European Newborn Study: Early Markers for a Better LifE

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Primary Objective: to develop and evaluate a machine learning (ML) prediction model of brain injury in neonates at high-risk for CP to predict motor, behavioral, and cognitive outcome more accurately.This aim will be achieved by: developing and...

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

Summary

ID

NL-OMON53431

Source
ToetsingOnline

Brief title
ENSEMBLE

Condition

- Congenital and peripartum neurological conditions

Synonym
cerebral palsy

Research involving
Human

Sponsors and support

Primary sponsor: Universitair Medisch Centrum Utrecht
Source(s) of monetary or material Support: Fondation Cérébrale Paralysie en Zoundream AG,Zoundream AG

Intervention

Keyword: 1. Early Diagnostics and Prediction, 2. High-risk newborns with perinatal brain injury, 3. Machine learning for prediction, 4. Open access database / open science

Outcome measures

Primary outcome

The creation of a ML algorithm (including standard clinical care assessment: MRI, EEG, and clinical data collected up to 3 months of age, including GMA and HINE) being able to early predict motor, behavioral, cognitive outcome. The creation and implementation of automated tools to analyze these early assessments in at-risk infants to obtain a more precise, individualized diagnosis and prognosis of CP based on harmonized scans and protocols (GMFCS, BSID-III, CBCL).

Secondary outcome

The development of recommendations to support parents in the process of disclosure of diagnosis and communication around prognosis of the development of their child, using questionnaires and interviews with parents.

Study description

Background summary

Cerebral palsy (CP) is the most common cause of physical disability in children but is still diagnosed too late. Consequently, many children with CP do not get specific intervention until their second birthday, which has consequences for motor and cognitive outcomes, as the great part of the entire neuroplastic window for motor learning is misspent. Specific and reliable tools for the early detection of infants with CP have been recently defined and are now part of the first International Clinical Practice Guidelines. Infants with perinatal risk factors for CP can reliably receive an early diagnosis of CP before 6 months using a combination of brain magnetic resonance imaging (MRI) and either

the general movement assessment (GMA) and/or the Hammersmith infant neurological examination (HINE). In addition, electroencephalography (EEG) is essential to define and monitor the level of brain maturation and seizures in high-risk newborns, thus contributing to outcome prediction. As CP is a heterogeneous condition, it is critical to be able to formulate and communicate 1) an early diagnosis and 2) the functional prognosis of the child at a very young age, so clinicians and families are informed and can make informed decisions on treatment goals and (novel) interventions. Nowadays the combinations of early assessments in one prediction model is lacking, as well as the precision in prediction.

Study objective

Primary Objective:
to develop and evaluate a machine learning (ML) prediction model of brain injury in neonates at high-risk for CP to predict motor, behavioral, and cognitive outcome more accurately.

This aim will be achieved by: developing and validating a ML prediction model that will include the following well-established diagnostic tools: MRI, EEG, GMA and HINE combined with the clinical variables during admission in infants with MRI diagnosed brain injury with high risk of CP. Next to automated scoring tools for each modality.

Secondary Objective(s):
1. a. To gain insight in parental mental well-being and family- and social functioning over the first two years after the birth of their child with brain injury, born preterm or full-term, at high risk of developing CP.
1. b. To examine the relation of parents* experiences around the disclosure of diagnosis, child-related factors and social support with parental mental well-being.
2. To understand the needs and preferences of parents related to the process of disclosure of diagnosis and related to the information they receive regarding prediction and prognosis, to identify what information is meaningful to families.

Study design

This is a longitudinal, prospective, observational multicenter study where several populations of newborn infants with brain injury and high-risk of CP will be enrolled.
We will collect multimodal data from a unique cohort of ~1000 newborn infants with brain injury who are at high risk of developing CP; we will focus on preterm and full-term infants with brain injury at high-risk for CP confirmed using neonatal MRI, please refer to the "inclusion criteria" in the protocol for elaboration.

These infants will be enrolled from 8 large EU neonatal centers with neonatal neurology expertise and followed closely from birth, including initial neuroimaging (MRI) and neurophysiologic assessment using aEEG and EEG, followed by behavioral, clinical, and neuropsychological evaluations through infancy up to 2 years of age (within this 5-year project). Parents also have the option to have their child's crying sounds automatically recorded, and to opt for a 50-minute autism spectrum disorder test for their child at 2 years old. Please refer to "Figure 1" in the added protocol.
The project will start in January 2023: 2,5 years of inclusion, followed by 2 years of follow-up of the infants .
After this 5-year project, we will continue to follow these children in order to define the prognosis regarding cognitive and behavioral domains; this long-term follow-up is particularly important, given that motor deficits are not the main factor that limits the child*s social participation, schooling, and employability.

Study burden and risks

Most of the data for this study are obtained from standard clinical care procedures. For the child, all data are collected from procedures done as part of standard clinical care. For the parents, however, there is an additional action outside of clinical care, namely completing two sets of questionnaires when their child is 4 months and 24 months old. These sets of questionnaire take the parent 20 minutes and 30 minutes respectively to complete. The burden and risks of participating in this study are very low. On the other hand, early prediction of CP by the ML model could improve long-term motor, cognitive and behavioural outcomes in future children. The questionnaires may improve future parental support.

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

-All infants with confirmed brain injury on MRI at high risk for cerebral palsy.
-Written informed parental consent (Dutch, English, French, German, Italian, Spanish).

Exclusion criteria

-Infants not matching the inclusion criteria
-Any proven or suspected severe congenital anomaly, genetic or metabolic disorder
-Presence of an infection of the central nervous system
-Parents < 18 years old
-Not being able to read one of the six Informed Consent languages

Study design

Design

Study type: Observational non invasive

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

Recruitment

NL

Recruitment status:	Recruiting
Start date (anticipated):	06-10-2023
Enrollment:	240
Type:	Actual

Ethics review

Approved WMO Date:	26-04-2023
Application type:	First submission
Review commission:	METC NedMec
Approved WMO Date:	29-02-2024
Application type:	Amendment
Review commission:	METC NedMec
Approved WMO Date:	07-03-2025
Application type:	Amendment
Review commission:	METC NedMec

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	NL83183.041.22