Finding suitable clinical endpoints for ARID1B-related intellectual disability

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- To determine between-subject and within-subject variability of the study endpoints.- To determine the differences between subjects and healthy controls regarding the study endpoints.- To identify suitable endpoints for future clinical trials in...

Ethical review	Approved WMO
Status	Recruitment stopped
Health condition type	Mental impairment disorders
Study type	Observational non invasive

Summary

ID

NL-OMON48746

Source
ToetsingOnline

Brief title
Endpoints in ARID1B patients

Condition

- Mental impairment disorders

Synonym
Coffin-Siris syndrom, intellectual disability

Research involving
Human

Sponsors and support

Primary sponsor: Centre for Human Drug Research
Source(s) of monetary or material Support: self-funded study

Intervention

Keyword: ARID1B, Biomarker, Intellectual disability

Outcome measures

Primary outcome

CNS tests, CHDR

All subjects:

- Saccadic eye movements

- Body sway

- Resting state electroencephalography

- Task based EEG

Visual evoked potential

Auditory steady state response

Passive auditory mismatch negativity

Group 2-4 (Subjects > age 4)

- Adaptive tracking

- Finger tapping

- Smooth pursuit eye movement

- Task based EEG

Active auditory mismatch negativity

- Memory tests

Animal fluency test

Stroop-like day-night test

Wearables, trial@home

All subjects:

- 6-day physical activity, heart rate, sleep (Nokia Steel HR)

- 6-day questionnaire

Secondary outcome

not applicable

Study description

Background summary

De novo truncating mutations in AT rich interactive domain 1B (ARID1B) are found in about 1% of patients with intellectual disability (ID). Recently, an ARID1B mouse model showed a reduction of inhibitory gabaergic interneurons, and that stimulation of the GABA system by clonazepam in these mice reverses their cognitive and behavioural phenotype. Although it would be of interest to eventually test clonazepam in ARID1B patients, there are currently few suitable clinical endpoints to determine treatment effects in these patients. The LUMC has an internationally recognized expertise centre for patients with ARID1B mutation and has access to an international cohort of about 150 patients. In the Netherlands, there are currently 35 known ARID1B patients. This puts LUMC in a unique position to perform research in this rare patient group. CHDR has a lot of experience conducting central nervous system (CNS) tests using the Neurocart® system. The Neurocart® consists of a battery of non-invasive tests that cover all functional domains of the CNS. It provides rapid retesting of both subjective and objective measures. Furthermore, the CHDR home-monitoring platform allows for the registration of physical activity, including heart rate and sleep in an at home-setting. This study aims to identify relevant endpoints for the detection of drug effects in children with ARID1B.

Study objective

- To determine between-subject and within-subject variability of the study endpoints.
- To determine the differences between subjects and healthy controls regarding the study endpoints.
- To identify suitable endpoints for future clinical trials in patients with ARID1B-related intellectual disability.

Study design

Observational, non-interventional case-control study to investigate possible endpoints to be used in future clinical trials.

Study burden and risks

This is a non-interventional study. The study assessments have been chosen because they are considered to be non-invasive and are relatively easy to perform. In an earlier study where the Neurocart® was used to perform measurements in children aged 8-13, tolerability was excellent and all the participants said to like the study *quite much* or *very much*. EEG electrodes were considered to be *non-annoying* by 66% of subjects and 66% of subjects would participate again in a similar study (3). Modifications to the Neurocart® will be made to make the environment as child-friendly as possible, for example with the use of a chair extender and a safe ramp to enable the completion of certain tests.
The actual burden for subjects consists of the time spend behind the Neurocart®, which is not longer than a typical outpatient clinic visit in the expertise centre of the LUMC. Study subjects will have no direct benefit from study participation. The value of this research is in gaining insights into the neurocognitive phenotype of ARID1B syndrome and develop possible endpoints for future clinical trials. Such knowledge is an important step in the research for therapeutic interventions. The proposed research can be considered group-related because it is only feasible by including patients themselves.

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

ARID1B group
- Informed consent provided by both parents or the legal guardian prior to any study-mandated procedure.
- Known mutation in ARID1B.
- Assent provided by the participant.
Healthy control subjects
- Informed consent provided by both parents or the legal guardian if aged 11 years or younger.
- Informed consent provided by both parents or the legal guardian, and the participant if aged 12 up and till 15 years.
- Informed consent provided by the participant if aged 16 years or older.

Exclusion criteria

Clear indication of not wanting to participate during the study
Use of drugs, benzodiazepines or any other medication or drug with the potential to influence study related endpoints in the investigator*s opinion.;Healthy control subjects:
- Presence of intellectual disability.

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):	22-11-2018
Enrollment:	24
Type:	Actual

Ethics review

Approved WMO Date:	22-11-2018
Application type:	First submission
Review commission:	BEBO: Stichting Beoordeling Ethiek Bio-Medisch Onderzoek (Assen)
Approved WMO Date:	11-01-2019
Application type:	Amendment
Review commission:	BEBO: Stichting Beoordeling Ethiek Bio-Medisch Onderzoek (Assen)

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	NL67086.056.18