Predicting treatment outcome in obsessive-compulsive disorder using neuroimaging biomarkers

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Ethical review	Approved WMO
Status	Recruiting
Health condition type	Anxiety disorders and symptoms
Study type	Interventional

Summary

ID

NL-OMON45849

Source
ToetsingOnline

Brief title
neuroimaging biomarkers for OCD treatment

Condition

- Anxiety disorders and symptoms

Synonym
Obsessive-compulsive disorder

Research involving
Human

Sponsors and support

Primary sponsor: Academisch Medisch Centrum
Source(s) of monetary or material Support: NWO

Intervention

Keyword: Cognitive Therapy, Neuroimaging, Obsessive-Compulsive Disorder, Serotonin Uptake Inhibitors

Outcome measures

Primary outcome

Classifier accuracy as the proportion of patients correctly classified as responder (sensitivity) and non-responder (specificity), differences in the proportion of responders between the randomized (first) and fMRI biomarker allocated (second) cohort, independent network components using resting-state fMRI, structural connectivity using diffusion tensor imaging (DTI), task related activity and connectivity using event-related fMRI, brain volume using structural MRI and cerebral bloodflow using Arterial Spin Labeling (ASL).

Secondary outcome

Response rate defined as at least a 35% pre-treatment to post-treatment reduction in YBOCS score (Farris et al. 2013), clinical Global Impression-Improvement (CGI-I) score of 1 ('very much improved') or 2 ('much improved').

Study description

Background summary

Treatment for OCD is based on stepped care, in which patients initially receive pharmacological treatment with selective serotonin reuptake inhibitors (SSRIs) orpsychological treatment with cognitive-behavioral therapy (CBT) (van Balkom et al. 2013). Both these treatments are effective, but 40-60% of patients do not benefit sufficiently (Pallanti et al. 2002; Eddy et al. 2004). Although multiple treatment steps ensure that the majority of patients do receive effective treatment, approximately 50% of patients are exposed to one or more

ineffective treatments, and therefore to prolonged treatment trajectories and avoidable disease burden, side effects, and risks. One of the main priorities of the European Commission and National Institute of Mental Health therefore is to move away from trial-and-error based clinical practice and develop biomarkers that enable personalized treatment (Insel 2009; Olatunji et al. 2013). Yet, despite the efforts taken, there are still no reliable markers to guide individual treatment decisions in psychiatry. Recently, using a machine learning technique called support vector classification combined with leave-one-out cross-validation, we discovered that a resting-state network centered around the dorsomedial prefrontal cortex could predict recovery from depression with 84% sensitivity and 85% specificity (van Waarde et al. 2015). To optimize treatment for OCD and reduce the burden and costs associated with unsuccessful therapy, we aim to discover treatment outcome biomarkers for OCD by combining neuroimaging with machine learning methods. Similar to studies on the prediction of treatment outcome, research on the longitudinal effects of treatment are scarce. In OCD, the disbalance between the ventral and the dorsal cortico-striato-thalamo-cortical circuit leads to increased anxiety, repetitive behaviors and the inability to modulate responses (van den Heuvel et al. 2015). The most common findings in neuroimaging studies investigating the effects of treatment are decreased activity in the ventral circuits and increased activity in the dorsal circuits (Thorsen et al. 2015). In addition to our other aim, we will investigate the longitudinal effects of OCD treatment on functional and structural neuroimaging. The analysis of CBT and SSRI-related changes at the level of brain areas and circuits will provide more perspective on the pathophysiology of OCD and the response to different treatments. In order to relate the alterations in functional imaging to actual treatment-induced changes instead of time-related changes or test-retest reliability, the comparison with a healthy population is crucial.

Study objective

Our primary objectives are 1) to discover and validate a treatment selection fMRI biomarker for allocating OCD patients to CBT or SSRIs, and 2) to determine the divergent longitudinal effects of SSRIs and CBT on functional and structural brain measures in OCD.

Study design

Patients in the first cohort will be treated with SSRI or CBT to develop and validate a treatment selection fMRI biomarker for allocating OCD patients and to determine the divergent longitudinal effects on brain measures of treatment in patients with OCD. Treatment will be performed as usual and in accordance with the national guidelines. In the second cohort, patients will be allocated to SSRI or CBT based on fMRI biomarkers identified in the first cohort.

Intervention

The subjects will be randomized between SSRI treatment and CBT. Treatment is as usual, consisting of a high dosed SSRI or group sessions CBT on a weekly basis for 16 weeks.

Study burden and risks

As the participates will be treated according to the national guidelines, the burden and risk of treatment will be the same as usual. The additional risk for participation in this study is limited to MRI scanning, which can be considered negligible. Randomization to SSRIs or CBT and participating in the neuroimaging study imposes an additional burden to patients which can be considered minimal. Given that our approach is expected to provide a large benefit for patients in the future, we consider this additional burden well justified.

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

* Diagnosis of obsessive compulsive disorder (OCD) according to the DSM-IV
* 18-70 years of age
* Willingness and ability to give written informed consent and willingness and ability to understand, to participate and to comply with the study requirements

Exclusion criteria

* Bipolar disorder, current or past psychosis, primary alcohol or drug abuse
* Contraindication for MRI such as metal implants, claustrophobia, left-handedness and pregnancy * Major head trauma or neurological disease, current or in history
* Adequate treatment of OCD with high dosed SSRI or CBT at the moment of screening or within 4 weeks before screening
* Current treatment with tricyclic antidepressant or antipsychotic medication

Study design

Design

Study type:	Interventional
Intervention model:	Other
Allocation:	Randomized controlled trial
Masking:	Open (masking not used)

Primary purpose: Treatment

Recruitment

NL

Recruitment status:	Recruiting
Start date (anticipated):	28-11-2016
Enrollment:	202
Type:	Actual

Ethics review

Approved WMO

Date:	01-09-2016
Application type:	First submission
Review commission:	METC Amsterdam UMC
Approved WMO Date:	03-11-2016
Application type:	Amendment
Review commission:	METC Amsterdam UMC
Approved WMO Date:	21-03-2017
Application type:	Amendment
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

ID: 23107
Source: NTR
Title:

In other registers

Register	ID
CCMO	NL57808.018.16
OMON	NL-OMON23107