Abnormal patterns of brain connectivity in major depression

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Ethical review	Approved WMO
Status	Recruiting
Health condition type	Mood disorders and disturbances NEC
Study type	Observational non invasive

Summary

ID

NL-OMON38392

Source
ToetsingOnline

Brief title
APOBCIMD

Condition

- Mood disorders and disturbances NEC

Synonym
"have the blues", mood disorder

Research involving
Human

Sponsors and support

Primary sponsor: Universiteit Maastricht
Source(s) of monetary or material Support: NWO/FES

Intervention

Keyword: Biomarkers, Connectivity, fMRI, Unipolar depression

Outcome measures

Primary outcome

Differences in structural T1, DTI, functional resting-state and functional task-related connectivity and effective connectivity between:

1)depressed patients and healthy controls

2)depressed patients and healthy participants with a genetic vulnerability to depression

3)healthy controls and healthy participants with a genetic vulnerability to depression

4)depressed patients before and after 9 months of treatment

Correlations between:

1)severity of depression and functional/anatomical connectivity

2)cognitive performance and functional/anatomical connectivity

3)treatment success and changes in functional/anatomical connectivity

Secondary outcome

Not applicable

Study description

Background summary

Major depression is characterized by persistent, pervasive feelings of sadness, guilt, and worthlessness. This baseline state has triggered a wealth of positron emission tomography (PET) or single photon computed tomography (SPECT) resting state studies. It was shown that patients suffering from major depression show decreased brain activation in prefrontal cortex regions, implicated in cognition, and increased activation in the regions involved in emotion processing. These neuroimaging methods have significant limitations which might be overcome by using non-invasive functional Magnetic Resonance Imaging (fMRI). Furthermore, newly developed fMRI methods that assess slow fluctuations in the blood oxygen level dependent (BOLD) response allow the investigation of the functional connectivity between brain regions. Insight into changes in functional connectivity will increase our knowledge about what goes wrong in *a depressed brain*.

Study objective

The objective of the study is to answer the following research questions:
1) What differences do exist in functional connectivity between patients with unipolar depression and healthy controls?
2) Can changes in functional connectivity be used as neurobiological marker for depression?
3) Do changes in anatomical connectivity underlie these changes in functional connectivity?
4) Is the severity of the depression related to the changes in functional/anatomical connectivity?
5) How does connectivity change after treatment?
6) Do healthy controls with an increased risk to develop depression, also show the changes in functional/anatomical connectivity that are found in depressed patients?
7) What is the effect of sad mood induction on effective connectivity, and is there a difference between the effect on healthy volunteers with and without a family history of depression and depressed participants?
8) Do depressed people have difficulty disengaging their attention from emotional stimuli compared to healthy participants, and
9) Does treatment modify the abnormal attentional patterns of depression?

Study design

Research questions 1 till 4 and questions 6-8 will be answered with a between-subject design: functional and anatomical connectivity, mood and cognition will be measured in all three groups of participants. Research questions 5 and 9 will be answered with a within-subject design: the group of depressed patients will be tested before and 9 months after treatment. Research question 7 will be answered with a within-subject design: effective

connectivity will be measured before and after a mood induction.

Study burden and risks

BURDEN
Depressed patients recruited from the participating centres will be tested on two occasions: once before treatment and once 9 months later. People with depression recruited from the general population who do not receive treatment will be tested once. For those participants a screening session of about 2 hours will take place before testing. Healthy volunteers will be tested once. A test session includes MRI scanning (63 min in total, including performing two cognitive tasks (25 min) and mood induction (10 min) and two resting state scans (8 min each)) and performing two cognitive tasks outside the scanner (50 min) and lasts in total about two hours. Additionally, all participants will be asked to complete a series of questionnaires at home (30 min) before each session.
RISKS
Although the risks involved in this study are minor, there is in MRI research the possibility of an incidental finding. Further, while the effects of musical sad mood induction procedure are considered transient, there is the possibility of a longer lasting effect on participants* mood.

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

PATIENTS
Between 18 - 70 years old and able to give voluntary informed consent
Diagnosis of unipolar depression. The diagnosis of depression will be made by the participants* treating psychiatrist/ psychologist and confirmed with the Structured Clinical Interview for DSM-IV (SCID-I).
Severity of the depression: moderate to severe (BDI-II score >=20)
Duration of the depression: longer than 2 months
Are already receiving or will receive in the coming weeks treatment for depression;HEALTHY PARTICIPANTS WITH FAMILY HISTORY OF DEPRESSION
Between 18 - 70 years old
No current or history of major psychiatric illness
A first-degree relative (i.e. father, mother, brother or sister) that has been diagnosed with unipolar depression. This diagnosis needs to be confirmed by the GP, psychologist or psychiatrist of the family member;HEALTHY CONTROLS
Between 18 - 70 years old
No current or history of major psychiatric illness
No family history of major depression

Exclusion criteria

PATIENTS
Meeting DSM-IV criteria for schizophrenia, schizo-affective disorder, bipolar disorder or an anxiety disorder as a primary diagnosis
Meeting DSM-IV criteria for drug dependence as a primary diagnosis
High suicidal risk (evaluated by the treating clinicians as part of standard therapy procedures)
MRI contra-indications, such as claustrophobia, metal parts in the body and, for women, current pregnancy or breastfeeding
Serious medical or neurological illness
Currently taking centrally acting medication which is known to have a large effect on brain functioning, such as benzodiazepam
HEALTHY PARTICIPANTS WITH FAMILY HISTORY OF DEPRESSION
Meeting DSM-IV criteria for drug dependence, except caffeine or nicotine
MRI contra-indications, such as claustrophobia, metal parts in the body and, for women, current pregnancy or breastfeeding

Serious medical or neurological illness
Currently taking centrally acting medication which is known to have a large effect on brain functioning, such as benzodiazepam
HEALTHY CONTROLS
Meeting DSM-IV criteria for drug dependence, except caffeine or nicotine
MRI contra-indications, such as claustrophobia, metal parts in the body and, for women, current pregnancy or breastfeeding.
Serious medical or neurological illness
Currently taking centrally acting medication which is known to have a large effect on brain functioning, such as benzodiazepam

Study design

Design

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

Recruitment

NL

Recruitment status:	Recruiting
Start date (anticipated):	08-11-2011
Enrollment:	150
Type:	Actual

Ethics review

Approved WMO

Date:	09-02-2011
Application type:	First submission
Review commission:	METC academisch ziekenhuis Maastricht/Universiteit Maastricht, METC azM/UM (Maastricht)

Approved WMO

Date:	09-03-2012
Application type:	Amendment
Review commission:	METC academisch ziekenhuis Maastricht/Universiteit Maastricht, METC azM/UM (Maastricht)

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	NL34583.068.10