PErsonalized PRognosis for children with traumatic brain injury (PEPR Study)

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We aim to develop an innovative personalized prognostic model for outcome of children with TBI, using a unique combination of demographic, pre-injury and clinical predictors. The value of innovative MRI techniques and promising machine learning...

Ethical review	Approved WMO
Status	Recruiting
Health condition type	Structural brain disorders
Study type	Observational non invasive

Summary

ID

NL-OMON54521

Source
ToetsingOnline

Brief title
PEPR Study

Condition

- Structural brain disorders

Synonym
traumatic brain injury; neurotrauma

Research involving
Human

Sponsors and support

Primary sponsor: Academisch Medisch Centrum
Source(s) of monetary or material Support: Cornelia Stichting & JANIVO Stichting

Intervention

Keyword: neuroimaging, pediatrics, personalized prognosis, traumatic brain injury

Outcome measures

Primary outcome

The primary outcomes of the study are motor functioning (Movement-ABC2), neurocognitive functioning (Wechsler Intelligence Test) and behavioral functioning (Child Behavior Checklist and Teacher Report Form), which will be used to construct an overall outcome score. Demographic, pre-injury and clinical predictors will be prospectively registered, as well as outcome at 6 months post-injury. Magnetic resonance imaging (MRI) will be performed at 1 month post-injury in a subsample of the children with TBI (aged >=8 years, n = 150). Outcome will be defined by the level of functioning for the child*s demographics and pre-injury functioning. This will be measured by an overall outcome score that will be constructed in three steps. First, total scores on each test for each outcome domain (motor, neurocognitive and behavioral functioning) will be transformed to z-scores, where the z-score describes the difference between each TBI patient*s score and the mean of the demographically-matched control group. Second, we will further adjust these z-scores for the influence of pre-injury functioning (parent reported pre-injury behavioral functioning and family functioning) by adding these variables as predictors to the linear regression analyses on each z-score pertaining to an outcome domain. The demographic and pre-injury adjusted z-scores will then be retrieved by extracting the standardized residuals of these regression analyses. Lastly, the overall outcome score will be calculated

by the sum of the adjusted z-scores. Since children with high pre-injury functioning and significant decrement in functioning can still perform in the average range of the general population, the demographic and pre-injury adjustment procedure will increase sensitivity of outcome prediction. The overall outcome score is used for the sake of clinical usability, enabling the development of one prognostic model for outcome in a range of relevant domains of functioning. Thanks to its cumulative nature, the overall outcome score will be sensitive to poor outcome across function domains. The prognostic model will also be used to predict outcome in each function domain separately in order to identify children with selective impairment.

Secondary outcome

• Health status (TBI group and control group): Health status will be assessed as a reference standard, allowing to investigate the relevance of primary study parameters for health status. We will use the Childhood Health Assessment Questionnaire, measuring heath status as defined by disability in a range of Activities of Daily Life.

• School functioning (TBI group and control group): School functioning will be assessed as a secondary outcome measurement in the subsample of children attending a primary school. CITO Pupil Monitoring System results will be used to assess school functioning. Based on the expected age range of this group (6-12 years), this information will be available for a subsample of (3,5*30=) 105 children with TBI. The size of this subsample allows to build a separate highly relevant prediction model for school outcome with a maximum of 7

predictors.

• Brain structure and function (TBI group only): Brain structure and function will be assessed in children with TBI in order to investigate the (1) value of innovative MRI for prognostic purposes and (2) neuroanatomical and neurophysiological mechanisms that underlie neurocognitive impairment and daily life problems. Brain structure and function will be measured using MRI sequences.

• Specific neurocognitive functioning (TBI group and control group): Specific neurocognitive functioning will be assessed in order to investigate the neurocognitive mechanisms that underlie daily life problems and will be measured using the Emma Toolbox for Computerized Neurocognitive Testing;

• Quality of life (TBI group and control group): Quality of life will be measured using the EQ-5D questionnaires for children and adults.

• Brain function (TBI and control group): Resting state brain activity in children will be assessed in order to investigate (1) the E-I balance in children following TBI, (2) assess its value towards explaining the heterogeneity in functional outcome. Brain function will be assessed using resting state EEG.

Study description

Background summary

Traumatic brain injury (TBI) is the leading cause of death and disability in children. TBI can cause poor outcome in crucial function domains, including motor, neurocognitive and behavioral functioning. However, large differences exist between patients, generated by the complex interplay between demographic factors, pre-injury functioning and clinical characteristics. Available clinical prediction tools are insufficient to account for the multifactorial differences in outcome and the complex interplay between predictors. Outcome prediction in children with TBI falls short, preventing clinicians to tailor medical decision making to the child*s individual risk profile. This contributes to overtreatment (i.e. unnecessary follow-up) and undertreatment (i.e. undetected impairment).

