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A neuroscience perspective on anxiety proneness - sex differences, monoaminergic pathways and treatment response

Submission date
08/07/2011

Recruitment status
No longer recruiting

Registration date
02/08/2011

Overall study status
Completed

Last Edited
27/06/2016

Condition category
Mental and Behavioural Disorders

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

Plain English summary of protocol

Background and study aims
Anxiety disorders are more common in women. It is not clear why but anxiety proneness may be related to imbalances in brain neurotransmitter systems such as the serotonin and dopamine systems. Escitalopram is a selective serotonin reuptake inhibitor and has previously been demonstrated to be effective in patients suffering from anxiety conditions like social anxiety disorder (SAD). SAD is characterized by excessive fear of being observed or scrutinized by unfamiliar persons. An individual with SAD is agonized by the potential risk of performing inadequately or showing overt signs of nervousness with resultant embarrassment or humiliation in social situations, for example when speaking in front of a group. SAD, and other anxiety disorders, can also be treated with psychosocial interventions like cognitive-behavior therapy (CBT). It has recently been demonstrated that CBT can be delivered as a structured self-help program via the internet. It is unclear, however, how effective a combination of drug and psychosocial treatments is. Moreover, it is not known how combined treatments change activity patterns in the brain. The aim of this study is to examine the brain processes underlying anxiety proneness, why anxiety proneness is elevated in women, and what biological processes are related to treatment outcome in patients with SAD.

Who can participate?
We will recruit 48 medication-free patients (men and women) between 20-65 years of age who fulfill the diagnostic criteria for social anxiety disorder (SAD). For comparison, we will also recruit 48 healthy people.

What does the study involve?
By use of neuroimaging techniques, this study examines serotonin and dopamine reuptake functions, as well as neural activation patterns during emotional stimulation, in patients diagnosed with SAD, before and after 9 weeks of treatment. Participants will be randomly allocated to receive either escitalopram in combination with Internet-delivered CBT, or a placebo (dummy) drug in combination with CBT. The effects of the treatment on serotonin and dopamine reuptake processes will be studied with positron emission tomography (PET). Moreover, neural activation patterns during emotional stimulation will be studied with

functional magnetic resonance imaging (fMRI). Brain activity will be recorded while patients experience anticipatory anxiety before making a public speech, and while they view images with varying degrees of emotional content. Assessments will be repeated after the 9-week treatment period. A group of healthy controls is also included in the study, for comparison with patients before treatment.

What are the possible benefits and risks of participating?
Escitalopram is usually well tolerated but may cause side effects like nausea for some individuals. Participants may experience discomfort while being assessed with PET or fMRI. During PET assessments short-lived radioactive tracer isotopes are injected. However, the radiation dose is well within established safety limits. We dont expect that participation in this study will lead to negative consequences provided that the safety regulations are followed.

Where is the study run from?
The study will be conducted at the Department of Psychology, Uppsala University, and University Hospital in Uppsala, Sweden.

When is the study starting and how long is it expected to run for?
September 2011 to December 2012

Who is funding the study?
The study is funded by the Swedish Council for Working Life and Social Research, the Swedish Research Council, and the Uppsala University Amersham fund.

Who is the main contact?
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Contact information

Type(s)
Scientific

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Clinical Trials Information System (CTIS)
2010-023007-10

Protocol serial number
TF2010

Study information

Scientific Title
A neuroscience perspective on anxiety proneness - sex differences, monoaminergic pathways and treatment response: a randomised controlled trial

Study objectives
1. Serotonin and dopamine reuptake functions are compromised in patients with social anxiety disorder, possibly more so in women than in men
2. Compromised serotonin reuptake functions are restored by successful treatment (escitalopram and CBT)
3. Patients on escitalopram, as compared to placebo, will possibly also demonstrate altered dopamine reuptake functions (due to an increased endogenous dopamine concentration or an effect by the medication on the transporter protein)
4. Serotonin and dopamine related genes affect reuptake functions and treatment success, possibly differently in women and men
5. Networks in the brain that generate and/or attenuate emotion, as measured by functional Magnetic Resonance Imaging (fMRI) during emotional activation, behave differently in women compared to men, and in patients with social anxiety disorder compared to healthy controls
6. Gray matter volume, measured with voxel-based morphometry (VBM), in emotion relevant areas in the brain, differ between women and men, and between patients with social anxiety disorder and healthy controls. That can also be true for white matter nerve fibers, measured with diffusion tensor imaging (DTI)
7. Women and men with social anxiety will differ from healthy controls regarding the extinction of learned (conditioned) fear, and women will demonstrate decreased extinction recall compared to men

Ethics approval required
Old ethics approval format

Ethics approval(s)
Research Ethics Committee, Uppsala, ref: 2010/226

Study design
Double-blind randomized controlled trial with two arms

Primary study design
Interventional

Study type(s)
Treatment

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

Interventions

1. A group of healthy controls is also included for pretreatment comparisons
2. Patients with social anxiety disorder will be randomized into one of two treatment conditions:
2.1. Either a escitalopram + CBT combination
2.2. Or a placebo + CBT combination
3. Principally, all other therapies will be avoided
4. Administration of escitalopram 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
5. Doses are packaged so that the patients take one capsule per day
6. Placebo is administered with a corresponding capsule without active substances
7. The CBT treatment consists of a previously evaluated self-help manual for social anxiety disorder that is divided into nine modules adapted for use over the Internet
8. Participants are asked to complete one module every week
9. Each module consists of information and exercises (homework assignments) and ends with a short quiz to check adherence
10. The CBT self-help program has been found efficacious in several previous trials

Intervention Type
Mixed

Primary outcome(s)
1. The Liebowitz Social Anxiety Scale (LSAS)
2. The Clinical Global Impression - Improvement (CGI-I) scale
3. Spielberger state-trait anxiety inventory (STAI-S) during antecipatory anxiety in the fMRI-setting

Key secondary outcome(s))
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. Karolinska Scale of Personality (KSP)
8. NEO PI-R
9. Spielberger state-trait anxiety inventory (STAI-T)

Completion date
31/12/2012

Eligibility

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

Healthy controls:
1. No psychiatric diagnosis and otherwise somatically healthy
2. Age 18 or older but not postmenopausal
3. Willingness to participate in a brain imaging trial

Participant type(s)
Patient

Healthy volunteers allowed
No

Age group
Adult

Lower age limit
18 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
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 investigations (e.g. implants or other metal objects in the body, brain and heart operations)

Date of first enrolment
01/09/2011

Date of final enrolment
31/12/2012

Locations

Countries of recruitment
Sweden

Study participating centre

Uppsala University
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Sponsor information

Organisation
Uppsala University (Sweden)

ROR
https://ror.org/048a87296

Funder(s)

Funder type
Research council

Funder Name
Forskningsrådet för Arbetsliv och Socialvetenskap

Alternative Name(s)
Swedish Council for Working Life and Social Research, FAS

Funding Body Type
Private sector organisation

Funding Body Subtype
Other non-profit organizations

Location
Sweden

Funder Name
The Uppsala University Amersham Fund (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	01/09/2016		Yes	No
Study website	Study website	11/11/2025	11/11/2025	No	Yes