Pharmacological enhancement of fear extinction in OCD; a randomized placebo controlled, double blind study.

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Ethical review	Approved WMO
Status	Pending
Health condition type	Psychiatric disorders
Study type	Interventional

Summary

ID

NL-OMON33819

Source
ToetsingOnline

Brief title
DCS addition in OCD

Condition

- Psychiatric disorders

Synonym
Obsessive Compulsive Disorder;

Research involving
Human

Sponsors and support

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

Intervention

Keyword: D-cycloserine, Exposure and Response Prevention, Fear Extinction, OCD

Outcome measures

Primary outcome

The change in Yale Brown Obsessive Compulsive Scale (Y-BOCS), time of onset of change on the Y-BOCS and time of administering DCS (directly pre- or post ERP).

Secondary outcome

VLGT : Verbal Learning and Memory Test

WCST: Wisconsin Card Sorting Test

TOL: Tower of London

ET: Extinction Task

CGI: Clinical Global Impression scale

BABS: Brown Assessment of Belief Scale

HDRS: Hamilton Depression Rating Scale

HARS: Hamilton Anxiety Rating Scale

SDS: Sheehan Disability Scales

WHOQOL World Health Organization Quality of Life

FSEC Fawcett side effects checklist

Tic-P: Trimbos/iMTA questionnaire for Costs associated with Psychiatric Illness

Study description

Background summary

Obsessive Compulsive Disorder (OCD) is a chronic and severe psychiatric disorder which affects 2-3% of the general population. The use of medication

for OCD is very common, but often less effective without psychotherapy. Behavioural therapy (Exposure and Response prevention) is currently the treatment of choice for OCD and aims to help patients changing their behaviours. Notwithstanding effective treatment 40-60 % of OCD patients fail to respond to behavioural exposure therapy. Procedurally, exposure is based on extinction of conditioned fear. Recent work in rodents and humans has demonstrated that acute treatment with D-cycloserine (DCS) a partial agonist of the NMDA-receptor enhances the learning and memory processes underlying extinction of fear. Adding DCS to exposure therapy might improve treatment outcome in OCD and at a faster rate.

Study objective

treatment outcome in OCD.
Objective: The objective for this study is fourfold. First we will determine whether DCS addition to behavioural exposure therapy may enhance fear extinction and improve symptoms in OCD. Our hypothesis is that improvement will occur and at a faster rate than with no addition of DCS. Additionally we aim to establish the optimal timing of administration of D-Cycloserine (directly pre- or post ERP). Furthermore, we will examine the underlying pathophysiologic mechanisms of fear extinction in OCD with neuro-imaging studies. The brain activity of the amygdale and cortico-striatal circuits will be assessed in fifty patients before and after behavioural exposure treatment and DCS by means of functional magnetic resonance imaging (fMRI) in a fear extinction paradigm. In addition, we will examine the fear extinction enhancement of DCS using a neuropsychological paradigm. We hypothesize based on rodent and limited human studies that DCS is a performance enhancer in different learning, memory and executive tasks. Finally, from a health economic perspective the question is whether the benefits of treatment only lead to an increased efficiency (less therapy sessions and thus costs for similar health outcomes),or better health outcomes for the same short term costs (therapy sessions). Thereby faster and/or better response could also reduce indirect costs (generated by lost productivity in paid work).

Study design

A randomized, double blind, placebo-controlled fixed dose study.

Intervention

Intervention: Half of the subjects will be randomly assigned to the placebo condition and the other half will be randomly Subjects will be randomized to treatment with either placebo, or single fixed dosages of 125mg in 1 of 3 possible conditions. Patients in condition 1 will receive DCS before and placebo after exposure sessions. Patients in condition 2 will receive Placebo both before and after exposure sessions. Patients in condition 3 will receive

placebo before and DCS after exposure sessions.

Study burden and risks

Side-effects of D-Cycloserine are limited, since study dosing is low (125 mg). Exept for this small chance on side effects, there are no serious risks associated to this study. Advantages to the subjects can be expected because of the potential therapeutic effect (faster reduction in OCD-symptoms and lower drop-out rates). Futhermore, the results can offer insight into the pathofysiology of OCD and may lead to future development of more effective treatmentmethods.

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

- All patients meet the DSM-IV criteria for OCD
- Y-Bocs score: * 18 if obsessions and compulsions; * 12 if only obsessions or compulsions
- Male and female, aged between 18-70 years
- Female patients of childbearing potential must have a negative pregnancy test and use reliable method of contraception.
- Written informed consent
- Eligible for exposure therapy

Exclusion criteria

- Presence of any of the following DSM IV conditions:
* Major depression (HDRS * 15)
* Bipolar Disorder
* Schizophrenia or any other psychotic disorder
* Tic disorder
* Substance related disorder during the past 6 months
* Epilepsy or any structural CNS disorder of stroke within the last year;- Presence of primary or co-morbid personality disorder
- Evidence of clinically significant and unstable cardiovascular, gastrointestinal, pulmonary, Renal, hepatic, endocrine or haematological disorders, glaucoma, myocardial infarction within de past year or micturition abnormalities.
- Currently taking benzodiazepines
- Patients at risk for suicide
- Multiple serious drug allergies of known allergy for DCS
- Inability to speak Dutch or English

Study design

Design

Study phase:	2
Study type:	Interventional
Intervention model:	Parallel
Allocation:	Randomized controlled trial
Masking:	Double blinded (masking used)
Control:	Placebo
Primary purpose:	Treatment

Recruitment

NL

Recruitment status:	Pending
Start date (anticipated):	01-04-2009
Enrollment:	60
Type:	Anticipated

Medical products/devices used

Product type:	Medicine
Brand name:	Seromycin
Generic name:	D-cycloserine

Ethics review

Approved WMO

Application type:	First submission
Review commission:	METC Amsterdam UMC

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
EudraCT	EUCTR2009-010919-32-NL
CCMO	NL24096.018.09