Study objective

We aim to develop an innovative personalized prognostic model for outcome of children with TBI, using a unique combination of demographic, pre-injury and clinical predictors. The value of innovative MRI techniques and promising machine learning algorithms will be investigated for prognostic purposes. Additional goals are to explore neurocognitive and neural mechanisms that contribute to poor outcome after paediatric TBI.

Study design

Observational controlled longitudinal study

Study burden and risks

TBI group:
The study procedures are associated with minimal risk. Parental questionnaires assessing demographic characteristics and premorbid child and family functioning will be administered shortly after admission of the child to the hospital (estimated duration: 30 minutes). At one month post-injury, a sample of 150 children aged >=8 years will revisit the hospital for magnetic resonance investigation (estimated duration: max. 1.5 hour). At six months post-injury, children (with at least one supervising parent) will revisit the hospital for outcome measurement (estimated duration: max. 3.5 hours). Altogether, the child and parent will visit the hospital twice (once if no MRI scan is made) in addition to regular care. The total duration of study procedures is 5 hours for children and 1-1.5 hour for parents (excluding 3.5 hours waiting time for parents). Given the specific effects of TBI on (the post-injury development of) children, it is crucial that this study is performed in a sample including

minors with TBI.

Control group:
The study procedures are associated with minimal risk. The outcome measurements will also be executed for children in the control group during one appointment with an estimated duration of max. 3.5 hours. The control group of typical developing children will be used as a reference group for the TBI group and is necessary to elucidate the impact of TBI on outcome measures, as corrected for age, sex and socio-economic status. Standardized population norms are available for some of the outcome measures, but these norms are only standardized for age while it is well-known that other demographic characteristics can have a considerable influence on child functioning. More specifically, children with low socio-economic status are over-represented in the TBI population, while socioeconomic status is known to have a strong influence on the impact and recovery of TBI. Therefore, the confounding influence of socio-economic status needs to be controlled for the construction of a valid and reliable personalized prognosis, which cannot be done using age-standardized population norms. This justifies the need to include a demographically matched typically developing control group in the current study.

Contacts

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Trial sites

Listed location countries

Netherlands

Eligibility criteria

Age
Adolescents (12-15 years)
Adolescents (16-17 years)
Adults (18-64 years)
Children (2-11 years)

Inclusion criteria

Inclusion criteria for the TBI group will be:
1. 4-18 years;
2. Fluent Dutch speaker;
3. Inhabitant of The Netherlands;
4. Hospital admission for mild to severe TBI.
5. No documented and/or parent-reported diagnosis of a neurological disorder (other than TBI).

Inclusion criteria for the control group will be:
1. 4-18 years;
2. Fluent Dutch speaker;
3. Inhabitant of The Netherlands;
4. No documented and/or parent-reported diagnosis of a neurological disorder (among which TBI).

Exclusion criteria

Participants who meets any of the following criteria will be excluded from participation in this study:
1. Absence or withdrawal of written informed consent;
2. Severe motor disability that interferes with outcome assessment at time of assessment;
3. Inability to comprehend testing instructions at time of assessment;
4. Somatic disorders unrelated to TBI and possibly affecting the outcome assessments at time of assessment.

Study design

Design

Study type:	Observational non invasive
Intervention model:	Other
Allocation:	Non-randomized controlled trial
Masking:	Open (masking not used)
Control:	Active
Primary purpose:	Basic science

Recruitment

NL

Recruitment status:	Recruiting
Start date (anticipated):	22-12-2020
Enrollment:	315
Type:	Actual

Ethics review

Approved WMO Date:	20-05-2020
Application type:	First submission
Review commission:	METC Amsterdam UMC
Approved WMO Date:	19-02-2021
Application type:	Amendment
Review commission:	METC Amsterdam UMC
Approved WMO Date:	15-04-2021
Application type:	Amendment
Review commission:	METC Amsterdam UMC
Approved WMO Date:	08-06-2021
Application type:	Amendment
Review commission:	METC Amsterdam UMC
Approved WMO Date:	14-06-2021

Application type:	Amendment
Review commission:	METC Amsterdam UMC
Approved WMO Date:	05-05-2022
Application type:	Amendment
Review commission:	METC Amsterdam UMC
Approved WMO Date:	20-07-2023
Application type:	Amendment
Review commission:	MEC Academisch Medisch Centrum (Amsterdam) Kamer G4-214 Postbus 22660 1100 DD Amsterdam 020 566 7389 mecamc@amsterdamumc.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

ID: 21973
Source: NTR
Title:

In other registers

Register	ID
CCMO	NL71283.018.19
OMON	NL-OMON21973