Search for genetic variations in neuropsychiatric disorders

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1. We will recruit 30 probands who meet DSM-IV inclusion criteria for a primary psychotic disorder or mood disorder with psychotic features: schizophrenia, schizoaffective disorder, delusional disorder, bipolar I disorder, psychotic depression, post...

Ethical review	Approved WMO
Status	Recruiting
Health condition type	Schizophrenia and other psychotic disorders
Study type	Observational invasive

Summary

ID

NL-OMON39216

Source
ToetsingOnline

Brief title
GEZIN study

Condition

- Schizophrenia and other psychotic disorders

Synonym
Psychosis, Schizophrenia

Research involving
Human

Sponsors and support

Primary sponsor: Erasmus MC, Universitair Medisch Centrum Rotterdam
Source(s) of monetary or material Support: Ministerie van OC&W,Economic Structure Enhancing Fund (FES): Life Sciences & Health;NeuroBsik Program Project;Work Package: Translation of animal model findings to human disease treatments

Intervention

Keyword: Bipolar Disorder, Genetic Variants, Psychosis, Schizophrenia

Outcome measures

Primary outcome

1. The identification of genetic variation in probands and their family members

2. Clinical characterization of the probands and their family members

Secondary outcome

n/a

Study description

Background summary

With recent technological developments in medicine, it has become possible to investigate the genetic basis of illnesses and disorders. Many scientists worldwide investigate the genetic underpinnings of psychiatric disorders such as depression and psychosis. It has proven to be difficult to pinpoint the exact area in the genetic material that is responsible for the vulnerability for psychiatric disorders. It is likely and generally assumed that the emergence of symptoms in psychiatry involves a complex interaction between a person*s genes and the circumstances and events one experiences in his or her life.

Genetic material is inherited from both parents and is partly similar in members of the same family. Therefore, it is possible to compare the genetic material of several family members in order to identify parts of the genetic material that may be involved in the emergence of psychiatric symptoms or disorders. In this study, we ask the question if there are areas in the genetic material that correlate with the expression of psychiatric symptoms.

Study objective

1. We will recruit 30 probands who meet DSM-IV inclusion criteria for a primary psychotic disorder or mood disorder with psychotic features: schizophrenia, schizoaffective disorder, delusional disorder, bipolar I disorder, psychotic depression, post-partum psychosis. These probands will be clinically assessed with blood drawn for the analysis of DNA and RNA. The DNA will be analyzed

with high-throughput sequencing and micro-array based comparative genomic hybridization to examine these subjects for the presence of potentially etiologic genetic variations. RNA expression analyses will investigate the impact of the genetic variants on gene transcription.

2. We will recruit up to 300 first-, second-, or third degree biological relatives of these probands who may or may not be affected with psychosis. These subjects will also be clinically assessed with blood drawn for the analysis of DNA and RNA. The DNA will be analyzed with high-throughput sequencing and micro-array based comparative genomic hybridization to examine these subjects for genetic variations observed in the probands. RNA expression analyses will investigate the impact of the genetic variants on gene transcription. A selection of patients and family members will be asked to cooperate with a skin biopsy in order to map the biological effect of the genetic difference on (nerve) cell characteristics.

3. Furthermore, we will recruit 20 probands and both their unaffected biological parents for de novo genetic analysis. These subjects will also be clinically assessed with blood drawn for the analysis of DNA and RNA. The DNA will be analyzed with high-throughput sequencing and micro-array based comparative genomic hybridization to examine these subjects for genetic variations observed in the probands. RNA expression analyses will investigate the impact of the genetic variants on gene transcription.

Study design

A naturalistic, single-center study focused on identifying genetic risk factors for psychosis in patients and their family members.

