A genetic study of left-handedness and language lateralization in extended pedigrees from a Dutch population isolate. An investigation of a possible endophenotype for psychosis

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To perform a genetic study of left-handedness and language lateralization as endophenotypes of schizophrenia. The study will make use of 30 extended multigenerational pedigrees with multiple left-handers from Urk, an isolated population in The...

Ethical review	Approved WMO
Status	Recruitment stopped
Health condition type	Neurological disorders NEC
Study type	Observational invasive

Summary

ID

NL-OMON30043

Source
ToetsingOnline

Brief title
lateralisation and left handedness

Condition

- Neurological disorders NEC
- Schizophrenia and other psychotic disorders

Synonym
decreased lateralization, left-handedness

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: genes, language lateralization, left-handedness, psychosis

Outcome measures

Primary outcome

1) co-segegration of left-handedness and decreased language lateralization 2) association of genomic candidate regions with left-handedness and decreased language lateralization 3) the association of identified candidate genes or genomic regions with left-handedness in an existing sample of schizophrenia patients and their association with schizophrenia in a case-control design.

Secondary outcome

not applicable

Study description

Background summary

A possible solution to investigate genetic backgrounds of schizophrenia is the use of mono, or oligogenic endophenotypes related to more fundamental aspects of the disease. Decreased language lateralization, i.e. a more bilateral pattern of cortical language representation has been associated with schizophrenia. Decreased language lateralization is correlated to left-handedness and both may serve as endophenotypes for schizophrenia. Both can be studied rather effectively in 30 families from an isolated population in large pedigrees regardless of the schizophrenia phenotype.

Study objective

To perform a genetic study of left-handedness and language lateralization as endophenotypes of schizophrenia. The study will make use of 30 extended

multigenerational pedigrees with multiple left-handers from Urk, an isolated population in The Netherlands. Chromosomal candidate regions will be identified by linkage analyses using left-handedness and language lateralization as traits. Revealed regions may contain schizophrenia susceptibility genes. Therefore, identified genomic areas or genes linked with left-handedness and/or decreased lateralization will be tested for association in an existing sample of more than 500 schizophrenia patients and a comparable healthy control group from an earlier research project (00-035).

Study design

Patients visiting their doctor are screened using a validated handedness questionnaire. Left-handed subjects with familial left-handedness will be contacted. We aim to include 30 large families with three or more left-handed subjects. Participation exists of three steps: 1) measurement of language lateralization with functional Transcranial Doppler. This device measures lateralization as a function of change in flow velocity in the right and left medial cerebral arteries. During a paced letter fluency task language areas of the dominant hemisphere will be activated to a higher degree than the contralateral areas, inducing an asymmetrical increase in bloodflow in the middle cerebral arteries. 2) subjects will participate in a Word production test and a Modified test of Remote Association or Semantic Distance. 3) a small blood sample (20ml) will be obtained for DNA extraction and genetic analysis.

Hereafter (co)segregation of handedness and language lateralization will be determined, as well as a genome-wide linkage analysis using the highly informative Linkage Mapping Set v2.5-MD10 of 400 microsatellite markers evenly spaced at 10cM intervals throughout the human genome (Applied Biosystems). Identified candidate genes or genomic regions will first be tested for association with left-handedness in an existing sample of schizophrenia patients with known handedness. When an association with left-handedness can be replicated in the schizophrenia sample, the identified genes will be tested in a case-control association design for their potential association with schizophrenia.

Study burden and risks

fTCD is a non-invasive Doppler technique that has been used extensively and has no known associated risks. People wear a headset to which the Doppler-probes are attached. When wearing the headset causes distress it can easily be adjusted or taken off. Bloodsamples from subjects will be taken by experienced medical doctors, thus decreasing the risk of haematomas. Participation takes only 60 minutes.

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. All grandparents born in the Netherlands
2. Age minimal 14 years
3. left handed or right handed within a family with 3 or more left handed members.

Exclusion criteria

1. age below 14 years
2. less than 3 left handed family members
3. not all grandparents born in the Netherlands

Study design

Design

Study type: Observational invasive

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

Recruitment

NL

Recruitment status:	Recruitment stopped
Start date (anticipated):	25-09-2006
Enrollment:	600
Type:	Actual

Ethics review

Approved WMO Date:	27-06-2006
Application type:	First submission
Review commission:	METC Universitair Medisch Centrum Utrecht (Utrecht)
Approved WMO Date:	15-05-2007
Application type:	Amendment

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	NL11620.041.06