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The effect of medication for social anxiety disorder upon the production of chemical messengers in the brain

Submission date
01/02/2019

Recruitment status
No longer recruiting

Registration date
08/02/2019

Overall study status
Completed

Last Edited
03/05/2023

Condition category
Mental and Behavioural Disorders

[X] Prospectively registered
[ ] Protocol
[ ] Statistical analysis plan
[ ] Results
[ ] Individual participant data
[ ] Record updated in last year

Plain English summary of protocol

Background and study aims
Serotonin and dopamine are two chemical messengers in the brain that are likely to be involved in the causes and treatments of anxiety disorders. A group of drugs, selective serotonin reuptake inhibitors (SSRIs), is recommended as first-line treatment for social anxiety disorder. However, it is not well understood how the SSRIs exert their anxiety-reducing effects in the brain. The main aim of the study is to examine changes in brain serotonin and dopamine production, in participants suffering from social anxiety disorder, after treatment with the SSRI escitalopram. Treatment-induced changes in these neurotransmitters will be assessed with positron emission tomography (PET) and related to altered brain activity patterns assessed with functional magnetic resonance imaging (fMRI).

Who can participate?
Men and women between 18-64 years old, suffering from social anxiety disorder (patient group) as well as healthy volunteers (healthy control group).

What does the study involve?
Participants will undergo brain scanning both before and after 9 weeks of treatment with the SSRI escitalopram for individuals with social anxiety disorder. PET scanning is used to assess the production of serotonin and dopamine (2 scans before as well as after treatment). Patterns of brain activity during emotionally relevant tasks, e.g. viewing faces expressing different emotions, will also be recorded with fMRI. Blood and saliva samples will be collected for analyses of biological markers of social anxiety.

What are the possible benefits and risks of participating?
Benefits include free treatment of a potentially serious anxiety conditon. Subjects will also receive a small economic compensation for participating (approximately 280 USD). The risks involved are minimal, i.e. the benefits by far outweigh 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 having metallic materials within the body may not be allowed to

participate. Also, individuals having heart pacemakers or having undergone surgery of the heart, may not participate. There may be unwanted side effects such as nausea or diminished libido from the study drug, although previous research indicates that escitalopram is 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 February 2019 (recruitment, initial neuroimaging, treatment) for the first subjects enrolled. Neuroimaging assessments will be repeated after 9 weeks of treatment along with clinical assessments. A one-year follow-up (with questionnaires) will also be conducted. The study is expected to be completed, for all participants, by May 2023.

Who is funding the study?
Funding has been provided by the Swedish Research Council and Riksbankens Jubileumsfond - The Swedish Foundation for Humanities and Social Sciences

Who is the main contact?
Professor Tomas Furmark, tomas.furmark@psyk.uu.se

Contact information

Type(s)
Scientific

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Additional identifiers

Clinical Trials Information System (CTIS)
2018-000207-17

Protocol serial number
TF2018

Study information

Scientific Title
Serotonin-dopamine interactions in social anxiety disorder

Study objectives
It is hypothesised that responders (as compared no nonresponders) to treatment with the selective serotonin reuptake inhibitor (SSRI) escitalopram will exhibit alleviated social anxiety concomitantly with reduced brain serotonin synthesis capacity, assessed with PET, and reduced threat-related activation of the amygdala assessed with fMRI.

The study further evaluates, with exploratory analyses, how SSRI treatment of social anxiety disorder affects:
- Brain dopamine synthesis capacity assessed with PET
- The balance between serotonin/dopamine synthesis, i.e neurotransmitter interactions
- Functional brain connectivity between the amygdala and prefrontal cortex
- Brain structure, i.e. grey matter volume
- Telomerase activity in leukocytes

Ethics approval required
Old ethics approval format

Ethics approval(s)
Approved 18/01/2018, Regional Research Ethics Committee, Uppsala (Box 1964, SE-751 49 Uppsala, Sweden; +46 18 4717400; registrator@uppsala.epn.se), ref: 2018/001

Study design
Interventional study; non-randomised, single-group, single-centre evaluation of open-label escitalopram in patients with social anxiety disorder assessed with neuroimaging

Primary study design
Interventional

Study type(s)
Treatment

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

Interventions
Patients with social anxiety disorder will be treated with escitalopram 20 mg (10 mg first week), 1 tablet/daily, for 9 weeks and assessed with positron emission tomography (PET) as well as functional magnetic resonance imaging (fMRI) before and after treatment. This is a non-randomised open-label trial without treatment control group focusing on SSRI drug effects on brain parameters. Pre-treatment differences between patients and a healthy control group will also be evaluated. The brain parameters to be studied are serotonin and dopamine synthesis capacity (PET), neural activations during emotional fMRI paradigms, functional connectivity patterns, and gray matter volume.

