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STRess and Outcomes in Neonatal Intensive Care Unit Graduates (STRONG)

Submission date
12/02/2019

Recruitment status
No longer recruiting

Registration date
25/02/2019

Overall study status
Completed

Last Edited
25/04/2025

Condition category
Pregnancy and Childbirth

[X] Prospectively registered
[_] Protocol
[_] Statistical analysis plan
[X] Results
[_] Individual participant data

Plain English summary of protocol

Background and study aims
Premature birth has many effects during childhood, such as delayed growth and developmental and behavioral problems. Being admitted to a Neonatal Intensive Care Unit and encountering many stressful circumstances may be a contributing factor. In the last decades, evidence has emerged concerning stress and its long-lasting effects with chemical modifications of DNA. The aim of this study is to identify the most stressful stimuli and lead to a better understanding of potential targets for early intervention. Moreover, we aim to investigate the associations between stress and childhood outcomes.

Who can participate?
Anyone who is admitted to the Neonatal Intensive Care Unit of the University Medical Center Groningen can take part.

What does the study involve?
The study involves participants being monitored closely during NICU stay and during the follow-up period of 1 year after birth. Data on stress exposure during NICU stay will be collected from medical files and from rating by nurses. Children will be videotaped twice to study general movements in relation to stress exposure. Biological samples will be collected regularly to investigate the epigenetic profile in relation to stress exposure. Parents will be asked to complete several questionnaires during the first year of life, to study the effects of stress on childhood outcomes.

What are the possible benefits and risks of participating?
The possible benefits of this cohort study that eventually we will find targets for stress reduction and neurodevelopmental improvement. We do not expect any burdens or risks for participants, as the study is purely observational.

Where is the study run from?
Neonatal Intensive Care Unit of the University Medical Center Groningen, Hanzeplein 1, Groningen, Netherlands

When is the study starting and how long is it expected to run for?
March 2019 until March 2021

Who is funding the study?
Universitair Medisch Centrum Groningen (University Medical Center Groningen)

Who is the main contact?
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Contact information

Type(s)
Scientific

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Additional identifiers

EudraCT/CTIS number
Nil known

IRAS number

ClinicalTrials.gov number
Nil known

Secondary identifying numbers
Nil known

Study information

Scientific Title
STRess and Outcomes in NICU Graduates (STRONG): Studying the effects of stress exposure on preterm infants' epigenetic profile and early childhood outcomes

Acronym
STRONG

Study objectives

To investigate the effects of stress exposure in preterm infants on their epigenetic profile, in particular, the NR3C1 and SLC6A4 genes, and evaluate the development of the epigenetic profile over time.

Ethics approval required
Old ethics approval format

Ethics approval(s)
Approved 30/07/2019, Medical Ethical Committee of the University Medical Center Groningen (Postbus 30.001, 9700 RG Groningen, The Netherlands; Tel: +31 (0)50 361 4204; metc@umcg.nl), ref: 2019.128

Study design
Observational cross-sectional cohort study with 1-year follow-up

Primary study design
Observational

Secondary study design
Cohort study

Study setting(s)
Hospital

Study type(s)
Other

Participant information sheet
Not available in web format, please use contact details to request a participant information sheet.

Health condition(s) or problem(s) studied
Stress exposure during Neonatal Intensive Care Treatment

Interventions
Participants in this observational cohort study will be treated according to usual care, we will collect data from medical files (stress measures) and ask nurses to rate stress. Children will be videotaped twice (i.e. during NICU stay and at 3 months when they are at home) to study the general movements. Moreover, we will ask parents to complete several questionnaires during stay in the Neonatal Intensive Care Unit (NICU) and during the follow-up period of 1 year after birth. Finally, we will non-invasively collect placenta, cord blood and stool during NICU stay and in the first year of life to determine the epigenetic profile. The duration of observation will thus be the NICU stay period and follow-up will last 1 year.

Intervention Type
Other

Primary outcome measure
DNA methylation pattern of our primary stress-related candidate gene (NR3C1 gene), measured in gastro-intestinal cells, cord blood and placenta using pyrosequencing, in relation to stress exposure measured at birth, before discharge, 3, 6, 9 and 12 months of age.

Secondary outcome measures
1. DNA methylation patterns of our other stress-related candidate genes measured in gastro-intestinal cells, cord blood and placenta using pyrosequencing, in relation to stress exposure
2. Stress levels of the child, measured by the neonatal infant stressor scale each day during stay in the neonatal intensive care unit,
3. Stress levels of the child according to the neonatal nurses, using a Likert scale each shift and using the COMFORT neo scores each shift.
4. Short-term neurological outcome, as assessed by General Movements Assessment at two weeks and three months of age
5. Long-term neurological outcome, as assessed by the Ages and Stages Questionnaire at 12 months of age
6. Infant quality of life, as assessed by the Infant Quality of Life Instrument at 3, 6, 9 and 12 months of age

Overall study start date
01/09/2018

Completion date
30/06/2022

Eligibility

Key inclusion criteria
1. Gestational age below 30 weeks and/or birth weight below 1000 grams
2. Admittance to Neonatal Intensive Care Unit of the University Medical Center Groningen
3. Written informed consent from both parents

Participant type(s)
Patient

Age group
Neonate

Sex
Both

Target number of participants
108

Total final enrolment
45

Key exclusion criteria
1. Inability of parents to speak/understand Dutch

Date of first enrolment
01/09/2019

Date of final enrolment

01/03/2021

Locations

Countries of recruitment
Netherlands

Study participating centre
University Medical Center Groningen
Hanzeplein 1
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Sponsor information

Organisation
Universitair Medisch Centrum Groningen

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Sponsor type
Hospital/treatment centre

ROR
https://ror.org/03cv38k47

Funder(s)

Funder type
University/education

Funder Name
Universitair Medisch Centrum Groningen

Alternative Name(s)

University Medical Center Groningen, UMCG

Funding Body Type
Government organisation

Funding Body Subtype
Local government

Location
Netherlands

Results and Publications

Publication and dissemination plan
We plan to publish our results in high-impact peer-reviewed journals.

Intention to publish date
30/06/2023

Individual participant data (IPD) sharing plan
The datasets generated during and/or analysed during the current study are available from the corresponding author on reasonable request

IPD sharing plan summary
Available on request

Study outputs

Output type	Details	Date created	Date added	Peer reviewed?	Patient-facing?
Results article	Course of stress	09/12/2021	10/07/2023	Yes	No
Results article	Quality of life	02/07/2021	25/04/2025	Yes	No
Results article		08/04/2024	25/04/2025	Yes	No