Genes and Mental Retardation

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Ethical review	Approved WMO
Status	Pending
Health condition type	Chromosomal abnormalities, gene alterations and gene variants
Study type	Observational invasive

Summary

ID

NL-OMON32197

Source
ToetsingOnline

Brief title
Genes and Mental Retardation

Condition

- Chromosomal abnormalities, gene alterations and gene variants
- Mental impairment disorders

Synonym
mental retardation, syndromes

Research involving
Human

Sponsors and support

Primary sponsor: Universitair Medisch Centrum Sint Radboud
Source(s) of monetary or material Support: VIDI

Intervention

Keyword: etiology, genes, mental retardation, microarrays

Outcome measures

Primary outcome

On basis of our own research as well as literature we expect in approximately

10% of the tested patients a microdeletion or duplication as the cause of their

mental handicap.

Secondary outcome

not applicable

Study description

Background summary

In the general population 2 to 3% of the children have a developmental delay or mental retardation. Mental retardation can be caused by genetic or non-genetic factors. For the majority of children with mental retardation it is currently not possible to reveal the cause of the delay. In spite of intensive genetic research over the last decades the genetic causes remains largely unknown as well. An exception are the X-linked mental retardation disorders as for these disorders large pedigrees are commonly available for genetic testing. Important genetic causes of mental retardation are chromosomal aberrations. The most frequent chromosomal aberration leading to mental retardation is a trisomy of chromosome 21 causing the well recognisable Down syndrome. Till recently most chromosome aberrations were identified by light-microscope analysis. Novel and more accurate techniques have allowed the detection of smaller chromosome aberrations not detectable by light microscope analysis so called microdeletions or microduplications. This has led to the identification of microdeletion syndromes that are causing mental retardation. Microdeletions cause the loss of a copy of one or more genes (single in stead of the normal two copies). So microdeletions will give information on the localisation of genes involved in mental retardation.

Study objective

The primary goal of this research project is the identification of genes involved in causing mental retardation. These genes will be part of genetic networks that play a role in normal brain development and function. With up-to-date bioinformatic tools those networks will be explored and further

expanded leading to a better understanding of normal physiological processes in the central neuronal system. Another goal is to get a better insight in the frequency of these specific microdeletions in individuals with mental retardation. In additional, new diagnostic tools will be developed in order to improve the detection of genetic defects that lead to mental retardation. This will improve the diagnosis of the patient with a mental handicap. A correct diagnosis will improve the care of the child and will allow for better counselling of the parents and other family members.

Study design

The study consist of the following parts:
1. The establishment of a phenotypic database of clinically well characterised patients with a mental handicap (under code) en the collection of DNA samples of an international cohort of patients with a mental handicap.
2. Identification of genomic disorders (microdeletions and microduplications) using the following methods:
a. genome-wide deletion mapping using the 500 K SNP array
b. genome-wide homozygosity mapping and expression profiling using the Human Exon 1.0 ST Array
3. The project will generate four datasets: phenotypes, genomic deletions and duplications, homozygosity- and expression data. These datasets will be subjected to an in-depth bioinformatics analysis to select candidate genes for mental retardation. Candidate genes will be prioritized by in silico analysis of genomic data and by text mining.
4. High throughput sequencing of candidate genes for mental retardation in patients with an unknown cause of their mental handicap

Study burden and risks

Minimal

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)
Children (2-11 years)
Elderly (65 years and older)

Inclusion criteria

A selection of patients with mental retardation, some with additional congenital malformations. Selection will partly be based on clinical characteristics (see pages 4-6 of the research protocol.

Exclusion criteria

Patients without mental retardation

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):	01-01-2008
Enrollment:	2250
Type:	Anticipated

Ethics review

Approved WMO

Application type:	First submission
Review commission:	CMO regio Arnhem-Nijmegen (Nijmegen)

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	NL19921.091.07