Fear acquisition and extinction mechanisms in relation to treatment outcome: a study in patients with anxiety disorders

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1) To study the predicitve value of fear acquisition and extinction mechanisms on treatment outcome in anxiety disordered patients. 2) To study pathological fear acquisition and extinction in anxiety disorders: what are the differences in...

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

Summary

ID

NL-OMON39222

Source
ToetsingOnline

Brief title
Fear acquisition & extinction mechanisms in relation to treatment outcome

Condition

- Anxiety disorders and symptoms

Synonym
Anxiety disorder

Research involving
Human

Sponsors and support

Primary sponsor: Universiteit Utrecht

Source(s) of monetary or material Support: Ministerie van OC&W

Intervention

Keyword: Anxiety, Fear conditioning, Polymorphisms, Treatment outcome

Outcome measures

Primary outcome

Primary endpoint measures of change indices are: State Trait Anxiety Inventory (state subscale) and Disorder specific ratings. Physiological (skin conductance response and electromyograhy) and self-reported (Visual analogue scales) measures are used to measure speed of fear acquisition, fear extinction and context learning. Various polymorphisms will be genotyped: serotonine (5HTTLPR, 5-HTR1A), dopamine (COMT Val158Met, DAT), cannabinoïd (CB1 rs2180619 en CB1 rs1049353) and glutamergic polymorfisms (SLC1A1/EAAC1 rs3780412, rs301430). Promising newly detected polymorphisms available through the literature will be tested as well.

Secondary outcome

Secondary objectives: several questionnaires and neuropsychological tests (see section 3.8 and 4.4 of the research protocol) were added to be able to control for possible modulating effects on fear conditioning, such as: depresion, memory function and life-events.

Study description

Background summary

Anxiety disorders are among the most prevalent psychiatric disorders, with substantial genetic involvement. Dysfunctional fear acquisition and extinction

mechanisms are postulated to underlie anxiety disorders. Fear acquisition and extinction are extremely suitable to systematically study in the laboratory using classical fear conditioning paradigms. These paradigms can be extended using contextual cues that signal safety or threat. Previous research in healthy participants indicated that participants who were unable to learn the association between a fearful conditioned stimulus and context, displayed higher trait anxiety than persons who learn to differentiate between contextual cues of threat and safety. Next step is to investigate pathological fear acquisition and extinction mechanisms in patients with anxiety disorders, and to investigate the predictive value of these mechanisms on treatment outcome. State of the art treatment of anxiety disorders is exposure with response prevention (ERP), a behavioral treatment in which anxiety extinction mechanisms are at the core of the procedure. The exact relationship between speed of fear acquisition -and extinction and subsequent treatment effect in patients with anxiety disorders is unclear.
Several genetic polymorphisms seem to be involved in dysfunctional fear conditioning, extinction and the development of anxiety disorders. Most genetic mechanisms related to fear acquisition and extinction have been investigated using animal models, and to date few studies have investigated relationships between genetic polymorphisms, fear acquisition and extinction mechanisms and outcome in anxiety disordered patients. Therefore, it seems highly worthwhile to study the relationship between genetic polymorphisms, fear acquisition and extinction mechanisms and treatment outcome in anxiety disorder patients.

Study objective

1) To study the predicitve value of fear acquisition and extinction mechanisms on treatment outcome in anxiety disordered patients.
2) To study pathological fear acquisition and extinction in anxiety disorders: what are the differences in conditioning mechanisms between patients with anxiety disorders and healthy controls.
3) To study the genetic underpinnings of fear acquisition and extinction. To study the second objective, associations are studied between genetic polymorphisms involved in dopamine, glutamate, neuronal growth and serotonin pathways, and speed of fear acquisition/ extinction in patients with anxiety disorders versus healthy controls.
4) To explore relationships between genotype, fear acquisition and extinction and treatment outcome; is a mediational versus a liability model likely? To study the third objective, results from objectives 1 and 2 are combined with model fitting procedures (using mplus) to test the most likely model to explain the relationship between genetic factors, speed of fear acquisition and extinction and treatment change.

Study design

250 patients with lifetime anxiety disorders are included in the study. With

respect to some of the research questions tested they are compared with respectively 60 helathy controls (conditioning task 1) and 150 healthy controls (conditioningtask 2, see METC protocol nr. NL31689.041.10). Patients are recruited at the Academic Anxiety outpatient clinics Altrecht (AAA). Part of the standars procedure at the AAA, is the assessment of standardized qualitative and quantitative measures of (general and disease specific) anxiety in all patients. These measurements are being assessed at pre-treatment, post treatment and 6 months after completing treatment to gain insight into the treatment effects. Beside these questionnaires that are part of the standardized care, several questionnaires and neuropsychological tests are being assessed primary for the present study. These will measure factors that may interfere with conditioning mechanisms (like memory). Further, two tasks are performed in a (virtual) computerized environment to assess fear acquisition and extinction using several contextual cues, in a quasi-experimental design. Lastly, in all participants blood is drawn by a trained research assistent (or in case of refusal buccal swabs are collected) to collect DNA using standardized procedures.

Study burden and risks

All participants are asked to visit the department of experimental psychology once for a period of three hours and forty minutes. Participants will possibly experience minor discomfort during the fear conditioning tasks, since shock administration is involved. No health risks are associated with the study.

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Trial sites

Listed location countries

Netherlands

Eligibility criteria

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

Inclusion criteria

a. Patients with a lifetime diagnosis of the following disorders as a primary diagnosis: Panic disorder with or without agoraphobia, social anxiety disorder, specific phobia, generalized anxiety disorder, post-traumatic stress disorder and obsessive compulsive disorder.
b. Males and females between 18 and 65 years old.
c. Command of the Dutch language (i.e. ability to understand procedures and questionnaires).
d. Normal or corrected normal vision.;The inclusion criteria for the healthy controls participating in conditioning task 1 are the same as described above, with the exception of criterium a.

Exclusion criteria

a. Current comorbid severe psychiatric disorder in the past 6 months: i.e. severe major depressive disorder (BDI * 30), bipolar disorder, psychotic disorder.
b. Lifetime history of substance dependence, or substance abuse within the last three months.
c. Mental retardation (IQ < 80)
d. History of any physical disease which may confound the results of the study according to the investigator, like brain damage.
e. Hearing/ vision problems
f. Current use of antipsychotic medication;The inclusion criteria for the healthy controls participating in conditioning task 1 are the same as described above.

Study design

Design

Study type:	Observational invasive
Intervention model:	Other
Allocation:	Non-randomized controlled trial
Masking:	Open (masking not used)
Control:	Active
Primary purpose:	Basic science

Recruitment

NL

Recruitment status:	Recruitment stopped
Start date (anticipated):	24-10-2011
Enrollment:	310
Type:	Actual

Ethics review

Approved WMO Date:	09-09-2011
Application type:	First submission
Review commission:	METC Universitair Medisch Centrum Utrecht (Utrecht)
Approved WMO Date:	17-07-2013
Application type:	Amendment
Review commission:	METC Universitair Medisch Centrum Utrecht (Utrecht)
Approved WMO Date:	25-11-2014
Application type:	Amendment
Review commission:	METC Universitair Medisch Centrum Utrecht (Utrecht)

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	NL35780.041.11