Cognitive dysfunction and developmental risks for severe psychopathology: insights from sex chromosomal disorders

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

Summary

ID

NL-OMON32524

Source
ToetsingOnline

Brief title
Neurodevelopmental risks in sex chromosomal disorders

Condition

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

Synonym
sex chromosomal aneuploidy, sex chromosomal disorder

Research involving
Human

Sponsors and support

Primary sponsor: Universiteit Leiden
Source(s) of monetary or material Support: NWO VENI-subsidie

Intervention

Keyword: autism, cognition, mri, sex chromosomal disorders

Outcome measures

Primary outcome

cognitive dysfunctions in relation to social behavioural difficulties,

differences between the groups in BOLD (blood oxygen level dependent) response

during cognitive tasks and FA (Fractional Anisotropy) as measured with MRI,

levels of testosterone as measured in saliva samples.

Secondary outcome

number of adverse events

Study description

Background summary

Social skills are crucial for adapting to an increasingly complex social world during development. The importance of impaired social skills and its implications for mental well-being has called for an investigation of cognitive and neurobiological mechanisms underlying severe social dysfunctioning in childhood. So far, our knowledge of these mechanisms is almost exclusively derived from studies on autism spectrum disorders. However, as the autism spectrum represents a limited sampling of the socially impaired population, these findings may not generalize to other children with social dysfunctions. A solution lies in a new strategy that we employ in this study, which is the study of sex chromosomal disorders associated with severe social dysfunctioning (Turner syndrome and Klinefelter syndrome).

Study objective

1. To what degree are the type of social difficulties similar or different in children with Klinefelter syndrome, Turner syndrome and autism?
2. Which cognitive dysfunctions are most strongly related to social difficulties in these different clinical populations?
3. To what degree are various neural circuits underlying social information processing differentially affected in children with Klinefelter syndrome and is

this pattern of brain organization similar or different as compared to children with autism?

Study design

observational study, case-control study

Study burden and risks

The burden and risks for the children and parents are minimal. The requested time investment is a total of 4.5 hours (distributed over 3 visits) for the non-clinical control group and 6.5 hours (distributed over 3 visits) for the clinical groups. The researchers are skilled in working with children and our experience is that children enjoy the cognitive computer 'games'. With regard to eyetracking, children will not notice the eyetracker (no devices are attached) and sit behind the p.c. monitor as any other monitor. Also, saliva collection (3 to 6 ml) will pose no significant burden as children can simply 'spit' in a tube. Also, our experience is that most of the parents are very much interested in reporting on their child's development and receiving reports on the results of the study.
There will be no clinical diagnostic assessments in this study. If parents wish clincial diagnostic assessment (medical, psychological), we will refer them to clinicians. With regard to the MRI session, other studies from the LIBC in which children participate in MRI research give us confidence that children will have no problems with this part of the study. Participants will be also thoroughly screened (using standard procedures) before scanning, resulting in negligible risks. Even though the MRI scans will not be diagnostically screened for abnormalities, the procedure in case of unexpected findings will be explained (in person and in writing) to parents of participants. The potential gains and benefits from this study (see C4) far outweigh the costs.

Contacts

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Trial sites

Listed location countries

Netherlands

Eligibility criteria

Age
Children (2-11 years)

Inclusion criteria

General inclusion criteria include age between 4 and 12 (for the fMRI study: age between 9 and 12), voluntary participation, Dutch speaking and signed informed consent from parents. The specific inclusion criteria for the four groups are as following:;Klinefelter syndrome: diagnosed with (non-mosaic) Klinefelter syndrome based on the presence of a 47,XXY chromosomal pattern as determined by karyotyping.
Turner syndrome: diagnosed with (non-mosaic) Turner syndrome based on the presence of a 46,XO chromosomal pattern as determined by karyotyping.
Autism spectrum condition: an autism spectrum diagnosis according to DSM-IV or ICD-10 criteria
Non-clinical controls: n/a

Exclusion criteria

Clinical groups:
- history of closed-head injury or neurological illness
- contraindications for MRI (part 2 study)
- premature birth;Non-clinical groups:
- use of psychotropic medication
- history of psychiatric illness, closed-head injury, neurological illness or endocrinological dysfunction
- contraindications for fMRI
- premature birth

Study design

Design

Study type: Observational invasive

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

Recruitment

NL

Recruitment status:	Recruitment stopped
Start date (anticipated):	20-04-2009
Enrollment:	200
Type:	Actual

Ethics review

Approved WMO

Date:	02-04-2009
Application type:	First submission
Review commission:	METC Leids Universitair Medisch Centrum (Leiden)

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	NL25924.058.08