European Network of National Schizophrenia Networks Studying Gene-Environment interactions (EU-GEI). Work package 5: GenexEnvironment in the Prodrome

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Main objectives: (1) To identify genetic, environmental and clinical determinants of psychosis vulnerability and onset. (2) To assess neural systems and behavioural substrates mediating gene environment interactions. (3) To test for gene-...

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

Summary

ID

NL-OMON34336

Source
ToetsingOnline

Brief title
Identifying genetic and environmental interactions in psychosis

Condition

- Schizophrenia and other psychotic disorders

Synonym
At Risk Mental State, Psychosis

Research involving
Human

Sponsors and support

Primary sponsor: Academisch Medisch Centrum
Source(s) of monetary or material Support: Europese Unie

Intervention

Keyword: Environment, Gene, Prodrome, Psychosis

Outcome measures

Primary outcome

The main outcome measure is transition status to first- episode psychosis

within 24months

post study entry. Transition is operationally defined via rating scales, as one

of:

1. Abnormal thoughts held with delusional intensity occurring every day for one

week or longer

2. True hallucinations in any modality occurring every day for one week or

longer

3. Formal thought disorder to the degree of incoherence and/or loose

associations occurring every day for one week or longer

Secondary outcome

1. We will examine exposure to the main environmental factors implicated in

psychosis: childhood urbanicity and trauma, ethnicity, adolescent cannabis use,

acute stress, social discrimination and social defeat.

2. Level of symptomatology, including depression, positive, negative, and basic

symptoms

3. Level of functioning across a range of domains including peer relations,

family

functioning, vocational, and occupational functioning. The following secondary

outcome cut points will be applied: Remission will be defined as at least a 50%

reduction in the CAARMS positive symptoms score. Recovery will be defined as at

least a 50% reduction in key symptom measures (as above) plus improvement in

functioning to premorbid level.

Study description

Background summary

Patients with psychotic disorders such as schizophrenia, usually experience early signs of psychosis for 1*5 years prior to the first episode of frank illness. This early state is known as at risk mental state (ARMS) or prodrome. Individuals with ARMS appear to be at extremely high risk of developing psychosis* about one-third will do so, while two-thirds will not make a transition to psychosis and their at-risk symptoms will either stay the same or improve. It is unclear why only a subset of those who are highly vulnerable to psychosis go on to develop the illness. There is increasing evidence that aetiological models of schizophrenia need to incorporate the role of genetic, social, psychological and biological factors, and to clarify how they interact. In this study, state-of-the-art methods will be used to examine the genetic, psychological and physiological interactions in individuals at high risk of psychosis. The ultimate aim of this work-package is to deliver a tool that can be used to help identifying genetic and environmental factors that, when they interact, predict who is more likely to develop schizophrenia.

Study objective

Main objectives: (1) To identify genetic, environmental and clinical determinants of psychosis vulnerability and onset. (2) To assess neural systems and behavioural substrates mediating gene environment interactions. (3) To test for gene-environment
interactions, as well as gene-gene and environment-environment interactions playing a role in psychosis vulnerability and onset. (4) To develop translational tools for the early prediction, diagnosis and course of psychosis. Secondary objective: To disseminate the results to a critical mass of stakeholders for policy counselling, integrating the expertise and views of the European Commission and all relevant stakeholders groups to develop policy

recommendations and guidelines.

Study design

Over a five-year period, we will prospectively study young people experiencing prodromal symptoms of schizophrenia in a naturalistic design.

The cohort of people with prodromal symptoms (n=400) will be collected by an established network of European centres (EARN* European At Risk Network) in London, Cambridge, Cologne, Munich, Amsterdam, Basel and Vienna. An additional site (ORYGEN, Melbourne) that also meets the inclusion criteria has applied to the Australian NHMRC for linked funding to participate in the proposal, as part of the NHMRC-EU collaborative grant scheme. Inclusion of this site, one of the largest clinical centres for the ARMS, does not incur costs to the EU. The subjects presenting to these sites are young adults with an ARMS who are seeking clinical help.

New patients are seen for the baseline clinical assessment, neuropsychological clinical assessment and MRI when they are accepted into the service. If the client agrees to take part to the research project, the information collected during the assessment will be anonymised and used for the study. Also a blood sample will be collected for DNA analysis.

We expect each participant to be in the study for 24 months. Participants will be assessed at baseline, a 12 months and after 24 months after baseline (or earlier if they make a transition to psychosis). Blood samples will only be collected at baseline.

In the Netherlands, all assessments will take place at Academic Medical Center, Amsterdam and at Parnassia, Den Haag.

Study burden and risks

Burden: All participants will be assessed using a number of clinical scales/interviews and neuropsychological tests. A potential hazard of clinical and cognitive assessment is that participants may experience anxiety and emotional distress related to their performance. In addition, 25 ml blood will be drawn for DNA and Serum purposes. No risks are attached to this study.

Contacts

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Trial sites

Listed location countries

Netherlands

Eligibility criteria

Age
Adolescents (12-15 years)
Adolescents (16-17 years)
Adults (18-64 years)
Elderly (65 years and older)

Inclusion criteria

1. Age 16 to 35
2. Adequate command of the Dutch language to complete the assessment
3. Meeting the criteria for an at risk mental state for psychosis as defined by the Personal Assessment and Crisis Evaluation Clinic (PACE) criteria (Yung et al 1998; Yung et al 2003). An individual meets criteria for the *at risk* mental state if they exhibit one or more of the following: 1) a schizotypal personality disorder or a first degree relative with psychosis plus a recent decline in function* 2) *attenuated* positive psychotic symptoms, like ideas of reference, odd beliefs, magical thinking, or unusual perceptual experiences* and 3) a brief psychotic episode of less than one week duration that resolves without antipsychotic medication.

Exclusion criteria

- Having had a psychotic episode for more than one week
- Symptoms relevant for inclusion are explained by a medical disorder or drugs or alcohol

dependency
- IQ <60

Study design

Design

Study type: Observational invasive

Masking:	Open (masking not used)
Control:	Uncontrolled
Primary purpose:	Basic science

Recruitment

NL

Recruitment status:	Pending
Start date (anticipated):	01-07-2010
Enrollment:	45
Type:	Anticipated

Ethics review

Approved WMO

Application type:	First submission
Review commission:	METC Amsterdam UMC

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	NL32721.018.10