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 a maximum of 14 days). Follow-up assessment with questionnaires will be conducted after 1 year.

Intervention Type
Drug

Phase
Not Applicable

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

Primary outcome(s)
Social anxiety, measured using:
1. The Liebowitz Social Anxiety Scale (LSAS), pre- and post-treatment
2. The Clinical Global Impression-Improvement (CGI-I) scale at post-treatment

Key secondary outcome(s))
Social anxiety measured pre- and post-treatment using:
1. Social Interaction Anxiety Scale (SIAS)
2. Social Phobia Scale (SPS)
3. Social Phobia Screening Questionnaire (SPSQ)
4. Montgomery-Åsberg Depression Rating Scale (MADRS-S)
5. Beck Anxiety Inventory (BAI)
6. Quality of Life Inventory (QOLI)
7. Spielberger state-trait anxiety inventory (STAI-S, STAI-T)

Additional measures for research purposes (not outcome measures):
8. Karolinska Scale of Personality (KSP)
9. NEO-PI-R, personality inventory
10. Temperament and Character Inventory (TCI)
11. Karolinska Sleepiness Scale (KSS)
12. Karolinska Sleep Questionnaire (KSQ)
13. Insomnia Severity Index (ISI)
14. Ritvo Autism and Asperger Diagnostic scale (RAADS-14)
15. Tellegen Absorption Scale (TAS)
16. Mystical Experiences Scale (MES)

Completion date
31/05/2023

Eligibility

Key inclusion criteria
1. Social anxiety disorder according to DSM-5, must be the main diagnosis as assessed with the structured clinical interview for DSM disorders (SCID) and the MINI interview
2. Otherwise somatically healthy
3. Age 18-64
4. Willingness to participate in a brain imaging trial (giving informed consent)

Participant type(s)
Patient

Healthy volunteers allowed
No

Age group
Adult

Lower age limit
18 years

Upper age limit
64 years

Sex
All

Total final enrolment
52

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 depressoin, bipolar disorder)
3. Suicidal ideation
4. Chronic use of other prescribed medication that could influence the results (e.g. antidepressants, anxiolytics, certain sleeping pills and herbal drugs like St John's Wort)
5. Abuse of alcohol or narcotics
6. Pregnancy of planned pregnancy during the study period
7. Menopause
8. Previous PET examination
9. Contraindications for MRI investigation (e.g implants or other metal objects in the body, brain and heart operations)
10. Heart insufficiency or previous heart surgery
11. Contraindications for treatment with escitalopram

Date of first enrolment
12/02/2019

Date of final enrolment
30/04/2023

Locations

Countries of recruitment
Sweden

Study participating centre
Uppsala university
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Sponsor information

Organisation
Uppsala university

ROR
https://ror.org/048a87296

Funder(s)

Funder type
Research council

Funder Name
Vetenskapsrådet

Alternative Name(s)
Swedish Research Council, VR

Funding Body Type
Government organisation

Funding Body Subtype
National government

Location
Sweden

Funder Name
Riksbankens Jubileumsfond

Alternative Name(s)
Bank of Sweden Tercentenary Foundation, Stiftelsen Riksbankens Jubileumsfond, Stiftelsen Riksbankens Jubileumsfond (RJ), RJ

Funding Body Type
Government organisation

Funding Body Subtype
National government

Location
Sweden

Results and Publications

Individual participant data (IPD) sharing plan
The data sharing plans for the current study are unknown and will be made available at a later date.

IPD sharing plan summary
Data sharing statement to be made available at a later date

Study outputs

Output type	Details	Date created	Date added	Peer reviewed?	Patient-facing?
Study website	Study website	11/11/2025	11/11/2025	No	Yes