Genetic and environmental influences on the brain, the immunesystem and gene expression in bipolar twin pairs - a cross-sectional and longitudinal study

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Study A: Show BP patients similar progression in brain volume change compared to schizophrenia patients. If so, can the progressive change in BP patients also be explained by genetic factors?Study B: Show BP patients and their non-bipolar cotwins...

Ethical review	Approved WMO
Status	Recruitment stopped
Health condition type	Manic and bipolar mood disorders and disturbances
Study type	Observational invasive

Summary

ID

NL-OMON33914

Source
ToetsingOnline

Brief title
Brain, immune system, gene expression in BP twins

Condition

- Manic and bipolar mood disorders and disturbances

Synonym
manic depressive disorder

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, longitudinal, MRI, twins

Outcome measures

Primary outcome

Study A: Change in brain volume (sMRI) or gray/white matter density (Voxelbased morphometry)

Study B: Change in immunology parameters

Study C: Fractional anisotropy and magnetisation transfer ratio

Study D: Genotype and gene expression data

All studies: Baseline values or parameters which might intervene with the main study parameter (age, gender, years of education, symptoms, level of functioning, medication intake, life events)

Secondary outcome

n/a

Study description

Background summary

Family and twin studies in bipolar disorder (BP) have established the importance of genetic factors in etiology of the illness. Moreover, BP shows high point estimates of heritability in liability to the illness, i.e. ~85%. Recently, we finished data collection of a large cohort op BP twin pairs. The purpose of collecting a BP twin cohort was two-fold. First, patients show structural brain abnormalities, but whether the abnormalities are due to genetic factors or disease related (non-genetic) factors remains largely unknown. Therefore, an MRI study was performed (study A). Secondly, the prevalence of thyroid dysfunction is higher in patients with mood disorder than in the general population. Therefore, blood samples were acquired to determine

parameters involved in the immune system (study B). Currently, this is the largest BP twin cohort worldwide.
Earlier, we carried out a longitudinal study in monozygotic (MZ) and dizygotic (DZ) twin pairs concordant or discordant for schizophrenia. Because of the apparent genetic overlap, and the overlap in phenotypic characteristics it is of particular interest to conduct a longitudinal study of our BP twin sample and compare the data to the results of the prospective study of schizophrenia twins.
We propose to carry out 4 studies, using the earlier collected bipolar disorder (BP) twin cohort of our department. In addition, we ask affected and unaffected siblings of these twin pairs to participate as well.
Study A: A longitudinal MRI study
Study B: A longitudinal study on neuroimmune parameters
Study C: A cross-sectional study into MRI measures that focus on integrity and connectivity in white matter structures.
Study D: A cross-sectional study into gene expression levels in discordant MZ twin pairs. Moreover, genetic information will be available to investigate the effect of genotype on brain volume (change) in BP twins.

Study objective

Study A: Show BP patients similar progression in brain volume change compared to schizophrenia patients. If so, can the progressive change in BP patients also be explained by genetic factors?
Study B: Show BP patients and their non-bipolar cotwins progression in TPO-Abs and other neuroimmune parameters compared to normal controls. If so, can the progressive change also be explained by genetic factors?
Study C: Since our baseline measures show a genetic contribution to the white matter volume abnormalities in BP we hypothesis that abnormal values of fractional anisotropy and magnetisation transfer ratio will also be influenced by the genetic risk to develop BP.
Study D-genotyping: What is the effect of genotype on brain volume (change) in BP, schizophrenia and healthy twin pairs, regarding specificity to diagnosis?
Study D-gene expression: Is there differential gene expression within discordant MZ twin pairs with either BP or SZ and are can these expression patterns explain discordancy?

Study design

Study A and B: longitudinal twin design
Study C and D: cross-sectional extended twin design

Study burden and risks

A magnetic resonance imaging (MRI) scan session of approximately 50 minutes will be performed: MRI is a non-invasive technique, so there is no need for

special preparation for the subject. There are no known risks associated with the MRI acquisition and the data are solely used for research purposes. However, structural cerebral pathology may be noticed. If medical treatment is indicated, the subject will be notified.
From each participant a small amount (4 x 10 ml) of EDTA blood will be taken, by means of a venapuncture. On request, the skin can be locally anesthetized prior to the venapuncture. If the participant refuses the puncture, a cotton swab of buccal mucosa can be taken. Since the number of blood samples is limited and the samples are small, the burden for participating subjects is expected to be negligible.
No immediate benefits are to be expected from participation in this study for the subjects. In the long run, increased understanding of the aetiology and pathophysiology of psychiatric illness in general and schizophrenia and bipolar disorder in particular, may contribute to diagnosis, early detection and/or prediction of treatment outcome.

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

Study A+B (longitudinal):
participation at baseline;Study A+B+C+D (cross-sectional)
New bipolar twin pairs
1) Part of a monozygotic or dizygotic twin pair
2) At least one twin has a diagnoses (life time) of Bipolar Disorder I or Bipolar Disorder II (DSM-IV criteria)
3) No history of drug or alcohol dependency (DSM-IV criteria) for the last half year
4) No history of Cognitive Disorder (DSM-IV criteria)
5) No history of serious neurological illness
6) No severe medical illness
7) Age between 18 and 60 years;New healthy control twin pairs
1) Part of a monozygotic or dizygotic twin pair
2) No history of axis I psychiatric disorder (DSM-IV criteria), on the basis of a SCID interview (Modules A-G)
3) No history of axis II personality disorder (DSM-IV criteria), on the basis of SIDP-V
4) No first degree relative with a history of specific axis I psychiatric disorder (DSM-IV criteria), on the basis of a FIGS interview
5) No history of drug or alcohol dependency (DSM-IV criteria) for the last half year
6) No history of serious neurological illness
7) No severe medical illness
8) Age between 18 and 60 years;Siblings
1) full sibling of an included twin pair
2) No history of axis I psychiatric disorder (DSM-IV criteria), on the basis of a SCID interview (Modules A-G)
3) No history of axis II personality disorder (DSM-IV criteria), on the basis of SIDP-V
4) No history of drug or alcohol dependency (DSM-IV criteria) for the last half year
5) No history of serious neurological illness
6) No severe medical illness
7) Age between 18 and 60 years

Exclusion criteria

Did not give written informed consent
2) Ferrous objects in or around the body (e.g. braces, glasses, pacemaker, metal fragments)
3) Drug or alcohol abuse over a period of six months prior to the experiment
4) History of closed-head injury
5) History of neurological illness or endocrinological dysfunction
6) Claustrophobia

Study design

Design

Study type:	Observational invasive
Intervention model:	Other
Allocation:	Non-randomized controlled trial
Masking:	Open (masking not used)

Primary purpose: Basic science

Recruitment

NL

Recruitment status:	Recruitment stopped
Start date (anticipated):	18-01-2010
Enrollment:	420
Type:	Actual

Ethics review

Approved WMO Date:	08-07-2008
Application type:	First submission
Review commission:	METC Universitair Medisch Centrum Utrecht (Utrecht)
Approved WMO Date:	29-09-2009
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	NL20509.041.08