Brain morphology in bipolar twin pairs compared with healthy control twin pairs - Follow up

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Objectives1. Are there differences in brain structures in bipolar twin pairs compared to their (healthy) co-twins and healthy control twin pairs?2. If there are changes in brain volume, will these changes differ across a 5 year interval between...

Ethical review	Not approved
Status	Will not start
Health condition type	Other condition
Study type	Observational non invasive

Summary

ID

NL-OMON30080

Source
ToetsingOnline

Brief title
BrABiT: Brain Anatomy in Bipolar Twins

Condition

- Other condition

Synonym
Affective Disorder, Manic-Depressive Disorder

Health condition

Psychiatrische stoornissen: Bipolar Disorder (Manisch-Depressiviteit)

Research involving
Human

Sponsors and support

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

Intervention

Keyword: Bipolar disorder, Follow up, Trimodal MRI, Twin pairs

Outcome measures

Primary outcome

- Volume changes across time: Volume change within subjects, in patients as well as in (healthy) co-twins and healthy control twin pairs. This means the difference in brain volumes for T0 and T5 (in years).

Secondary outcome

- Diagnosis. Do patients have more and larger structural brain abnormalities compared to healthy control twin pairs, but also compared to their (healthy) co-twin.

- Zygosity: Do patients have more and larger structural brain abnormalities compared to healthy control twin pairs and is there a difference between mono- and dizygotic twin pairs.

- Sexe. Is there a difference in structural brain abnormalities between males and females.

Study description

Background summary

Bipolar Disorder (BD) is a common, severe, and often life-threatening condition with a lifetime prevalence of about 1-2 percent. Symptoms during a depression include a persistent sad mood; loss of interest or pleasure in activities that were once enjoyed; significant change in appetite or body weight; difficulty sleeping or oversleeping; physical slowing or agitation; loss of energy; feelings of worthlessness or inappropriate guilt; difficulty thinking or concentrating; and recurrent thoughts of death or suicide. Patients in a manic episode show abnormally and persistently elevated (high) mood or irritability occurring with at least three of the following: overly-inflated self-esteem; decreased need for sleep; increased talkativeness; racing thoughts; distractibility; increased goal-directed activity or physical agitation; and excessive involvement in risky behaviors or activities (e.g., unwise spending sprees, reckless driving, sexual affairs).
Family and twin studies in BD have established the importance of genetic factors in the aetiology of the illness. Environmental are also of great importance, given that the concordance rate among monozygotic twin pairs is approximately 70%. However, the precize interaction between genetic vulnerability for BD (genotype) and environmental factors remains unknown.
There is evidence that there are structural brain abnormalities in BD. However, relatively little MRI research has been performed (as compared to schizophrenia) and the results are sometimes inconsistent for brain structures. The most pronounced abnormalities show an increase of lateral ventricular volume, a decrease of gray matter in the prefrontal cortex and an enlargement of the amygdala.

The prevalance of thyroid dysfunction is higher in patients with mooddisorders than in the general population. Previous research indicates that autoimmune thyroiditis with increased TPO-Abs levels seems to be a marker which is related to the genetic vulnerability to develop bipolar disorder rahter than to the disease process itself.
Furthermore, there is increasing evidence that the immune system, in close interaction with the central nervous system and the endocrine system, plays a rol in the pathophysiology of bipolar disorder.

Study objective

Objectives
1. Are there differences in brain structures in bipolar twin pairs compared to their (healthy) co-twins and healthy control twin pairs?
2. If there are changes in brain volume, will these changes differ across a 5 year interval between bipolar twin pairs, their (healthy) co-twins and healthy control twin pairs?

