Developmental Outcome in Congenital Heart Disease in Kids

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Primary Objective: To investigate motor developmental outcome at school age of children with CHD compared to typically developing peers.Secondary Objective(s): - To investigate neurodevelopmental outcom eat school age on several developmental...

Ethical review	Approved WMO
Status	Pending
Health condition type	Congenital cardiac disorders
Study type	Observational non invasive

Summary

ID

NL-OMON57272

Source
ToetsingOnline

Brief title
DUCK

Condition

- Congenital cardiac disorders
- Cardiac and vascular disorders congenital

Synonym
heart disease, heart problems

Research involving
Human

Sponsors and support

Primary sponsor: Universitair Medisch Centrum Groningen
Source(s) of monetary or material Support: Stichting Hartonderzoek Nederland

Intervention

Keyword: congenital, heart, neurodevelopment

Outcome measures

Primary outcome

The study parameters are the scores obtained through the assessments and questionnaires to assess developmental disorders. The scores of the MABC-2 are dichotomized as *at risk of DCD* (<=16th percentile) or not. As a secondary endpoint also the raw MABC-2 scores will be used. For all other study parameters we will calculate the total scores (except for neurological condition). These total scores will be used as continuous variables in our primary analyses. In some of the exploratory analyses the total scores are also dichotomized, by using valid cut-off points as mentioned in the corresponding manuals as well.

Main study parameter/endpoint:

The Movement Assessment Battery for Children - second edition (MABC-2; Henderson & Sugden, 2007): a valid, reliable, and easily administered motor assessment for children aged 3 to 16 years which is developed to assess DCD. It measures competences in three areas of motor performance; manual dexterity, aiming and catching and balance. The MABC-2 is a composite of two complementary assessments; a checklist and a performance test. In the current study only the performance test is used. The dichotomized total score (composite of the three areas) is the primary outcome parameter in our analysis. A score <=16th

percentile means *at risk of DCD*, as mentioned in the corresponding manuals.

Secondary outcome

Other primary study parameters are:

Tests:

- Minor Neurological Dysfunction assessment (MND; Hadders-Algra, 2010): neurological age-specific examination to detect minor neurological dysfunction. The assessment includes traditional neurological items, such as the evaluation of posture in various positions, muscle tone and reflexes, as well as developmental items, i.e. the items dealing with coordination, fine manipulative abilities and associated movements. The assessment can distinguish between two basic forms of MND: simple MND (s-MND) and complex MND (c-MND).
- Wechsler Intelligence Scale for Children V (WISC-V-NL): IQ test for children aged 6-16 years with sub-indexes on verbal understanding, spatial awareness, fluid reasoning, random access memory and processing speed (Hendriks and Ruiter, 2017).
- Personal Well-being Index: School Children (PWI-SC): an instrument which measures personal well-being in school-aged children with 7 questions on standard of living, personal health, achievement in life, personal relationships, personal safety, feeling part of the community, and future security (Cummins and Lau, 2005).

Parental questionnaires:

- Child Behavior Checklist (CBCL): Questionnaire to screen for behavioural problems, ADHD, anxiety, ASD and depression in children aged 6 to 18 years

(Achenbach, 2006)

- Behavior Rating Inventory of Executive Function (BRIEF): Questionnaire to screen for executive functioning in 5- to 18 year olds (Huizinga and Smidts 2020).
- Social Responsiveness Scale (SRS-2): Questionnaire to screen for social shortcomings associated with ASD (Constantino & Gruber 2012, Roeyers et al. 2015).
- Conners* Rating Scale Revised (CRS-R): Questionnaire to screen for ADHD (Conners 1997).
- The Developmental Coordination Disorder Questionnaire-revised (DCDQ): to assist in the identification of DCD in children (Wilson et al., 2009, Dutch translation; Schoemaker et al., 2006).
- General questionnaire on presence of illnesses, medication use and visual and auditory problems, known developmental problems and history of related therapy, current school of the children, socio-economic background, psychiatric and developmental disorders in the parents. For the children with CHD number of cardiac interventions/surgeries and actual medical information such as latest ECG, ultrasound data and saturation will be collected from their electronic patient files.

Clinical data:

For the children with congenital heart disease we will collect medical history and current medical status, including ECG and ultrasound results. We will also use the previously collected data on prenatal cerebral perfusion and postnatal

cerebral oxygenation in order to correlate this with the current neurological

results.

Study description

Background summary

Children with severe congenital heart disease (CHD) are at increased risk for a different neurodevelopmental development in comparison to healthy peers. Think of cognitive difficulties, problems with executive and adaptive functioning, motor difficulties and language problems. In addition, CHD has been associated with more externalizing and internalizing behavioural problems, attention deficit hyperactivity disorder (ADHD) and autism spectrum disorder (ASD) (Mebius et al. 2017, Huisenga et al. 2020). These developmental problems are related to altered cerebral oxygenation and circulation, already in utero, causing suboptimal brain development. (Sun L et al., 2015). Delayed neonatal brain development is related to less favorable early motor outcomes (Stegeman R et al., 2022). Early detection is key to optimizing developmental outcomes through early intervention at young age when brain plasticity is highest (Kolb et al. 2017). In addition, early recognition of developmental problems is important for children with CHD and their parents for getting the appropriate guidance and support, knowing that part of the developmental problems will persist into adulthood (Mebius et al. 2017).

