ACTIVITIES AND PARTICIPATION AFTER MILD TRAUMATIC BRAIN INJURY

THE BRAINS AHEAD! STUDY

IRENE RENAUD

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Irene Renaud

Cover	Nina van Styrum
Printed by	Proefschriftmaken.nl || Uitgeverij BOXPress
ISBN	978-94-6380-549-0

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PROEFSCHRIFT

ter verkrijging van de graad van doctor aan de Universiteit Maastricht,

op gezag van de Rector Magnificus, Prof. dr. Rianne M. Letschert,

volgens het besluit van het College van Decanen,

in het openbaar te verdedigen

op woensdag 23 oktober om 12:00 uur

door

Maria Irene Renaud

Geboren, 7 juni 1986 te Delft

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Prof. dr. A.M.C.F Verbunt

Het Brains Ahead! project werd financieel mogelijk gemaakt door het Johanna Kinderfonds (award number 2012/0040-1552) in samenwerking met het Revalidatiefonds (award number R2012175).

Het verschijnen van dit proefschrift werd mede mogelijk gemaakt door financiële steun van Maastricht University en Revant Revalidatiecentrum te Breda.

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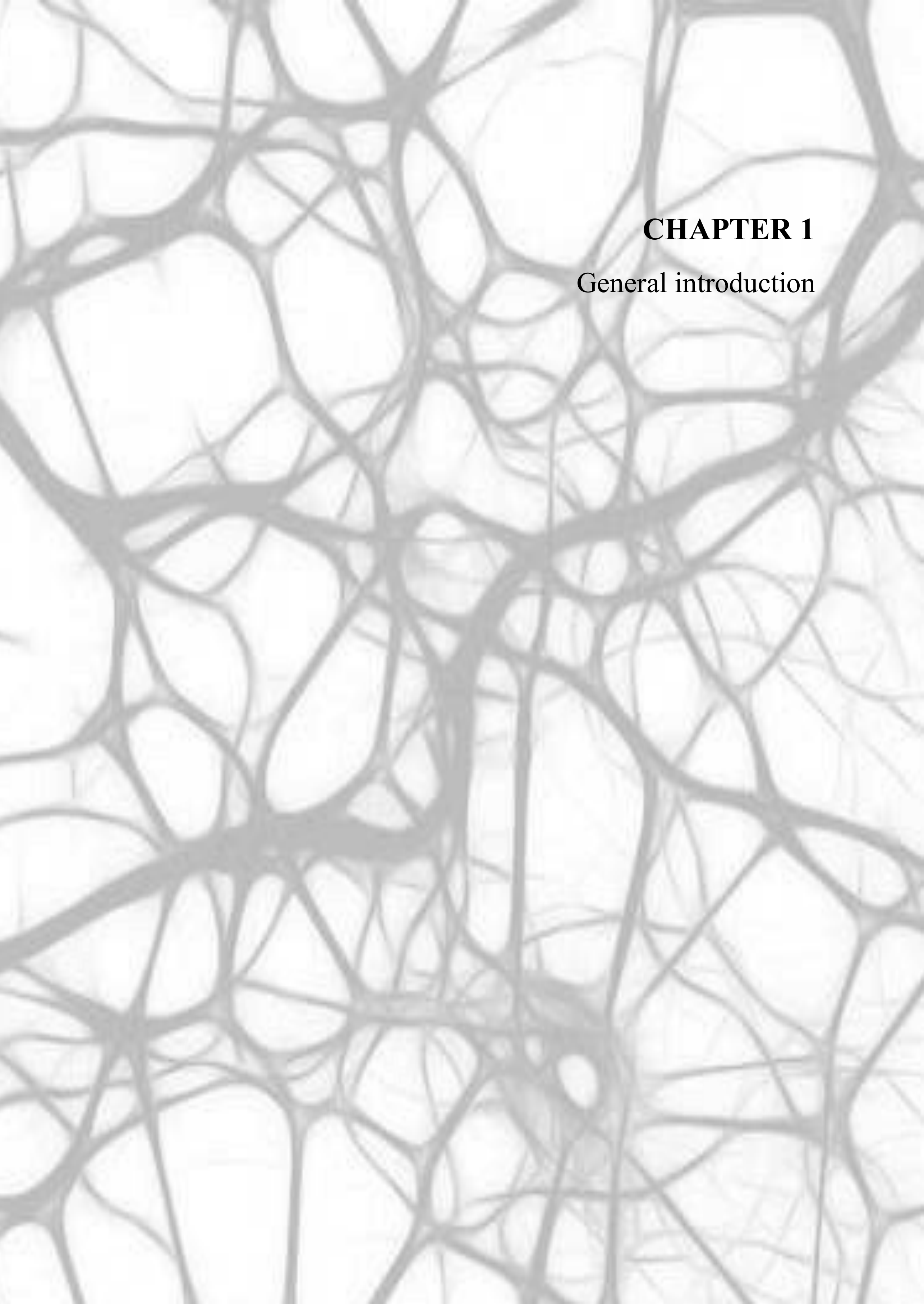
CHAPTER 1

