Brain network analysis in preterm infants using electro-encephalography

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

Summary

ID

NL-OMON44140

Source
ToetsingOnline

Brief title
Brain network analysis in preterm infants

Condition

- Congenital and peripartum neurological conditions

Synonym
premature, preterm

Research involving
Human

Sponsors and support

Primary sponsor: Kinderneurologie
Source(s) of monetary or material Support: Ministerie van OC&W

Intervention

Keyword: Brain, EEG, Network, Preterm infants

Outcome measures

Primary outcome

Phase 1: Retrospective study

Exploration of measures of coupling and organisation of EEG functional brain networks in relation to gestational age by using measures for general connectivity: the Phase Lag Index (PLI) and directed connectivity (the Phase Transfer Entropy) and network organization (Minimum Spanning Tree analysis (leaf number, diameter, betweenness centrality)).

Phase 2: Prospective study:

Main study endpoints are differences in measures of coupling and organisation of EEG functional brain networks between the preterm and term born children at baseline and at the (corrected) age of 2 years and the longitudinal network changes between baseline and at 2 years.

Importantly, baseline EEG network measures will be correlated with neurodevelopmental outcome at 2 years of (corrected) age.

As measures for general connectivity the Phase Lag Index (PLI) and the Phase Transfer Entropy will be used. In addition, Minimum Spanning Tree analysis (leaf number, diameter, betweenness centrality) will be used.

Secondary outcome

see primary study parameters

Study description

Background summary

In the Netherlands 1-2% of live-born infants are born very preterm (<32 weeks of gestation). Multiple factors, such as hypoxia, infection and inflammation, can damage the extremely vulnerable brain of preterm infants and cause brain injury such as periventricular leukomalacia (PVL) and intraventricular haemorrhage (IVH). This brain injury is associated with compromised long term developmental outcome and social behaviour in preterm children. Although the neurological complications of very preterm birth can be visualised, to a certain extent, using cranial ultrasound and MRI of the brain in early stages, it remains difficult to give an accurate prognosis of neurodevelopment for the individual patient.

In addition to structural investigation of brain damage related to preterm birth, brain activity can be measured using electro-encephalography (EEG), magnetic-encephalography (MEG) or functional MRI (fMRI). From this activity, functional brain networks can be derived by measuring the strength, and sometimes direction, of the functional coupling between different brain regions. The architecture of functional brain networks is associated with cognitive performance in adults, especially in complex cognitive functions, such as attention, executive functioning and memory.Recent studies show that during development in healthy children the organisation of these functional networks mature from more random to efficient *small world* network structures, necessary for optimal cognitive functioning, and that in preterm born children differences in these networks can be demonstrated at the age of 6 years.

Better insight in the pattern of functional brain network disruption associated with very preterm birth can lead to a better understanding of the underlying processes and may lead to improved individual prognostication and eventually, may serve as a marker for new intervention strategies in this patient group.

We hypothesize that functional brain network measures may serve as a marker for (disrupted) neurodevelopment in very preterm born infants.

Study objective

We hypothesize that functional brain network measures may serve as a marker for (disrupted) neurodevelopment in very preterm born infants.

Objective: we propose to perform two studies aiming to answer the following questions.

Phase 1: Retrospective study:
Detecting and characterizing functional brain networks in a spectrum from very preterm to term born infants (cross-sectional). How can we optimally perform functional brain network analyses in this type of patients; which network measures can be optimally used in these young infants? Can we estimate sample sizes needed for future studies based on the observed results? How do functional brain networks relate to gestational age?

Phase 2: Prospective study:
1 Detecting and characterizing functional brain network differences in very preterm born infants at TEA and at 2 years in comparison to term born controls (cross-sectional).
2 Detecting and characterizing longitudinal functional brain network development changes between baseline and the (corrected) age of 2 years. Questions that are addressed are: is there a change in brain network topology over time. And if that is the case is there a difference in development of brain networks between the preterm and term born children? (longitudinal)
3 Relating functional brain network changes to specific neurodevelopmental deficits. If patterns of change in functional brain network topology are found, can a relationship with neurological performance be established at the (corrected) age of 2 years? And are there region specific changes related to certain neurodevelopmental deficits?

Study design

Phase 1: Explorative retrospective study
In the database of the department of clinical neurophysiology EEGs of approximately 75 neonates performed from 2012 until 2015 are available for exploring the optimal methods for network analyses in the very young. These EEGs were performed in routine clinical practice in infants admitted at the NICU of the VUMC (from 25 weeks of gestational age to term born patients). All EEG data and clinical information will be analysed anonymously.

Phase 2: Prospective study

Preterm born infants from the NICU at the VUMC (n=10-20, gestational age: 28-32 weeks) and a healthy, term born, control group (n=10-20) from the maternity ward at the VUMC (healthy term borns who are admitted because of maternal indication only) will be investigated. These are relatively small numbers, after we have conducted the retrospective study we might be able to better estimate accurate sample sizes for the current study. We estimate that at the NICU of the VUmc inclusion will take approximately 12 months. At baseline (TEA for preterm born infants and in the first week after birth for the term borns)

and at 2-year follow-up an EEG will be recorded. At the age of 2 years neurodevelopment will be assessed using the Bailey Scales of Infant Development III (BSIDIII). Preterm born infants will be investigated at TEA and at the corrected age of 2 years. Term born infants will be investigated within the first week of life and at the age of 2 years. To evaluate possible brain injury, which could influence network development, all patients will undergo a cerebral ultrasound at TEA for preterm infants and in the maternity ward for term born infants.

Study burden and risks

EEGs are routinely used diagnostic procedures in standard clinical care at the NICU at the VUmc. EEG measurements are non-invasive, taking approximately 45-60 minutes. The procedure is not considered to be painful or difficult and has negligible risks. Regular clinical follow-up of the preterm born infants includes a BSIDIII assessment at the corrected age of 2 years and we will ask parents for permission to register a second EEG in addition. The term born infants are invited for a second EEG and a BSIDIII assessment at the VUMC at the age of 2 years, meaning one extra trip to the hospital. All participants will be examined using cerebral ultrasound, which is also a routine diagnostic procedure in infants. It is a non-invasive, pain-free examination with negligible risks. There is no individual benefit from the EEG or the cerebral ultrasound. Unexpected findings which could lead to medical treatment will be discussed with caregivers of participants.

Contacts

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Trial sites

Listed location countries

Netherlands

Eligibility criteria

Age
Children (2-11 years)

Inclusion criteria

retrospective part: all infants (28-42 weeks gestational age) who underwent EEG in the last three years.
Prospective part: very preterm born infants (28-32 weeks gestational age) admitted to the NICU of the VUmc and term born control infants born in het VUmc.

Exclusion criteria

Antenatal congenital infection, Congenital malformation or syndrome, Invasive respiratory support, Severe complications during NICU admission

Study design

Design

Study type:	Observational non invasive
Intervention model:	Other
Allocation:	Non-randomized controlled trial
Masking:	Open (masking not used)

Primary purpose: Basic science

Recruitment

NL

Recruitment status:	Recruitment stopped
Start date (anticipated):	08-08-2017
Enrollment:	40

Type:	Actual

Ethics review

Approved WMO Date:	04-04-2016
Application type:	First submission
Review commission:	METC Amsterdam UMC

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	NL54151.029.15