# CANDY MULTIPLEX STUDY

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Last updated: 13-06-2024

1) Assess the whole genome sequence (WGS) and clinical profile of the MPX families to identify how rare and common genetic variants interact to produce shared versus distinct NDDs and clinical features in individuals, or different combinations of...

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| **Ethical review** | Approved WMO |
| **Status** | Recruiting |
| **Health condition type** | Mental impairment disorders |
| **Study type** | Observational invasive |

## Summary

### ID

NL-OMON52192

**Source**
ToetsingOnline

**Brief title**
Multiplex

### Condition

- Mental impairment disorders
- Developmental disorders NEC

**Synonym**
Neurodevelopmental Disorder

**Research involving**
Human

### Sponsors and support

**Primary sponsor:** Radboud Universitair Medisch Centrum
**Source(s) of monetary or material Support:** Horizon2020 programme of the EU (project □CANDY□);grant number 847818

## Intervention

**Keyword:** ADHD, Autism Spectrum Disorder (ASD), Epilepsy, Intellectual Disability

## Outcome measures

### Primary outcome

1) Complete genetic profile of all participants (including rare and common genes).

2) Refined phenoptyping of all participants by means of questionnaires and interviews in terms of: ASD symptoms and traits, Cognitive and neurocognitive level, Developmental level, Somatic comorbidities (clinical epilepsy, allergies, immune disease, gastro-intestinal problems) and Psychiatric comorbidities.

A subsample of the participants will be invited for a nested follow-up study with assessment of EEG/ERP, eye-tracking and cognition; for this, we will submit an amendment at due time.

### Secondary outcome

n.a.

# Study description

### Background summary

Neurodevelopmental disorders (NDDs) are frequent and significantly impact peoples* lives. According to the DSM-5, NDDs include Autism Spectrum Disorder (ASD), Attention Deficit Hyperactivity Disorder (ADHD), Intellectual Disability (ID), specific learning disorders, language disorders and motor disorders.

ADHD, ID and epilepsy co-occur more often within an individual with ASD than in the general population. Further, NDDs are highly heritable and cluster in partly the same families. Most studies investigate families with a single affected member but few studies have investigated the other family members who are likely to be affected by NDDs or epilepsy. The relationship between genotype and phenotype is only partially understood, especially in families in which several individuals are affected by heterogeneous forms of NDDs.
In the current study, we will investigate the shared and distinct genetic and biologic mechanisms involved in those NDDs by recruiting so-called multiplex (MPX) families in which there are at least two patients, one proband with ASD, and at least one other first-degree or second-degree relative with epilepsy, ASD, ID or ADHD.

**Study objective**

1) Assess the whole genome sequence (WGS) and clinical profile of the MPX families to identify how rare and common genetic variants interact to produce shared versus distinct NDDs and clinical features in individuals, or different combinations of NDDs and/or epilepsy in an individual.

Nota Bene: We will not perform whole genome sequencing analysis in participants younger than 16 years, but only assess variation in "common genes".

2) Identify the molecular pathways that are involved in the clinical phenotype and cut across NDD in relationship with the genetics variants by combining different technique used to identify (i) mutated genes; (ii) common genetic variants; (iii) the genetic background; and (iv) the clinical profile of the individual.

**Study design**

The CANDY multiplex study is an observational multi-centre study conducted at five sites: Robert-Debré Hospital (Paris), King*s College London (London), Radboudumc (Nijmegen), Ghent University and Karolinska Institutet (Stockholm). The study will be conducted over 36 months (time between the first and last visit).

**Study burden and risks**

We will collect biosamples by means of venapuncture in all participants for genetic studies and immune profiling, and collect data by questionnaires and interviews. In addition to adults and adolescents, children of 3 years and older will be included in this study, as we are also investigating the development of and emergence of NDDs over a wide age range. A study of very young and young children through to adults is vital to understanding how the clinical and genetic/ biomarker profile of NDDs changes at different time

points. As this is an explorative study, the hypotheses that are generated as a result of these experiments will stimulate and inform future NDD research. Overall, this work will lead to new insights into the common and distinct genetic and biologic mechanisms that underpin ASD, ADHD, ID and epilepsy. This will lead to better counseling of families with NDDs and development of targeted treatments.

## 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)

### Inclusion criteria

Multiplex (MPX) families will be enrolled when there are at least two diagnosed individuals, one with ASD, and at least one other first or second-order member

with epilepsy, ASD, ID or ADHD (age 3 years and older). All unaffected first-degree relatives of an MPX family will be invited to participate as well.

### Exclusion criteria

None of the biological parents of the ASD proband is available / willing to participate

## Study design

### Design

**Study type:** Observational invasive

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

### Recruitment

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| Recruitment status: | Recruiting |
| Start date (anticipated): | 05-06-2023 |
| Enrollment: | 100 |
| Type: | Actual |

## Ethics review

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| Approved WMO Date: | 12-01-2022 |
| Application type: | First submission |
| Review commission: | CMO regio Arnhem-Nijmegen (Nijmegen) |
| Approved WMO Date: | 18-05-2022 |
| Application type: | Amendment |
| Review commission: | CMO regio Arnhem-Nijmegen (Nijmegen) |
| Approved WMO | |

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| Date: | 06-04-2023 |
| Application type: | Amendment |
| Review commission: | CMO regio Arnhem-Nijmegen (Nijmegen) |
| Approved WMO Date: | 01-08-2023 |
| Application type: | Amendment |
| 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 | NL76487.091.21 |