General introduction



Each year, approximately 13,000 children and adolescents aged between 0-24 years old, suffer a traumatic brain injury (TBI) in The Netherlands due to a fall or accident, the majority (80%) of which are mild (MTBI).[1-2] Usual care for children and adolescents with moderate and severe TBI consists (at least) of follow-up care from a neurologist or physiatrist.[3] Since most children with MTBI are expected to recover completely, they do not receive such follow-up care.[3] In several studies was however found that between 6-43% of the children with MTBI suffer from a variety of post-concussive symptoms (PCS) in the physical (e.g. headache), cognitive (e.g. trouble concentrating), emotional (e.g. stress), and behavioural (e.g. irritability) domains up to six months post-injury or longer.[4-8] These long-term symptoms can have a negative impact on activities and participation such as in school, social relations and play.[9-11]

MTBI: lasting consequences and impact on activities and participation

Long-term symptoms accompanying paediatric MTBI, such as cognitive or behavioural problems, are often difficult to recognize and to associate with the MTBI.[12-13] Delayed recognition and underestimation of symptoms may also contribute to limitations on activities and participation.[5,14-15] Studies on the impact of paediatric MTBI on activities and participation specifically are scarce, but in studies of children who had experienced other forms of acquired brain injury (ABI; such as stroke), or studies that investigated mixed samples including more severe forms of TBI, it was found that children who suffer from long-term symptoms may also be at risk for limitations on activities and participation.[9-11] For this reason, both long-term outcomes on activities and participation and predictors of activities and participation after paediatric MTBI remain unclear.[12,16-19]

Studies on PCS, functional-, and family-outcome after paediatric MTBI suggest that both health condition-related-related (e.g. Glasgow Coma Scale score, loss of consciousness, post-traumatic amnesia), environmental (e.g. parental socioeconomic status, pre-injury family functioning), and personal (e.g. age of the child at injury,) factors affect outcome.[20-23] Missing from the literature, are well-designed, longitudinal studies that investigate how the natural course of activities and participation is affected, and that investigate a broad range of factors that may predict long-term problems on activities and participation after paediatric MTBI.