3. Investigate whether the structural brain changes during a 5 year interval in twin pairs concordant and discordant for bipolar disorder are mediated by genetic and/or environmental factors.
4. Investigate whether white matter disparities as detected by DTI and MTR imaging are mediated by genetic and/or environmental factors.
5. Since the same MRI protocol is used for both the schizophrenia and the BP twin pairs, we can compare the results and find out whether there are differences between both patient groups.
6. Is there a connection between structural changes in brain anatomy and (certain) genes?
7. Are there differences in TPO-Abs levels in bipolar twin pairs compared to their (healthy) co-twins, their healthy siblings and healthy control twin pairs?
8. If there are changes in TPO-Abs levels, will these changes differ across a 5 year interval between bipolar twin pairs, their (healthy) co-twins and healthy control twin pairs?
9. Investigate whether the TPO-Abs levels changes during a 5 year interval in twin pairs concordant and discordant for bipolar disorder are mediated by genetic and/or environmental factors.
10. Is there a connection between TPO-Abs levels and (certain) genes?
11. Are there differences in neuroimmmune parameters or organ-specific antibodies in bipolar twin pairs compared to their (healthy) co-twins, their healthy siblings and healthy control twin pairs?
12. If there are changes in neuroimmmune parameters or organ-specific antibodies, will these changes differ across a 5 year interval between bipolar twin pairs, their (healthy) co-twins and healthy control twin pairs?
13. Investigate whether the neuroimmmune parameters or organ-specific antibodies changes during a 5 year interval in twin pairs concordant and discordant for bipolar disorder are mediated by genetic and/or environmental factors.
14. Is there a connection between neuroimmmune parameters or organ-specific antibodies and (certain) genes?

Study design

The research will be performed in a double blind study design. All subjects are coded, this accounts for the questionaires and interviews as well as the MRI scan.
The subjects will be asked to fill in some questionaires, and participate in a couple of interviews e.g. to determine how the severity of the symptoms.
Also, an abbreviated version of the WAIS IQ test will be performed to get an idea of the average IQ of the subjects.
Furthermore, a small bloodsample will be taken. This will be used to determine zygosity, to assess functioning of the pancreas and autoimmune levels, and for future objectives in genetics.
The MRI scan will be used to acquire the volumes of several brain structures.
The DTI and MTI scan (both are made during the MRI sequence) will be used to

detect and quantify white matter abnormalities.

Study burden and risks

It is of great importance to know which brain structures are involved in bipolar disorder, and if these changes are progressive (or not) across time and have a genetic background or if they are more influenced by environmental factors.

There are no risk concerning this research project.
For the follow-up measurements subjects will be occupied for approximately3-4 hours. First, interviews and questionaires will be held. Second, a blood sample will be taken. Subsequently, there will be a break before starting with the MRI scan.
The same activities are applied for the new subjects. However, the questionaires and interviews will be more extensive, because no background information is yet available.
It will also be possible to spread the study over two days, to decrease any pressure.
Some questionaires can be filled in at home, others have to be held at the UMC Utrecht. This will take approximately 2-2.5 hours. The scan will take 45 minutes.
Subjects can also stop at moment if they find the examination too exhausting.

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:
1) Part of a monozygotic or dizygotic twin pair
2) For monozygotic twin pairs at least one twin (MZ concordant and MZ discordant) and for dizygotic twin pairs only one twin (DZ discordant) has a diagnoses (life time):
- Bipolar Disorder I or Bipolar Disorder II (DSM-IV criteria)
- For the interview and blood sample: not in a acute (hypo)manic or major depressive episode
3) Age between 18 and 60 years;Healthy controls:
1) Part of a monozygotic or same-sex dizygotic twin pair
2) Matched to patient groups on age, sex and zygosity
3) Age between 18 and 60 years

Exclusion criteria

Patients:
1) No history of drug or alcohol dependency (DSM-IV criteria) for the last half year
2) No history of Cognitive Disorder (DSM-IV criteria)
3) No history of serious neurological illness
4) No severe medical illness
Healthy controls:
1) No history of specific axis I psychiatric disorder (DSM-IV criteria), on the basis of a SCID interview (Modules A-G)
2) No history of axis II personality disorder (DSM-IV criteria), on the basis of SIDP-V
3) No first degree relative with a history of specific axis I psychiatric disorder (DSM-IV criteria), on the basis of a FIGS interview
4) No history of serious neurological illness
5) No severe medical illness
6) No history of drug or alcohol dependency (DSM-IV criteria) for the last half year

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:	Will not start
Enrollment:	220
Type:	Anticipated

Ethics review

Not approved

Date:	16-01-2007
Application type:	First submission
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	NL12339.041.06