Predicting treatment success in anxiety disorder patients by use of biomarkers

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Ethical review	Approved WMO
Status	Recruitment stopped
Health condition type	Anxiety disorders and symptoms
Study type	Observational non invasive

Summary

ID

NL-OMON46417

Source
ToetsingOnline

Brief title
Predictive biomarkers for treatment of anxiety

Condition

- Anxiety disorders and symptoms

Synonym
anxiety

Research involving
Human

Sponsors and support

Primary sponsor: Radboud Universitair Medisch Centrum
Source(s) of monetary or material Support: Ministerie van OC&W

Intervention

Keyword: anxiety disorder, fMRI, individualized treatment, Prediction

Outcome measures

Primary outcome

In the fMR session three paradigms will be tested to determine the neural phenotype:

prefrontal regulation task

salience processing task

face processing task

Therapy evaluation:

A therapy evaluation is routinly in place at pro Persona including a questionnaire battery. We will analyze the aquestionnaire data regarding the therapy outcome and relate results to previously determined neural mechanisms in the individual patient.

Secondary outcome

questionnaires:

FEELE (Emotional Adjustment Questionnaire for Adults, Grob & Horowitz, 2014)

Biological markers for stress:

heart rate

skin conductance

pupil dilation

shoulder muscle tension (MEG)

Study description

Background summary

Symptoms of anxiety are based on amygdala responsiveness, which can be evoked by the activation of multiple different brain circuits. We aim to characterize the following neural mechanisms that might cause amygdala hyperresponsiveness* high locus coeruleus drive, low prefrontal control or increased amygdala sensitivity. We hypothesize that variation in local sensitivity and variation in specific control mechanisms may explain why certain individuals are more fearful than others. The same phenotype may
result from different neural mechanisms.
State-of-the-art treatment for anxiety disorders is cognitive behavioral therapy, in particular exposure therapy. As we know that cognitive therapy improves prefrontal control processes, we assume that patients with a low prefrontal control have the highest benefit from cognitive therapy compared to patients with other non-prefrontal mechanisms.
The aim of this study is to identify which biomarkers predict the outcome of cognitive behavioral therapy. If we can define a reliable biomarker, it would be possible to select the most beneficial therapy for a patient based on his or her individual biomarker leading to symptoms of anxiety. Predictive biomarkers would help to individualize treatment and shorten treatment time and costs.

Study objective

We select patients that have a diagnosed anxiety disorder and are already enrolled to start an intensive exposure therapy program at Pro Persona/Overwaal. In an fMRI session their individual underlying neural mechanism (biomarker) associated with their symptoms of anxiety will be determined. After completion of the therapy program an evaluation questionnaire battery is in place at Pro Persona. We will analyze the data of the evaluation in regard to potential predictive power of previously established biomarkers in a patient. Our aim is to identify biomarkers that reliably predict the treatment success of cognitive behavioral therapy for the individual patient.

Study design

Patients will be informed about the study by their therapist. Two weeks before starting the intensive therapy program, a preparation meeting is routinely scheduled for all patients. During this appointment, the therapist will inform the patient about the rational of the study and hand out information material. Patients will be asked if they agree to share their contact data with the

researcher to be contacted in case they decide to participate. The researcher contacts the patient 2 days after they received the information material to schedule an appointment for an exposure session and the MRI session at the Donders institute.
First, an exposure session will be conducted by a psychologist to familiarize the patient with the scanner set-up and to decrease potential anxiety of lying in the scanner. After a successful exposure session patients take part in the fMRI session. At the institute, participants will be fully informed about the rationale and procedure of the fMRI investigation and will be asked to give their consent. During the fMRI investigation, three tasks will be applied to classify the dominant neuronal mechanism in the individual patient. A pre frontal regulation task will be applied to monitor activity in the prefrontal cortex. Amygdala reactivity will be monitored by applying an emotional face processing task. Salience processing will be used to monitor activity in the locus coeruleus. Stimulus materials for visual stimulation are taken from standardized stimulus sets. Tactile stimulation is applied using stimulation by electrodermal stimulation.
After the fMRI session, participants are asked to complete a set op questionnaires evaluating anxiety, depression, personality traits and emotion regulation strategies.
Therapy outcome is evaluated at pro Persona right after the treatment - this evaluation is conducted for all patients, regardless if they particpated in the study or not. Participants of the study fill in the same set of questionnaires again three months after completing their treatment in order to measure long-term benefit of exposure therapy.

Study burden and risks

MRI is a non-inversive imaging technique. Only occasionally (< 0,5%) subjects report vertigo-like sensations and/ or slight nausea symptoms due to movement in the static field of the scanner. Sensitivity to these effects varies considerably between individuals. In rare cases, minimal muscle contractions due to nerve stimulation abating when the scanning procedure stops. Acoustic noise from the MRI scanner can be reduced wearing shielded earphones during the scanning procedures.
Burdens and risks are very minimal to negligible. Since we are dealing with a highly anxious population, an MRI measurement might create more stress than in a healthy population. Therefore, an exposure session in the dummy scanner will be scheduled before the actual MRI session, to familiarize patients with the MRI environment and to decrease potential fears.

Incidental neurological findings during the fMRI session are reported to the participant's GP.

Contacts

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Trial sites

Listed location countries

Netherlands

Eligibility criteria

Age
Adults (18-64 years)
Elderly (65 years and older)

Inclusion criteria

diagnose of anxiety disorder
enrollment at intensive exposure therapy program at Pro Persona/Onderwaal Nijmegen
cognitive competent, 18-65 years
fMRI compatibility

Exclusion criteria

History of or current or previous neurological disorders, psychosis or delusional disorders
History of current brain surgery or epilepsy
Pregnancy
Metal parts in the upper body, implants, medical devices or medicinal plasters

Claustrophobia

Study design

Design

Study type: Observational non invasive

Masking:	Open (masking not used)
Control:	Uncontrolled
Primary purpose:	Basic science

Recruitment

NL

Recruitment status:	Recruitment stopped
Start date (anticipated):	05-04-2019
Enrollment:	75
Type:	Actual

Ethics review

Approved WMO

Date:	12-07-2018
Application type:	First submission
Review commission:	CMO regio Arnhem-Nijmegen (Nijmegen)

Study registrations

Followed up by the following (possibly more current) registration

No registrations found.

Other (possibly less up-to-date) registrations in this register

No registrations found.

In other registers

Register	ID
CCMO	NL64610.091.18