Adolescent neurobiological predictors of developing psychosis

Published: 26-08-2010
Last updated: 02-05-2024

The two primary objectives of this study are:(1) to explore whether UHR in adolescence is associated with neurobiological differences at baseline and/or changes in the course of 4-8 year of follow-up as measured using MR-techniques and compared with...

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

Summary

ID

NL-OMON36521

Source
ToetsingOnline

Brief title
NeuroImaging of Risk for Psychosis (NIRP)

Condition

- Schizophrenia and other psychotic disorders

Synonym
psychosis, schizophrenia

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: developmental neuroimaging, MRI, psychosis, ultra high risk

Outcome measures

Primary outcome

The primary outcome measures are:

(1) Cortical thickness, as assessed using a standard anatomical MRI scan

(3D-FFE)

(2) White matter integrity, as assessed using track-based FA measures from DTI

Secondary outcome

The secondary outcome measures are:

(1) Volume of brain structures, as assessed using a standard anatomical MRI

scan (3D-FFE)

(2) Connectivity of resting state networks, as assessed with resting state fMRI

(3) Genotype on candidate risk genes for psychosis

Study description

Background summary

Psychosis is a severe psychiatric condition with a lifetime prevelance of approximately 3%. The onset of psychosis is often preceded by prodromal signs and symptoms. This has lead to the development of the clinical- or ultra high-risk (UHR) approach to psychosis research. This approach identifies individuals at increased risk of developing psychosis on the basis of prodromal symptoms, allowing researchers to track them over time, as psychosis develops. The incidence of psychosis is high in UHR studies and conversion occurs in relatively close temporal proximity to initial intake (16-35% in 2-2.5 year follow-up). Such an approach allows for the investigation of changes that accompany the onset of psychosis, including brain changes, behavioural and cognitive changes. Such research has the potential to improve our understanding of how psychosis develops, in particular when it compares psychotic development

to typical developmental trajectories. By investigating the impact of risk factors, such as brain changes and genetic risk factors, we can improve our understanding of the role of such risk factors. Studies that elucidate the neurobiology of psychosis will ultimately facilitate future design of new and effective ways to treat this disorder. Furthermore, a knowledge of the underlying biological substrate will improve accurate identification of individuals at high-risk.
Several research groups have reported premorbid neuro-anatomical and -functional changes in subjects at clinical high-risk for psychosis in both grey and white matter areas. Researchers have most often focused on the age range of 20-25 years, when psychosis typically first occurs. However, on average the earliest prodromal signs occur up to 5 years before psychosis onset.
An earlier study by our group investigated brain structure volumes in a well-defined sample of young adolescents at UHR for psychosis (aged 12-18 years) . Preliminary results from our own data show that adolescents at risk for psychosis who develop psychosis within two years of the initial MRI-scan show a greater decrease in cortical thickness, in particular in areas implicated in psychosis. However, research into such grey matter changes is very limited and these findings should be considered preliminary and need to be replicated. Clearly, further research is needed. Also new techniques are now assessible to investigate white matter integrity and connectivity of resting state networks.
Furtermore, there is evidence that psychosis is hereditary, with heritability estimates for psychotic disorders between 82% and 85%. The genes involved are not known, but some candidates have been identified. The impact of these genes on brain development and particular on the developmental trajectory to psychosis has not yet been established. Therefore, we propose to include an exploratory analysis of candidate risk genes for psychosis in this protocol.

Study objective

The two primary objectives of this study are:
(1) to explore whether UHR in adolescence is associated with neurobiological differences at baseline and/or changes in the course of 4-8 year of follow-up as measured using MR-techniques and compared with typically developing controls.
(2) to assess association and potential predictive value of (changes in) cortical thickness and resting state brain activation for the development of subsequent psychosis.

For the second objective we will focus on two hypotheses:
(1) Adolescent cortical thickness as assessed in the course of time (but before first occurrence of psychosis) is associated with the occurrence of psychosis within 8 years (duration of earlier study and follow-up in the current protocol).
(2) Adolescent white matter integrity, as assessed with DTI in the course of time (but before occurrence of psychosis) is associated with the occurrence of

psychosis within 4 years (duration of follow-up in the current protocol).