This research project consists of a follow-up project to the study by Mebius et al. from 2020, performed at the UMCG. This study investigated the association between prenatal cerebral perfusion, postnatal cerebral oxygenation and neurological outcome at the age of 3 months in children with CHD. Inclusion took place between May 2014 and August 2016, with the inclusion criteria being the presence of a prenatally diagnosed heart condition with NICU indication. Forty-five fetuses were eligible in this timeframe. Postnatal exclusion criteria were prematurity <36 weeks and/or serious chromosomal, genetic or structural defects. Based on these exclusion criteria nine neonates were excluded. In the neonatal period, seven neonates died. This resulted in a final study population of 29 neonates with follow-up until the age of 3 months. Tests included prenatal doppler imaging of the middle cerebral artery and the umbilical artery, resulting in a cerebroplacental ratio as a proxy for prenatal cerebral perfusion. Furthermore, postnatal Near-InfraRed Spectroscopy (NIRS), and assessment of the general movements at the age of 7 days and 3 months were performed. In addition, the Motor Optimality Score (MOS) was used to assess the motor repertoire in detail. Main result was that prenatal cerebral perfusion was found to be associated with neurologic outcome at the age of three months. In addition, neonates with both prenatal and postnatal perfusion or oxygenation

problems had the highest risk of having a deviant neurological condition.

To the best of our knowledge, no research has been done yet on the association between prenatal cerebral perfusion, postnatal cerebral oxygenation and neurodevelopmental outcome at school age in children with severe CHD. The UMCG CHD study group provides an excellent opportunity to investigate this. The current study therefore consists of a follow-up study in which the CHD-group will be re-invited for neurodevelopmental assessments to associate previous cerebral perfusion and oxygenation with cognitive development, neurological condition, motor development, adaptive and psychosocial functioning and signs of ASD and ADHD. An age and sex matched control group of typically developing children will be added for comparison.

We think the results of this study will add to the quality of care for children with CHD and their parents and that it will provide more insight in the pathophysiological background of brain damage and developmental problems in this specific group of patients.

Study objective

Primary Objective:
To investigate motor developmental outcome at school age of children with CHD compared to typically developing peers.

Secondary Objective(s):
- To investigate neurodevelopmental outcom eat school age on several developmental domains other than motor development of children with CHD compared to typically developing peers.
- To investigate associations between prenatal cerebral perfusion, postnatal cerebral oxygenation and neurodevelopmental outcome at school age of children with CHD.

Study design

Study design
This study is a longitudinal cohort study and is a follow-up study of the previous project of Mebius et al. (Mebius et al. 2020) in which a group of 29 children with CHD was assessed pre- and postnatally until the age of 3 months. For the current project these participants will be re-invited via mail and a control group of healthy, age- and sex-matched typically developing children will be recruited via social media and/or local primary schools.

Both groups will perform multiple assessments to investigate development, while their parents fill in additional questionnaires. Tests will be performed at the UMCG and if possible combined with regular check-ups at the cardiology department. The test procedure will take maximum 3 hours, including a small

break in between. Children at this age, with or without developmental problems, have shown to be able to endure such test durations, so we are confident this will be achievable. Tests will be carried out by well-trained medical students and recorded on video, allowing further supervision. Parents will be in the same room as their child during the whole assessment and will be asked to fill in a set of questionnaires on an Ipad.

Study duration
We aim to finish the study within 1.5 years, using the following time schedule. The study will start in November 2024 and will be finished in March 2026.

Setting
The assessments will take place at the child-lab of the department of Developmental Neurology in the University Medical Center Groningen. For the CHD group the appointment will, if possible, be combined with the regular follow-up visit at the paediatric cardiology department. Travel costs and parking costs of the parents will be re-imbursed

Study burden and risks

In our opinion the burden of this study, namely a 3 hour visit to our hospital with playful tests for the children and questionnaires for the parents, is very much acceptable for the benefits of learning more about neurodevelopmental problems in children with congenital heart disease with which we hope to be able to provide better guidance.

Contacts

Public
Universitair Medisch Centrum Groningen

Hanzeplein 1
Groningen 9713GZ
NL
Scientific
Universitair Medisch Centrum Groningen

Hanzeplein 1
Groningen 9713GZ
NL

Trial sites

Listed location countries

Netherlands

Eligibility criteria

Age
Children (2-11 years)

Inclusion criteria

Inclusion patient group: all children who participated in the first study
Control: age- and sex-matched healthy and typically developing children who attend regular school.

Exclusion criteria

Control group: congenital abnormalities, other medical conditions, special education, ASD/ADHD/neurodevelopmental disorder

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:	Pending
Start date (anticipated):	01-11-2024
Enrollment:	58
Type:	Anticipated

Ethics review

Approved WMO Date:	17-01-2025
Application type:	First submission
Review commission:	METC Universitair Medisch Centrum Groningen (Groningen)

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	NL87417.042.24