Identifying genetic and metabolic risk factors for mild non-specific mental retardation and borderline intellectual functioning in parent offspring trios.

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The main aim of this project is to identify genetic and metabolic risk factors for mild MR and borderline intelligence.

Ethical review	Approved WMO
Status	Completed
Health condition type	Neurological disorders congenital
Study type	Observational non invasive

Summary

ID

NL-OMON34844

Source
ToetsingOnline

Brief title
RISK MR

Condition

- Neurological disorders congenital

Synonym
1. mild non-specific mental retardation and borderline intelligence 2. mild intellectual disability

Research involving
Human

Sponsors and support

Primary sponsor: Vrije Universiteit Medisch Centrum

Source(s) of monetary or material Support: Ministerie van OC&W

Intervention

Keyword: aetiology, genetics, mental retardation, risk factors

Outcome measures

Primary outcome

- Genetic variation (Single Nucleotide Polymorphisms, SNPs).

- Metabolite concentration in urine and plasma.

- IQ as measured by an IQ test.

Secondary outcome

Attention and social skills, abnormal child behaviour scores, daily functioning

will be measured using questionnaires.

Study description

Background summary

Mental retardation (MR) is a complex phenotype defined by the DSM-IV as an IQ< 70 with deficits in two or more adaptive skills starting in a childhood age. Borderline intelligence is defined as an IQ of 70-85. (American psychiatric association, DSM-IV 1994) Children with borderline intelligence may have deficits in adaptive skills as well. The causes of MR and/or borderline intelligence are very heterogeneous, including environmental causes and genetic causes. Although a large number of genetic and non-genetic causes for MR have been identified, the cause of (especially mild non-specific) MR remains unknown in 50-70% of the cases. We hypothesise that mild non-specific MR and borderline intelligence is to a large extent caused by multiple genetic and environmental factors together.

Study objective

The main aim of this project is to identify genetic and metabolic risk factors for mild MR and borderline intelligence.

Study design

We will develop a database containing genotypic and phenotypic data of 1000 children with mild non-specific mental retardation or borderline intelligence and their parents for etiologic research. We plan to do a genetic association study (a transmission disequilibrium test) using a gene network approach to find groups of functionally related genes that are associated with mild MR and borderline intelligence. For the metabolic risk factors we will use a Case-control design, comparing metabolite concentrations of patients with a reference population.

Study burden and risks

The burden for participants in this study is minimal. These children are all referred to the clinical genetic department for diagnostic purposes. The standard diagnostic protocol includes physical examination, DNA and metabolic analysis. No extra blood samples of the children or physical test are needed for this study, but we however do intent to take an IQ-test in all children and the parents are asked to fill out 3 questionnaires, to perform an IQ-test and to donate 15-20 ml of blood and a urine sample. The child and the parents will need to pay one extra visit in most instances. The child and his/her parents might benefit from a recent IQ-test and the questionnaire on psychological functioning of the child as these gives insight in the abilities and developmental needs of the child. The understanding of the risk factors for MR and borderline intelligence is important for designing optimal, customized learning programs for (cognitively impaired) children and possibly to minimize exposure to relevant environmental factors or to develop medical treatment of MR.

Contacts

Public
Vrije Universiteit Medisch Centrum

Postbus 7057
1007 MB Amsterdam
NL
Scientific
Vrije Universiteit Medisch Centrum

Postbus 7057
1007 MB Amsterdam
NL

Trial sites

Listed location countries

Netherlands

Eligibility criteria

Age
Adolescents (12-15 years)
Adolescents (16-17 years)
Children (2-11 years)

Inclusion criteria

1. borderline intellectual functioning (IQ 70-85) or mild mental retardation (IQ 50-70)
2. age 4-18 years
3. parents are available (at least one) and capable of communication in the Dutch language

Exclusion criteria

1. major congenital malformation
2. suspicion of a syndrome based on physical examination and/or history, judged by a clinical geneticist
3. a known cause for the mild a-specific MR or borderline intellectual functioning

Study design

Design

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

Recruitment

NL

Recruitment status:	Completed
Start date (anticipated):	01-03-2011
Enrollment:	3000
Type:	Actual

Ethics review

Approved WMO

Date:	20-12-2010
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	NL31526.029.10