Two secondary objectives are to
(1) explore if development of resting state brain activation is associated with developing psychosis using longitudinal RS-fMRI
(2) explore the association of candidate risk genes for psychosis with the measures of brain structure that are identified as predictors.
structure. The second is an exploratory analysis of resting state networks, as assessed with resting state fMRI.

Study design

Our study design will be similar to the earlier study. We propose a longitudinal study, where diagnosis (UHR for psychosis vs control) will be the between-subject grouping variable. The first cohort will include a maximum of 140 subjects from our earlier study. They will be approached to participate in two follow-up measurements. The second cohort will consist of participants from a new recruitment. They will be asked to participate in two measurements (1 follow-up). Follow-up MR-scans will take place approximately 24 months after the preceding scan.
Participants will receive a set of questionnaires by mail and will be asked to complete them. Participants that still go to school will also be asked to approach a teacher for a questionnaire. During the first visit participants will be asked to particpate in an abbreviated IQ assessment and one or two interviews (depending on age participant). Parents will (depending on age participant) be asked to participate in an interview at the same time. In the last part of the first visit, all subjects will be offered to participate in a MRI-simulation. In a MRI practice session, subjects will be desensitized to the scanner environment with the use of a simulator. If a child does not successfully complete the simulation session, or indicates verbally that he or she no longer wishes to take part in the study, or if the child, the parent or the experimenter assesses the child as too anxious, the actual scanning session will be cancelled. During the second visit, the MRI-scan will be made and DNA will be collected via venepuncture or by using a spit cup (depending on age participant).

Study burden and risks

Participation will consist of questionnaires, interviews, an abbreviated IQ assessment, an MRI-scan (with the option of an MRI simulation session beforehand), and the collection of saliva or blood (depending on age). Study participation will be divided over two days and a visit will never take longer than 4 hours. There are no known risks associated with MRI acquisition, or any of the proposed methodologies, and we believe the impact on the subjects will be minimal. As only a single vial of blood will be collected during venepuncture, the burden for participating subjects is expected to be minimal.

If veneouncture is not preferred by partcipant or parent(s), they will be asked if DNA can be collected using a spitcup. Donation of DNA is strictly voluntarily. Subjects may discontinue study participation at any time, without giving a reason.

Contacts

Public
Universitair Medisch Centrum Utrecht

Heidelberglaan 100
3584 CX Utrecht
NL
Scientific
Universitair Medisch Centrum Utrecht

Heidelberglaan 100
3584 CX Utrecht
NL

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

This is a follow-up study. Inclusion criteria will be the same as initial intake.
General inclusion criteria:
- For subjects who initially participated in the DUPS study: Age between 12 and 18 years at initial inclusion

- For new subjects: Aged between 12 and 24 years at initial inclusion (to allow us to supplement the DUPS sample)
Inclusion criteria for Ultra High Risk for Psychosis (UHR) Group:
- No previous psychotic episode for more than one week
- No clear organic etiological factor
- Voluntary participation (informed consent)
- Meets criteria for UHRP (page 19-21 of protocol)
Inclusion criteria for controls:
-No history of psychiatric disorder (axis 1, DSM-IV) according to diagnostic interview (DISC or SCAN)
-No history of psychotic disorder in first or second-degree family members

Exclusion criteria

-Mental retardation (IQ < 70)
-Claustrophobia
-Presence of metal objects in or around the body

Study design

Design

Study type:	Observational invasive
Intervention model:	Other
Allocation:	Non-randomized controlled trial
Masking:	Open (masking not used)
Control:	Active
Primary purpose:	Basic science

Recruitment

NL

Recruitment status:	Recruitment stopped
Start date (anticipated):	20-10-2010
Enrollment:	264
Type:	Actual

Ethics review

Approved WMO Date:	26-08-2010
Application type:	First submission
Review commission:	METC Universitair Medisch Centrum Utrecht (Utrecht)
Approved WMO Date:	28-04-2011
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	NL30592.041.10