

# 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...

|                              |                                             |
|------------------------------|---------------------------------------------|
| <b>Ethical review</b>        | Approved WMO                                |
| <b>Status</b>                | Recruiting                                  |
| <b>Health condition type</b> | Schizophrenia and other psychotic disorders |
| <b>Study type</b>            | 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; NeuroBsic 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

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### Scientific

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## 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,  $FIQ \geq 55$ ) 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 |