Mechanisms underlying the development of autism: a multi-site prospective study in very young high-risk siblings and controls

Published: 03-09-2013
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Primary objective: To identify early cognitive, neural, behavioural and bio-markers which precede the onset of clinical symptoms of ASD, through obtaining measures of eye tracking, EEG/ERP, NIRS, cognitive performance and collecting DNA and...

Ethical review	Approved WMO
Status	Recruitment stopped
Health condition type	Developmental disorders NEC
Study type	Observational non invasive

Summary

ID

NL-OMON41412

Source
ToetsingOnline

Brief title
Development of autism

Condition

- Developmental disorders NEC

Synonym
Autism Spectrum Disorder; autism

Research involving
Human

Sponsors and support

Primary sponsor: Universitair Medisch Centrum Sint Radboud

Source(s) of monetary or material Support: Europese Unie (Innovative Medicines Initiative - IMI); dit is een subsidie gebaseerd op public-private partnership van de EU en EFPIA,Hoffmann-La Roche,Janssen-Cilag,Vifor

Intervention

Keyword: Autism Spectrum Disorder, Early biomarkers, Early clinical symptoms, EEG/ERP, NIRS and eye-tracking

Outcome measures

Primary outcome

The main dependent measure is the diagnosis of ASD and the severity of ASD

symptoms at age 36 months.

The main predictive measures for cognition, eye tracking and EEG/ERP are:

- Cognitive functioning (Mullen Scales of Early Learning)

- Time locked voltage changes (µV) at different electrode sites (EEG)

- Amplitude of event-related potentials wave to stimuli (ERPs)

- Evaluation of EEG power spectrum (frequency and time frequency analysis) (EEG)

- Power changes (µV2) at different electrode sites (EEG)

- Oxygenated and deoxygenated hemoglobin concentration changes (NIRS)

- Location of eye gaze and timing of eye movements (eye tracking)

- Anticipatory eye movements (eye tracking)

- Fixation duration (eye tracking)

Secondary outcome

Not applicable

Study description

Background summary

Young infants who have an older sibling with Autism Spectrum Disorder (ASD) have a substantially increased risk for developing ASD themselves. The cognitive, neural and behavioural mechanisms that underlie the development of ASD are still unknown. This study is designed to examine the early cognitive, neural, behavioural and bio-markers which precede the onset of clinical symptoms of ASD in high-risk siblings and in healthy controls.

Study objective

Primary objective: To identify early cognitive, neural, behavioural and bio-markers which precede the onset of clinical symptoms of ASD, through obtaining measures of eye tracking, EEG/ERP, NIRS, cognitive performance and collecting DNA and biochemical measures.
Secondary objective: To increase our understanding of early clinical symptoms of ASD.

Study design

Prospective longitudinal observational study. Measures will be taken at age 5, 10, 14, 24, 36 months.

Study burden and risks

The study of the early markers that precede the clinical symptoms of ASD can only be performed in very young children. All measures proposed have been used earlier by the research team. There are no known risks associated with participation in the proposed research. Blood for DNA and biochemistry will be obtained at age 36 months through venipuncture by an experienced nurse. Additionally, urine will be collected at this time point. The burden for both participant and caregiver are kept as low as possible, see for a more elaborate description the research protocol.

Contacts

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Trial sites

Listed location countries

Netherlands

Eligibility criteria

Age
Children (2-11 years)

Inclusion criteria

High-risk siblings:
- Age between 4 months and 6 months OR younger than 11 months
- Older full sibling with ASD (clinical diagnosis autism, PDD-NOS or Asperger syndrome)
- At least one parent speaks Dutch to child at home (does not need to be parent*s native language);Controls:
- Age between 4 months and 6 months OR younger than 11 months
- Older full sibling with typical development (by parent report)
- At least one parent speaks Dutch to child at home (does not need to be parent*s native language)

Exclusion criteria

High-risk siblings:
- Diagnosis of epilepsy or history of fits/convulsions
- Presence of genetic syndrome (in proband or infant) clearly related to ASD (e.g. Tuberous Sclerosis, Fragile-X)
- Presence of known significant uncorrected vision or hearing impairment in infant (reported to parent by a doctor or health professional)
- Infant was premature (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, foetal alcohol syndrome);Low-risk:
- Diagnosis of epilepsy or history of fits/convulsions
- Presence of known significant uncorrected vision or hearing impairment in infant (reported to parent by a doctor or health professional)
- Infant was premature (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)
- Interested in study because parents are concerned that their infant is developing ASD, despite negative family loadings
- 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:	Recruitment stopped
Start date (anticipated):	19-05-2014
Enrollment:	105
Type:	Actual

Ethics review

Approved WMO

Date:	03-09-2013
Application type:	First submission
Review commission:	CMO regio Arnhem-Nijmegen (Nijmegen)
Approved WMO Date:	11-03-2015
Application type:	Amendment
Review commission:	CMO regio Arnhem-Nijmegen (Nijmegen)
Approved WMO Date:	04-06-2015
Application type:	Amendment
Review commission:	CMO regio Arnhem-Nijmegen (Nijmegen)
Approved WMO Date:	18-06-2015
Application type:	Amendment
Review commission:	CMO regio Arnhem-Nijmegen (Nijmegen)
Approved WMO Date:	28-12-2015
Application type:	Amendment
Review commission:	CMO regio Arnhem-Nijmegen (Nijmegen)
Approved WMO Date:	23-06-2016
Application type:	Amendment
Review commission:	CMO regio Arnhem-Nijmegen (Nijmegen)
Approved WMO Date:	05-10-2016
Application type:	Amendment
Review commission:	CMO regio Arnhem-Nijmegen (Nijmegen)
Not approved Date:	19-12-2016
Application type:	Amendment
Review commission:	CMO regio Arnhem-Nijmegen (Nijmegen)
Approved WMO Date:	06-04-2017
Application type:	Amendment
Review commission:	CMO regio Arnhem-Nijmegen (Nijmegen)
Approved WMO	

Date:	03-05-2017
Application type:	Amendment
Review commission:	CMO regio Arnhem-Nijmegen (Nijmegen)
Approved WMO Date:	13-09-2017
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	NL42726.091.13