Systematic Hospital-based Assessment of Rotterdam*s critically Ill children, their Neurodevelopment and Growth

Published: 10-03-2020
Last updated: 09-04-2024

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Ethical review	Approved WMO
Status	Recruiting
Health condition type	Cardiac and vascular disorders congenital
Study type	Observational invasive

Summary

ID

NL-OMON52751

Source
ToetsingOnline

Brief title
S.H.A.R.I.N.G.

Condition

- Cardiac and vascular disorders congenital
- Neonatal and perinatal conditions
- Neonatal respiratory disorders

Synonym
Neonatal critical illness

Research involving
Human

Sponsors and support

Primary sponsor: Erasmus MC, Universitair Medisch Centrum Rotterdam

Source(s) of monetary or material Support: Sophie Stichting Wetenschappelijk Onderzoek (Lichtjesactie)

Intervention

Keyword: follow-up, neonatal critical illness, neurodevelopment

Outcome measures

Primary outcome

The main study parameter is the relationship between hippocampal volume before discharge and memory at five and eight years of age in all subjects.

Secondary outcome

- The association between factors associated with critical illness (e.g. hypoxia, hyperoxia, anesthetic and analgosedative exposure) and severity of illness (e.g. duration of ICU admission, PRISM, PIM, SNAP-II, VIS) and hippocampal volume at eight years of age
- The association between factors associated with critical illness (e.g. hypoxia, hyperoxia, anesthetic and analgosedative exposure) and severity of illness (e.g. PRISM, PIM, SNAP-II, VIS) and memory at five and eight years of age
- The difference between hippocampal development between the survivors of neonatal critical illness and healthy controls (Generation R NEXT population)
- The difference between memory outcome between the survivors of neonatal critical illness and the reference population (Dutch normative data)

Study description

Background summary

Over the last decade, the number of children admitted to neonatal intensive care units has increased significantly worldwide.1,2 Due to medical improvements, the majority of these children now survive to discharge1,2, necessitating our focus to broaden from prevention of mortality to long-term outcome. Knowledge has emerged that even the so-called *good survivors* are at risk of neuropsychological impairments and school problems, despite having generally average intelligence.3
Strikingly, the incidence of academic difficulties has been found to be high across common causes of neonatal critical illness such as preterm birth, complex congenital cardiac and non-cardiac anomalies and severe respiratory failure in need of treatment with extracorporeal membrane oxygenation (ECMO).4-9 As intelligence is generally normal, the school problems are likely related to specific neuropsychological deficit rather than general intellectual functioning. Indeed, memory deficits in particular are frequently reported following neonatal critical illness.7,8,10-16
The hippocampus, a grey matter structure within the brain*s limbic system, is the critical hub for memory formation and has been found to be particularly vulnerable to conditions associated with critical illness.17-19 Recently, we have described a common neurodevelopmental pathway across critically ill neonates, where early hippocampal alterations result in long-term memory deficits, irrespective of the underlying diagnosis or gestational age.3 However, the exact pathophysiological mechanisms of these long-term neurodevelopmental deficits following neonatal critical illness remain unknown. This is problematic as patients at risk of long-term deficits are generally not identified until the problems have affected school functioning and daily life activities. Furthermore, targeted and early intervention or even prevention is impossible without proper knowledge of what causes these long-term deficits.

Study objective

The main objective of this longitudinal study is to gain insight into the neurodevelopmental trajectories following neonatal critical illness, from the perinatal period to school-age compared to healthy controls. This insight may lead to the identification of early biomarkers of long-term memory deficits in survivors of neonatal critical illness that will improve early identification and treatment of survivors at risk of school problems later in life.

