UNIQUE, center for autism spectrum disorders with a rare genetic origin

Published: 07-06-2021
Last updated: 17-01-2025

We aim to study the association between (clusters of) genes or genetic pathways and phenotype in a population of people with a rare genetic variant and a (suspected) ASD. We will do this by 1) describing the individual participant, 2) comparing...

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

Summary

ID

NL-OMON54421

Source
ToetsingOnline

Brief title
ASD with a rare genetic origin

Condition

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

Synonym
autism, Autism spectrum disorder

Research involving
Human

Sponsors and support

Primary sponsor: Erasmus MC, Universitair Medisch Centrum Rotterdam
Source(s) of monetary or material Support: Stichting Vrienden van het Sophia

Intervention

Keyword: Autism spectrum disorder, genotyping, phenotyping, rare

Outcome measures

Primary outcome

We will use 16 primary outcome measures of our 5 domains of interest related to phenotype (Physical health, Mental health, Cognitive functioning, Brain functioning and Quality of life). The 16 primary outcome measures are:

- Physical health: Van Wiechen developmental test
- Mental health: ADOS-2, Kiddie-SADS, SRS-2 / SRS-A, RBS-R / RBQ-2A, CBCL / YSR / ASR
- Cognitive functioning: IQ test, BRIEF-P / BRIEF / BRIEF-A, 3 neuropsychological assessment scores: memory, visuospatial and attention/EF, Vineland screener
- Brain functioning: 1 eye-tracking task: Talking/Singing Face paradigm, 2 fNIRS tasks: Talking/Singing Face paradigm and Go/No-Go task; 3 eye reflex meassurements: eyeblink conditioning, acoustic startle response, startle habituation.
- Quality of life: ITQoL / CHQ / SF-36

Secondary outcome

Our second endpoint for this study is to create a biobank and database for this and future research on rare genetic variants and ASD.

Study description

Background summary

Research has demonstrated that 64-91% of the variability in ASD can be explained by genetic influences, as shown in twin studies (Tick, Bolton, Happe, Rutter, & Rijsdijk, 2016). Yet, the genetic background of ASD remains complex and hard to grasp.
The diversity of clinical phenotypes in ASD is in part caused by the underlying genetic heterogeneity of ASD. Genes that share the same genetic pathway might also share correlated phenotypes. Yet, duplications or deletions of the same genes could lead to contrasting molecular, cellular and clinical phenotypes. This illustrates how ASD might result from various types of neuropathology.

We know from previous studies that, on the one hand, ASD can be caused by a single rare variant with a large effect (rare deleterious variants), and on the other hand, the interaction of various genes involved, each with a small additive effect (common variants), can also lead to an ASD phenotype (Woodbury-Smith & Scherer, 2018).
Pathogenic single gene variants and de novo copy number variations are present in 10 to 20% of the patients with an autism spectrum disorder (Abrahams & Geschwind, 2008). These pathogenic variants are the types of disorders UNIEK wants to study.

Study objective

We aim to study the association between (clusters of) genes or genetic pathways and phenotype in a population of people with a rare genetic variant and a (suspected) ASD. We will do this by 1) describing the individual participant, 2) comparing participants with the same genetic variant (if available) and lastly 3) by comparing clusters of genes/genetic pathways.
We want to gain more insight into the underlying pathophysiology of ASD by biologically and behaviourally phenotyping children, adolescents and adults known to have a rare genetic variant and a (suspected) ASD. We hope to achieve this specifically for the unique participants in our study, but also for autism spectrum disorders in general.

Our secondary objective is to create a national biobank and database to benefit future ASD research.

Study design

The design used for this study is a multidisciplinary, exploratory, longitudinal, observational study. We aim to collect data in the following domains: genetics, physical health, mental health, cognitive functioning, brain

functioning, quality of life and demographic data.

Study burden and risks

The visit consists of the following components for the participant:
- 3D photograph of the face (15 minutes)
- Computer games (measuring cortical activity and eye movements) (45 minutes)
- Blood collection (1 x 28 ml) (10 minutes)
- Eye reflex meassurements (20 minutes)
- (Tasks and games with researcher, only if this information is missing (time depends on the tests to be taken))

Only minimally invasive methods (peripheral blood) will be used to collect blood. Side effects of blood collection are usually fairly minor.
There are no known risks or side effects for conducting neuropsychological tasks ((computer) games and tasks) and completing questionnaires. The neuropsychological tasks are adjusted to the cognitive level of the participant. Eye tracking, fNIRS and 3dMD are particularly child-friendly to use and there are no known medical risks associated with these measurements.

The burden is minimal because most research data will already be available and can be requested.

This study focuses on people with a rare genetic variant and a (suspected) ASD. Studying their developmental characteristics is crucial in finding the effect of the genetic variants on ASD phenotypes. Diagnostic tests that are best suited for investigating these characteristics are mostly taken when the patients are young and benefit their care. Because of this, and because of the rareness of the variants of interest, no other study groups can be used instead.

Contacts

Public
Erasmus MC, Universitair Medisch Centrum Rotterdam

Wytemaweg 80
Rotterdam 3015 CN
NL
Scientific
Erasmus MC, Universitair Medisch Centrum Rotterdam

Wytemaweg 80
Rotterdam 3015 CN

NL

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)

Inclusion criteria

- Have a rare genetic variant
- Have a (suspected) ASD diagnosis

Exclusion criteria

- Unable to give informed consent to all aspects of the study (i.e. no parent or caregiver can provide informed consent (in case of minors and adolescents/adults with intellectual disability)).
- Physically unable to participate in the study

Study design

Design

Study type: Observational invasive

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

Recruitment

NL

Recruitment status:	Recruiting
Start date (anticipated):	01-11-2021
Enrollment:	108
Type:	Actual

Ethics review

Approved WMO Date:	07-06-2021
Application type:	First submission
Review commission:	METC Erasmus MC, Universitair Medisch Centrum Rotterdam (Rotterdam)
Approved WMO Date:	21-12-2021
Application type:	Amendment
Review commission:	METC Erasmus MC, Universitair Medisch Centrum Rotterdam (Rotterdam)
Approved WMO Date:	22-02-2022
Application type:	Amendment
Review commission:	METC Erasmus MC, Universitair Medisch Centrum Rotterdam (Rotterdam)
Approved WMO Date:	31-03-2023
Application type:	Amendment
Review commission:	METC Erasmus MC, Universitair Medisch Centrum Rotterdam (Rotterdam)
Approved WMO Date:	18-12-2024
Application type:	Amendment
Review commission:	METC Erasmus MC, Universitair Medisch Centrum Rotterdam (Rotterdam)

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	NL73226.078.20