Neuropsychological assessment in X-linked adrenoleukodystrophy

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

Summary

ID

NL-OMON43496

Source
ToetsingOnline

Brief title
Neuropsychological assessment in X-ALD

Condition

- Neurological disorders congenital
- Congenital and peripartum neurological conditions

Synonym
Schilder's disease, X-ALD, X-linked adrenoleukodystrophy

Research involving
Human

Sponsors and support

Primary sponsor: Academisch Medisch Centrum
Source(s) of monetary or material Support: De reiskosten van proefpersonen worden gefinancierd uit het budget van de afdeling kinderneurologie.

Intervention

Keyword: Adrenoleukodystrophy, Neuropsychological assessment, X-linked

Outcome measures

Primary outcome

The main study parameter is neuropsychological function.

Secondary outcome

The secondary study parameter is neuropsychological test data correlated to

neuroimaging (MRI).

Study description

Background summary

X-linked adrenoleukodystrophy (X-ALD) is a rare genetic metabolic disorder. The clinical spectrum is broad with involvement of the adrenal glands, myelum and peripheral nerves. Some, but not all, develop a devastating and fatal progressive cerebral demyelinating disease, which can be treated with haematopoetic stem cell transplantation (HSCT). Candidates for transplantation are selected depending on the severity of MRI abnormalities and neuropsychological testing results. The latter are used to evaluate functional consequences of demyelination. Low Performance Intelligence Quotient scores (< 80) are associated with decreased functional outcome after HSCT. Neurocognitive function in patients not (yet) affected by cerebral demyelination is thought to be normal, although previous published results are inconsistent.

In 52 patients with a mean age of 6.4 years (range 2.1-14.6) with normal brain MRI, neuropsychological testing did not reveal any cognitive deficiencies when tested as a group, although 4 individual participants had moderate deficiencies in some cognitive functional domains. The authors assumed these deficiencies were probably not related to X-ALD.
In another group of boys without radiological abnormalities (age range 3.92-14.58 years) 2/8 patients had a significantly lower Performance Intelligence Quotient in comparison to the Verbal Intelligence Quotient, in 3/6 patients Kaufmann Asessment Battery for Children was significantly decreased and in 5/7 Frostig Developmental Test of Visual Perception results were abnormal.
In a group of 12 adult patients neurocognitive evaluation was solely abnormal

in the 3 patients with cerebral disease7. Controversially, neuropsychological testing in 57 adult patients (41 males and 16 females) revealed cognitive dysfunction in 60%. The pattern of impairment was mostly subcortical with defects in frontal-executive functions and memory. It is unclear however how many of these patients were affected by active cerebral demyelinating disease when tested.

We aim to assess neuropsychological function in X-ALD patients without active cerebral demyelinating disease and to correlate these findings to neuroimaging data. Now that newborn screening may be implemented in The Netherlands this data will be particularly valuable to expand our knowledge of the disease spectrum.

Study objective

The primary objective is to assess neuropsychological function in X-ALD patients without active cerebral demyelinating disease. Data of minors will be compared to matched healthy controls. Data of adults will be compared to reference values. The second objective is to correlate these findings to MRI imaging data.

Study design

This study is a cross-sectional cohort study, requiring one visit to the hospital.

Study burden and risks

Research on rare diseases is often restricted by the maximum cohort size available for studies. To investigate the neurocognitive function of X-ALD patients it is especially important to include minors because they form a significant section of the cohort. Taking in mind that newborn screening for X-ALD will be implemented in the Netherlands the necessity to expand our knowledge on all aspects of the disease spectrum in the different age groups is higher than ever. The number of newly diagnosed patients will rise substantially and thorough studies have to be done to be able to inform parents as completely as possible. Moreover, the results of this study have the potential to improve individual patient care if results suggest neurocognitive problems in X-ALD patients. This test battery is relatively brief and therefore not suitable to make any individual statements. However when indicated appropriate follow-up will be initiated. Risks of participation are negligible and the burden of a NPA is considered minimal. The tests are conducted playfully and are usually not considered tedious by children.

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

In order to be eligible to participate in this study, a patient must meet all of the following criteria:
- age for which follow-up is normally recommended (2 years and older)
- male patients with X-ALD (confirmed by ABCD1 mutation analysis)
- MRI data available
- informed consent obtained from participant or legal guardian in case of a minor;Healthy controls must meet all of the following criteria:
- male sex
- classmate of X-ALD patient (age matched)

- informed consent obtained from participant and/or legal guardian

Exclusion criteria

A patient (potential subject) who meets any of the following criteria will be excluded from participation in this study:
- co-existing neurological disease making interpretation of acquired data difficult (for instance, multiple sclerosis)
- active cerebral demyelinating disease, defined as white matter abnormalities with enhancement of the rim on MRI after intravenous gadolinium administration ;A potential control who meets any of the following criteria will be excluded from participation in this study:
- neurological disease making interpretation of acquired data difficult

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:	Other

Recruitment

NL

Recruitment status:	Recruitment stopped
Start date (anticipated):	21-06-2016
Enrollment:	55
Type:	Actual

Ethics review

Approved WMO

Date:	30-03-2016

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	NL56368.018.16