Study design

This study is a single-center prospective, longitudinal study conducted at the department of IC and Pediatric Surgery, the department of Pediatrics (subdivisions Neonatology and Pediatric Cardiology), the department of Radiology, the Department of Obstetrics and Gynecology, the department of Anesthesiology, and the department of Child- and Adolescent Psychiatry/Psychology at the Erasmus MC - Sophia Children*s Hospital. The study

will be conducted over a period of 9 years as children will be asked to return for follow-up visits at five years of age and eight years of age.
To compare the neurodevelopmental trajectory and outcome following neonatal critical illness to typical neurodevelopment, we will use the Generation R NEXT cohort as a reference sample. In this pediatric population study children will undergo neuroimaging during the neonatal period and again around 9 years of age.32 We will use the Generation R MRI scanner and will synchronize our scan protocol with the protocol used in the Generation R NEXT study (MEC-2016-589) to optimize comparison.

Study burden and risks

We regard the risk for participants in this prospective research project to be negligible. An MRI exam is non-invasive and can be reliably performed in infants without sedation.11,20 For the MRI exam at eight years of age, we will use a mock-scanner before the actual MRI to familiarize children with the MR-environment.21 Our extensive experience with non-clinical MRI exams in school-age survivors of neonatal critical illness have shown MRI research to be highly feasible, not harmful and well tolerated by children.21-23 The MRI exam and mock-scanner has been previously approved by the METC in children (Protocol ID NL33603.078.10 and Protocol ID NL47335.078.13). The main burden associated with participation will be the time spent on extra neuropsychological testing at five years of age and extra neuropsychological testing as well as an MRI exam at eight years of age. From previous experience, we have found that children in general enjoy these assessments.
In terms of direct or short-term benefits, the results from the neuropsychological assessments will be shared with the patients, as is part of routine care. As the incidence of academic difficulties and learning problems following neonatal critical illness is significant but often poorly understood, these results from the neuropsychological assessments will help patients and their care takers and teachers to better understand where potential problems lie. Specifically, from previous experience we know that parents have shared these results with school in order to help their child perform better in the classroom. Furthermore, participation in this study increases our insight into long-term neurodevelopmental outcome in survivors of neonatal critical illness, which is needed to improve early identification, and eventually intervention, of patients at risk of learning problems at a later age.

Contacts

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Trial sites

Listed location countries

Netherlands

Eligibility criteria

Age
Children (2-11 years)
Babies and toddlers (28 days-23 months)
Newborns
Premature newborns (<37 weeks pregnancy)

Inclusion criteria

In order to be eligible to participate in this study, a subject must meet the following criteria:
- Admitted within the first 2 days of life to the NICU or PICU of Erasmus MC-Sophia Children*s hospital, and:
- Born between 24-28 weeks of gestation, or;
- Born with complex congenital cardiac anomalies (i.e. aortic arch anomalies; univentricular hearts; transposition of the great arteries), or;
- Born with congenital diaphragmatic hernia, or;
- Neonatal severe respiratory failure in need of treatment with extracorporeal membrane oxygenation within the first 28 days of life

Exclusion criteria

A potential subject who meets any of the following criteria will be excluded from participation in this study:
- Syndromes known to affect neurodevelopment

- For the MRI: metal implants (e.g. certain pacemakers), claustrophobia or other problems such as movement disorders.

Study design

Design

Study type: Observational invasive

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

Recruitment

NL

Recruitment status:	Recruiting
Start date (anticipated):	16-06-2022
Enrollment:	55
Type:	Actual

Ethics review

Approved WMO Date:	10-03-2020
Application type:	First submission
Review commission:	METC Erasmus MC, Universitair Medisch Centrum Rotterdam (Rotterdam)
Approved WMO Date:	23-12-2021
Application type:	Amendment
Review commission:	METC Erasmus MC, Universitair Medisch Centrum Rotterdam (Rotterdam)
Approved WMO Date:	12-12-2022
Application type:	Amendment
Review commission:	METC Erasmus MC, Universitair Medisch Centrum Rotterdam (Rotterdam)

Not approved	
Date:	22-02-2024
Application type:	Amendment
Review commission:	METC Erasmus MC, Universitair Medisch Centrum Rotterdam (Rotterdam)

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	NL67183.078.19