Early cognitive, social and neural mechanisms that precede clinical onset of ASD in a community sample

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Objectives: 1) Assess neural and cognitive biomarkers (through eye-tracking, EEG/ERP and cognitive measures) in a community sample of infants at heightened non-familial risk for ASD and in age and gender matched low-risk controls. The HR group is...

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

Summary

ID

NL-OMON49325

Source
ToetsingOnline

Brief title
Early mechanisms of autism

Condition

- Mental impairment disorders
- Communication disorders and disturbances

Synonym
Autism Spectrum Disorder

Research involving
Human

Sponsors and support

Primary sponsor: Radboud Universitair Medisch Centrum
Source(s) of monetary or material Support: Marie-Curie scheme for ITN (project

SAPIENS)

Intervention

Keyword: Autism Spectrum Disorder (ASD), biomarker, cognitie, EEG

Outcome measures

Primary outcome

Behavioural

Communication and Social development Signals (CoSoS)

Social Responsiveness Scale (SRS)

Autism Diagnostic Observation Schedule (ADOS-2)

EEG/Eye-Tracking

Amplitude/latency of event-related potentials (ERPs) to visual and auditory

stimuli

Evaluation of EEG power (time frequency analysis)

Location of eye gaze and fixation duration (eye-tracking)

Secondary outcome

n.a.

Study description

Background summary

Over the last few years, there has been an increasing interest in the investigation of early cognitive and neural biomarkers that precede the clinical onset of autism spectrum disorder (ASD) to promote an earlier detection and intervention, and thus, improved long-term outcomes. Indeed, ASD is a neurodevelopmental disorder associated with a heterogeneous set of

deficits. For this reason, a clinical diagnosis is rarely made before three or four years of age as the expression of ASD is subtle and not captured consistently through behavioural measures. However, the majority of these studies has been focusing on prospective longitudinal studies of infants at high familial risk for ASD (HR-sibs), that is, infants who have an older sibling with a clinical ASD diagnosis.
Prospective longitudinal HR-sibs studies have provided unique and valuable insights regarding the early ASD phenotype. However, it remains unclear whether these studies are representative of all children with ASD. In fact, this population may not be representative, hampering generalization for the estimated 89% children from community settings who cannot be identified based on known genetic risk factors (such as having an older sibling with ASD). Thus, it is important to determine the suitability of using HR*siblings as a reference group for the development of ASD, as well as to further inform possible etiologic heterogeneity. In the proposed study, we aim to investigate the neural and cognitive correlates (through eye-tracking, EEG/ERP and cognitive measures) in a community sample of infants at heightened non-familial risk for ASD (HR) and in age and gender matched low-risk controls (LR). Moreover, we aim to explore whether early social abnormalities in children identified as high-risk from community settings (HR) are associated with atypicalities in early cognitive and neural markers of ASD in HR-sibling designs.

Study objective

Objectives: 1) Assess neural and cognitive biomarkers (through eye-tracking, EEG/ERP and cognitive measures) in a community sample of infants at heightened non-familial risk for ASD and in age and gender matched low-risk controls. The HR group is defined as at *risk* based on the display of early social abnormalities. 2) Explore whether atypicalities in biomarkers in a community high-risk sample are associated with atypicalities in early cognitive and neural markers of ASD as found in familial high-risk designs. 3) Assess the ASD diagnostic status of both groups of infants at 36 months.

Study design

A non-invasive explorative longitudinal study which will make use of eye-tracking, electroencephalography and behavioural measures. Measures will be taken at ages 18-24 months. At 36 months, we will determine the ASD diagnostic status of both groups of infants with the administration of the ADOS-2.

Study burden and risks

The proposed research concerns the early cognitive and neural markers of infants from a community sample at risk for ASD and controls. Investigating early ASD markers has the potential of improving our understanding of

underlying mechanisms of ASD, further validating previous findings from HR-sibs literature. The identification of early cognitive and neural markers that precede the onset of ASD symptoms is of great scientific and clinical relevance for an earlier intervention and, thus, improved long-term outcomes.
Autism is a developmental disorder which is characterized by its onset in early childhood. As our aim is to identify biomarkers of early ASD, the main research question of the current project cannot be answered by testing older children, adolescents and adult participants. EEG and eye-tracking are techniques that do not pose any risk to the subjects.There are no invasive measures, the risks associated with these measurements are negligible, no adverse events are expected, and the burden for the participants is considered to be minimal. The research team has extensive experience with high-risk and control infants of similar or even younger age, and thus, has ample experience working with infants and training researchers. Moreover, this means that the our age group is relatively easily accessible by our research team, since recruitment is supported by the SCOPE project (NL65479.091.18) and the Well-Baby Offices for the high-risk children and by the Baby & Child Research Center (Radboud University, Nijmegen) for the low-risk children. Our study will require a visit to the Donders Center for Cognitive Neuroimaging (DCCN) with a time investment of about 2 to hours, including breaks in between, and another visit at 36 months for assessing diagnostic outcome.

Contacts

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Trial sites

Listed location countries

Netherlands

Eligibility criteria

Age
Children (2-11 years)

Inclusion criteria

High-risk infants
Age between 18 months and 24 months old
At least one of the parents understands and speaks Dutch
Positive screen on the Communication and Social development Signals (CoSoS) (with a score >=3)
Caregiver and/or well-baby office professional (doctor, nurse) has ASD-specific concerns about their child

Low-risk infants
Age between 18 months and 24 months old
At least one of the parents understands and speaks Dutch
Negativescreen on the Communication and Social development Signals (CoSoS) (with a score <3)
Caregiver and/or professional does not have any ASD-specific concerns about the child

Exclusion criteria

High-risk infants
Diagnosis of epilepsy or history of fits/convulsions in infant (not including febrile convulsions);
Known presence of genetic syndrome (in proband or infant) clearly related to ASD (e.g. TSC, FXS, 22q11, 16p11.2, Rett*s)
Presence of known significant uncorrected vision or hearing impairment in infant (reported to parent by a doctor or health care professional)
Infant was born prematurely (pre 36 weeks)
Infant is looked after by the state (e.g. foster care), or other situation in which neither birth parent is involved in the infant*s care.

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Diagnosis of epilepsy or history of fits/convulsions in infant;
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Presence of known significant uncorrected vision or hearing impairment in infant (reported to parent by a doctor or health care professional)
Infant was born prematurely (pre 36 weeks)

Infant is looked after by the state (e.g. foster care), or other situation in which neither birth parent is involved in the infant*s care.
Presence of known significant developmental or medical condition in infant likely to affect brain development or infant*s ability to participate in the study (e.g. Cerebral Palsy, Down*s syndrome, cystic fibrosis)
Presence of ASD in 1st degree relatives

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:	Recruiting
Start date (anticipated):	10-03-2021
Enrollment:	100
Type:	Actual

Ethics review

Approved WMO Date:	11-11-2020
Application type:	First submission
Review commission:	CMO regio Arnhem-Nijmegen (Nijmegen)
Approved WMO Date:	30-12-2020
Application type:	Amendment
Review commission:	CMO regio Arnhem-Nijmegen (Nijmegen)

Approved WMO Date:	16-02-2023
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	NL72555.091.20