Preterm brain injury, long-term outcome and brain development study

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To investigate the association between preterm brain injury, impaired brain development and neurodevelopmental outcomes 9-10 years after VPT birth

Ethical review	Approved WMO
Status	Recruitment stopped
Health condition type	Congenital and peripartum neurological conditions
Study type	Observational non invasive

Summary

ID

NL-OMON47239

Source
ToetsingOnline

Brief title
PROUD study

Condition

- Congenital and peripartum neurological conditions
- Neonatal and perinatal conditions

Synonym
brain development, Preterm brain injury

Research involving
Human

Sponsors and support

Primary sponsor: Leids Universitair Medisch Centrum
Source(s) of monetary or material Support: Chiesi Farmaceutici,Chiesi Pharmaceuticals B.V.

Intervention

Keyword: Brain development, Brain injury, Outcome, Preterm birth

Outcome measures

Primary outcome

Relationship between common structural neonatal MRI abnormalities (white matter injury and cerebellar injury) and neurodevelopmental outcome on different domains (i.e. neuromotor outcome, cognitive outcome, neuropsychological outcome, executive functions and behavioural outcome) 9-10 years after preterm birth.

Relationship between neonatal MRI findings and brain development (i.e. brain tissue growth and markers of brain maturation) and connectivity (EEG and fMRI) 10 years after preterm birth.

Secondary outcome

Relationship between brain development and connectivity 9-10 years after preterm birth and motor, cognitive, neuropsychological, executive and behavioural functioning.

Study description

Background summary

Very preterm (VPT) birth causes brain injury and affects brain development. This leads to a broad spectrum of neurodevelopmental disabilities, including severe motor deficits in 5-10%, and cognitive, behavioural, and socialization deficits in 25-50% of infants. These problems often first manifest at school age. At present, our challenge is to detect children at risk of neurodevelopmental disabilities at an early stage, in order to start early intervention programs, stimulate development, and minimize the long-term impact of prematurity.

Magnetic resonance imaging (MRI) enhances the detection of preterm brain injury and altered brain development. Although neonatal MRI can assist in the prediction of neurodevelopmental outcome, its prognostic value is still under debate. Up to now it is not recommended as standard of care for VPT infants. If MRI proves to predict long-term outcome accurately, it can help to identify infants at risk of impaired neurodevelopmental outcome. Therefore, long-term follow-up studies in VPT infants investigated with MRI are essential.
Both preterm birth and brain injury lead to changes in brain volume, maturation and connectivity in later life that are related to neurodevelopmental impairments. Reduced cerebral volumes have been reported in childhood and adolescence in individuals with a history of preterm birth. However, longitudinal analyses are sparse, and most existing studies do not include neonatal MRI findings. Therefore, the consequences of nowadays frequently encountered types of brain injury in preterm infants, such as white matter injury and cerebellar injury, on subsequent brain development, maturation, activity and connectivity are still unknown. A longitudinal MRI study that combines early neonatal MRI findings with childhood neurodevelopmental follow-up, MRI, and EEG will provide more clarity on the association between preterm birth, brain injury and subsequent brain development and function. This is crucial to understand the link between neonatal neuroimaging findings, brain development and plasticity, and long-term neurodevelopmental outcome.

Study objective

To investigate the association between preterm brain injury, impaired brain development and neurodevelopmental outcomes 9-10 years after VPT birth

Study design

Non-randomized, single centre, observational cohort study

Study burden and risks

Follow-up visits are part of routine care for very preterm infants born with a gestational age <30 weeks, birth weight < 1000 grams, fetal therapy and/or severe brain injury. Visits are performed according to the guidelines of the Dutch working party on follow up for preterm infants. Parents and children will receive a report of the test results and, where necessary, advice for further support and interventions.
Participating children will not benefit directly from the MRI and EEG examination. Although, when abnormalities on EEG or MRI are found that require further treatment, the paediatric neurologist will inform the parents and advise and treat the infants.
At group level, the results of this study will improve the prediction of (long-term) neurological prognosis of individual preterm infants and the understanding of maturational and pathological processes in the brain following

preterm birth. Ultimately this will allow clinicians to provide more informed prognostic counselling to future parents and anticipatory planning. This can lead to early and targeted interventions with the potential to prevent disability and improve outcome.

The risks associated with study participating involving MRI scanning and EEG are negligible.
The MRI protocol involves a limited number of sequences and takes 20 minutes. The procedure will be practiced in advance, using a MR simulator. A monitor will be appointed to monitor the child throughout the MR procedure for verbal or physical signs of anxiety or resistance. For this purpose a microphone and camera are present in the MR room. Parents are encouraged to stay with their children in the MR room. To promote comfort ear protection will be provided using headphones and music will be offered. If any verbal or physical sign of resistance is observed by MRI personnel, investigator, monitor or parents the examination will be interrupted or terminated. No sedatives or anaesthetics will be used.

EEG examination is performed by experienced staff members to minimize the duration of registration. During the whole EEG registration parents can stay with their child. A bed is available for the children during the registration process to rest on.

Contacts

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Trial sites

Listed location countries

Netherlands

Eligibility criteria

Age
Children (2-11 years)

Inclusion criteria

VPT children (GA<32 weeks), born between May 2006 and October 2007, who participated in a previous longitudinal cohort study on neonatal brain imaging and short term outcome, and who underwent MRI examination at TEA

Exclusion criteria

Lack of informed consent of parents (including parental refusal or unable to explain because of language barrier)
Congenital or acquired abnormalities of the central nervous system, other than those caused by preterm birth
Any medical condition, device or implant that pauses a safety issue for MRI examination (exclusion for MRI investigation)
Children in whom a proper preparation for the MRI or EEG procedure is not possible because of severe motor, behavioural or cognitive handicaps or severe anxiety (both for MRI and EEG examination)

Study design

Design

Study type: Observational non invasive

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

Recruitment

NL

Recruitment status:	Recruitment stopped
Start date (anticipated):	16-09-2017
Enrollment:	110
Type:	Actual

Ethics review

Approved WMO Date:	22-06-2017
Application type:	First submission
Review commission:	METC Leiden-Den Haag-Delft (Leiden) metc-ldd@lumc.nl

Approved WMO Date:	21-08-2018
Application type:	Amendment
Review commission:	METC Leiden-Den Haag-Delft (Leiden) metc-ldd@lumc.nl

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	NL59355.058.17

Study results

Date completed:	29-11-2018
Actual enrolment:	67