

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	<input type="checkbox"/> Prospectively registered
Registration date 17/03/2014	Overall study status Completed	<input type="checkbox"/> Protocol
Last Edited 17/10/2017	Condition category Mental and Behavioural Disorders	<input type="checkbox"/> Statistical analysis plan
		<input checked="" type="checkbox"/> Results
		<input type="checkbox"/> 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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Study website
<http://www.sfstudie.se>

Contact information

Type(s)
Scientific

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Additional identifiers

EudraCT/CTIS number
2013-002962-38

IRAS number

ClinicalTrials.gov number

Secondary identifying numbers

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

Secondary study design

Randomised controlled trial

Study setting(s)

Other

Study type(s)

Treatment

Participant information sheet

<http://www.sfstudie.se/#tabs-3>

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 measure

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

Secondary outcome measures

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

Overall study start date

15/03/2014

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

Age group

Adult

Lower age limit

18 Years

Upper age limit

65 Years

Sex

Both

Target number of participants

48 individuals diagnosed with social anxiety disorder

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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Sponsor information

Organisation

Uppsala University (Sweden)

Sponsor details

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Sponsor type

University/education

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

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	01/10/2017		Yes	No