council.

Who is the main contact?
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Contact information

Type(s)
Scientific

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Additional identifiers

Clinical Trials Information System (CTIS)
2013-002962-38

Protocol serial number
TF2013

Study information

Scientific Title
Mechanisms of action of selective serotonin reuptake inhibitor (SSRI) pharmacotherapy for social anxiety disorder: a randomised neuroimaging trial

Study objectives
It is hypothesised that treatment with the selective serotonin reuptake inhibitor (SSRI) escitalopram will alleviate social anxiety accompanied by attenuated neural responsiveness to emotional challenges in limbic brain regions including the amygdala and insula cortex. The study further evaluates, with exploratory analyses, how SSRI treatment of social anxiety disorder affects:
1. Functional brain connectivity between the amygdala and prefrontal cortex
2. Brain structure, i.e. gray matter volume and white matter integrity
3. Brain monoaminergic processes, i.e. serotonin and dopamine reuptake efficiency
It is also examined how monoamine-related gene variants influence the brain parameters above.

Ethics approval required
Old ethics approval format

Ethics approval(s)
Regional Research Ethics Committee, Uppsala, ref. 2013/184

Study design
Randomised controlled trial

Primary study design
Interventional

Study type(s)
Treatment

Health condition(s) or problem(s) studied
Social anxiety disorder (social phobia)

Interventions
Patients with social anxiety disorder will be randomised into one of two treatment conditions: Escitalopram 20 mg or active placebo. All other therapies will be avoided.

1. Administration of escitalopram, 1 tablet daily, is based on the accepted recommended dose 10 mg per day during the first week and 20 mg per day for the rest of the treatment period. Participants are informed that this drug has been effective in previous controlled trials.
2. Active placebo is administered with a similar capsule. Participants are informed that it is a neurokinin-1 receptor antagonist lacking the crucial anxiolytic substance, and hence that it has been ineffective in previous controlled trials.

The treatment period is 9 weeks (63 days). Participants have an extra drug supply for another 14 days because the day of the last neuroimaging assessment may vary (hence treatment could be prolonged for maximum 14 days). Participants will undergo neuroimaging assessment with fMRI (n=48) and PET (n=24) before and after the 9 week treatment period. After the initial 9 week treatment period and neuroimaging assessments, all participants are offered Internet-delivered

Cognitive Behavior Therapy (ICBT) for an additional 9 week period. This ICBT treatment is optional. The ICBT program has been found efficacious in several previous trials. Follow-up assessment (questionnaires) will be conducted after one year.

Intervention Type
Drug

Phase
Not Applicable

Drug/device/biological/vaccine name(s)
Escitalopram

Primary outcome(s)
1. The Liebowitz Social Anxiety Scale (LSAS)
2. Spielberger state anxiety inventory (STAI-S) during anticipatory anxiety in the fMRI-setting

Primary measures will be administered at 4 times: baseline, posttreatment after nine weeks of drug treatment, after nine weeks of additional (voluntary) cognitive behaviour therapy, and at 12 month follow-up

Key secondary outcome(s))
1. The Clinical Global Impression Improvement (CGI-I) scale
2. Social Interaction Anxiety Scale (SIAS)
3. Social Phobia Scale (SPS)
4. Social Phobia Screening Questionnaire (SPSQ)
5. Montgomery-Åsberg Depression Rating Scale (MADRS-S)
6. Beck Anxiety Inventory (BAI)
7. Quality of Life Inventory (QOLI)
8. Karolinska scale of personality (KSP)
9. NEO-PI-R, personality inventory
10. Spielberger trait anxiety inventory (STAI-T)

Secondary measures will be administered at 4 times: baseline, posttreatment after nine weeks of drug treatment, after nine weeks of additional (voluntary) cognitive behaviour therapy, and at 12 month follow-up

Completion date
31/12/2015

Eligibility

Key inclusion criteria
1. Social anxiety disorder (social phobia), according to DSM-5, must be the main diagnosis as assessed with the structured clinical interview for DSM disorders (SCID)
2. Otherwise somatically healthy
3. Age 18-65, but not postmenopausal
4. Willingness to participate in a symptom provocation brain imaging trial

Participant type(s)

Patient

Healthy volunteers allowed
No

Age group
Adult

Lower age limit
18 years

Upper age limit
65 years

Sex
All

Key exclusion criteria
1. Treatment of social anxiety within the three months preceding the study
2. Current serious or dominant psychiatric disorder other than social anxiety disorder (e.g. psychosis, major depressive disorder, bipolar disorder)
3. Suicidal ideation
4. Chronic use of prescribed medication that could influence the results (e.g. other anxiolytic or antidepressant drugs, certain hypnotics or herbs like St Johns Wort)
5. Abuse of alcohol or narcotics
6. Pregnancy or planned pregnancy during the study period
7. Menopause
8. Previous positron emission tomography (PET) examination
9. Contraindications for MRI investigation (e.g. implants or other metal objects in the body, brain and heart operations)

Date of first enrolment
15/03/2014

Date of final enrolment
31/12/2015

Locations

Countries of recruitment
Sweden

Study participating centre
Uppsala University
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SE-75142

Sponsor information

Organisation
Uppsala University (Sweden)

ROR
https://ror.org/048a87296

Funder(s)

Funder type
Government

Funder Name
The Swedish Council of Health, Working Life and Welfare (FORTE) (Sweden)

Funder Name
The Swedish Foundation for Humanities and Social Sciences (Sweden)

Funder Name
Vetenskapsrådet

Alternative Name(s)
Swedish Research Council, VR

Funding Body Type
Government organisation

Funding Body Subtype
National government

Location
Sweden

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	01/10/2017		Yes	No
Participant information sheet	Participant information sheet	11/11/2025	11/11/2025	No	Yes
Study website	Study website	11/11/2025	11/11/2025	No	Yes