Study burden and risks

There are no direct benefits connected to participation in this study. Participation helps physicians and researchers to gain more insight into biology of psychiatric disorders. This may lead to the development of new forms of treatment. A downside of participation is that it will take about 2 hours of the time of each participant. Furthermore, on one occasion a sample of blood is drawn. A selection of patients and family members will be asked to cooperate with a skin biopsy in order to map the biological effect of the genetic difference on (nerve) cell characteristics. This is a minimally invasive procedure that is not very painful, but might produce some discomfort. It is possible that some scarr tissue will form and a small chance to develop an infection. An MRI will be performed to exclude the possibility that the neuropsychiatric symptoms arise from structural brain abnormalities.

Contacts

Public
Erasmus MC, Universitair Medisch Centrum Rotterdam

'S Gravendijkwal 230
Rotterdam 3000CA
NL
Scientific
Erasmus MC, Universitair Medisch Centrum Rotterdam

'S Gravendijkwal 230
Rotterdam 3000CA
NL

Trial sites

Listed location countries

Netherlands

Eligibility criteria

Age
Adults (18-64 years)
Elderly (65 years and older)

Inclusion criteria

A. Inclusion criteria for probands
1. All subjects must give signed, informed consent.
2. Probands must have a DSM-IV consensus diagnosis of primary psychotic disorder or mood disorder with psychotic features (schizophrenia, schizoaffective disorder, delusional disorder, bipolar I disorder, psychotic depression, post-partum psychosis). A concurrent diagnosis of idiopathic seizure disorder or learning disability will not be an exclusion factor. Accordingly, subjects with mild MR (as determined clinically, FIQ>=55) will be included, if their psychiatric symptoms and history can be clearly established.
3. Subjects must be over 18 years of age at interview, male or female.;B. Inclusion criteria for informants
1. The informant will have known the subject for at least two years, be familiar with their psychiatric history, and have at least one hour of contact per week with the proband (first-

degree family members preferred). As for the probands, informants must give signed, informed consent and be over 18 years of age at interview.
2. Exclusion criteria are the same as for the probands given above.;C. Inclusion criteria for family members of probands
1. First-, second-, or third degree biological family member of participating probands. As for the probands, family members must give signed, informed consent and be over 18 years of age at interview.
2. Exclusion criteria are the same as for the probands given above.
3. Family members may, but are not required, to meet criteria for a DSM-IV consensus diagnosis of primary psychotic disorder or mood disorder with psychotic features.

Exclusion criteria

1. Unable to give informed consent to all aspects of the study.
2. Unable to speak and be interviewed in Dutch or English (to ensure validity of the interviews).
3. Psychosis is deemed secondary to substance use by the consensus diagnostic procedure because psychotic symptoms are limited to periods of likely intoxication or withdrawal, or there are persistent symptoms which are likely to be related to substance use (i.e., increasing paranoia after years of amphetamine use; symptoms limited to visual hallucinations after extensive hallucinogen use).
4. The seizure disorder is deemed secondary to causative factors, such as medication (e.g., clozapine), head injury, psychogenic polydispsia, or alcohol withdrawal.
5. Subjects with severe mental retardation (MR).

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:	Recruiting
Start date (anticipated):	08-09-2010

Enrollment:	1160
Type:	Actual

Ethics review

Approved WMO Date:	11-08-2010
Application type:	First submission
Review commission:	METC Erasmus MC, Universitair Medisch Centrum Rotterdam (Rotterdam)
Approved WMO Date:	03-12-2010
Application type:	Amendment
Review commission:	METC Erasmus MC, Universitair Medisch Centrum Rotterdam (Rotterdam)
Approved WMO Date:	15-07-2011
Application type:	Amendment
Review commission:	METC Erasmus MC, Universitair Medisch Centrum Rotterdam (Rotterdam)
Approved WMO Date:	23-12-2011
Application type:	Amendment
Review commission:	METC Erasmus MC, Universitair Medisch Centrum Rotterdam (Rotterdam)
Approved WMO Date:	20-11-2012
Application type:	Amendment
Review commission:	METC Erasmus MC, Universitair Medisch Centrum Rotterdam (Rotterdam)
Approved WMO Date:	14-10-2013
Application type:	Amendment
Review commission:	METC Erasmus MC, Universitair Medisch Centrum Rotterdam (Rotterdam)

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	NL32184.078.10