Therefore, we developed a multicenter prospective cohort study (the Brains Ahead! study) that investigates outcome on activities and participation in children during the first six months post-MTBI and possible predictors within the categories of human functioning following the International Classification of Functioning, Disability and Health, children and youth version (ICF-CY).[24]

The results of this study may enable the application of early and focused interventions on long-term problems on activities and participation.[20,23]

Interventions for children with MTBI

Activities and participation are very important for the development of a child, because it helps children to develop different skills and competencies, develop physically and cognitively, develop their own identity, and set different life goals.[25] Early and focused interventions after MTBI may help prevent long-term problems on activities and participation. Only a few interventions for children after MTBI have been studied. Most interventions designed to reduce PCS report positive results.[14-15,26-29]

Evidence for interventions that prevent long-term limitations on activities and participation after paediatric MTBI is scarce. From literature on MTBI intervention studies aimed at preventing long-term problems, we know that early interventions should contain information and education on MTBI, with additional follow-up consultation, including individualized advice on returning to activities and participation and personalized reassurance, and should be offered to patient and family.[14-15,26-34] For this reason, we developed such an early intervention, which combines an inventory of symptoms, reassurance, standardized- and individualized psychoeducation and follow-up (‘The Brains Ahead! intervention’), aimed to prevent long-term problems on activities and participation in children and adolescents after MTBI.

The Brains Ahead! study

The present thesis describes the Brains Ahead! study, which consists of two umbrella study-concepts. First, in a multicenter longitudinal prospective cohort study, we examined the course of activities and participation after MTBI in children and adolescents and predictors for outcome. Next, we developed and examined the effectiveness and feasibility of The Brains Ahead! intervention for children and adolescents with MTBI and their caregivers in a randomized controlled trial study, which was nested in the prospective cohort study. Because literature shows that outcome based on the perspective of the parent may differ from outcome based on the perspective of the child,[35] both perspectives were included in the study. The Brains Ahead! study was a result of a collaboration between Maastricht University, Revant Rehabilitation Centre, and Erasmus University Hospital/ Sophia Children’s Hospital.

Aims of this thesis

The aims of the Brains Ahead! study were to examine activities and participation during the first six months after MTBI in children and adolescents and to identify outcome predictors. Furthermore this study aimed to develop an early psychoeducational intervention focused at preventing problems on activities and participation and evaluate its process and effectiveness. As a result, this thesis addresses the following research questions:

1. What is the natural course of activities and participation during the first six months after MTBI in children and adolescents and for how many children long-term problems on activities and participations are reported?
2. Which factors within the health condition, function, activities, environment, and personal categories predict outcome on activities and participation six months after mild traumatic brain injury in children and adolescents?
3. What is known about early interventions for children after MTBI and what are the recommendations for development of such interventions?
4. How feasible is the early psychoeducational Brains Ahead! intervention for children and adolescents with MTBI and their caregivers aimed at preventing problems on activities and participation?
5. Is the early psychoeducational Brains Ahead! intervention for children and adolescents with MTBI and their caregivers aimed at preventing problems on activities and participation more effective compared to the usual care?

Outline of the thesis

This thesis represents the results of the Brains Ahead! study. It consists of the following parts:

- *Chapter two* describes the study protocol of the Brains Ahead! study into activities and participation of children and adolescents after mild traumatic brain injury and the effectiveness of an early intervention.
- *Chapter three* presents the results of the prospective longitudinal cohort part of the Brains Ahead! study on the course of activities and participation after mild traumatic brain injury in children and adolescents.
- *Chapter four* examines the predictive value of factors within the health condition, function, activities, environment, and personal categories for outcome on activities and participation six months after mild traumatic brain injury in children and adolescents.
- *Chapter five* presents an overview of early interventions in improving the level of activities and participation in youths after mild traumatic brain injury.

- *Chapter six* presents the rationale behind and description of the early psychoeducational ‘Brains Ahead! intervention’ for children and adolescents with mild traumatic brain injury and their caregivers.
- *Chapter seven* discusses the outcomes of the process evaluation study of the ‘Brains Ahead! intervention’.
- *Chapter eight* discusses the outcomes of the randomized controlled trial evaluating the effectiveness of the ‘Brains Ahead! intervention’ compared to the usual care.
- *Chapter nine* presents the general discussion, describing the main findings of the Brains Ahead! study, methodological strengths and considerations, as well as implications for clinical practice and recommendations for further research.

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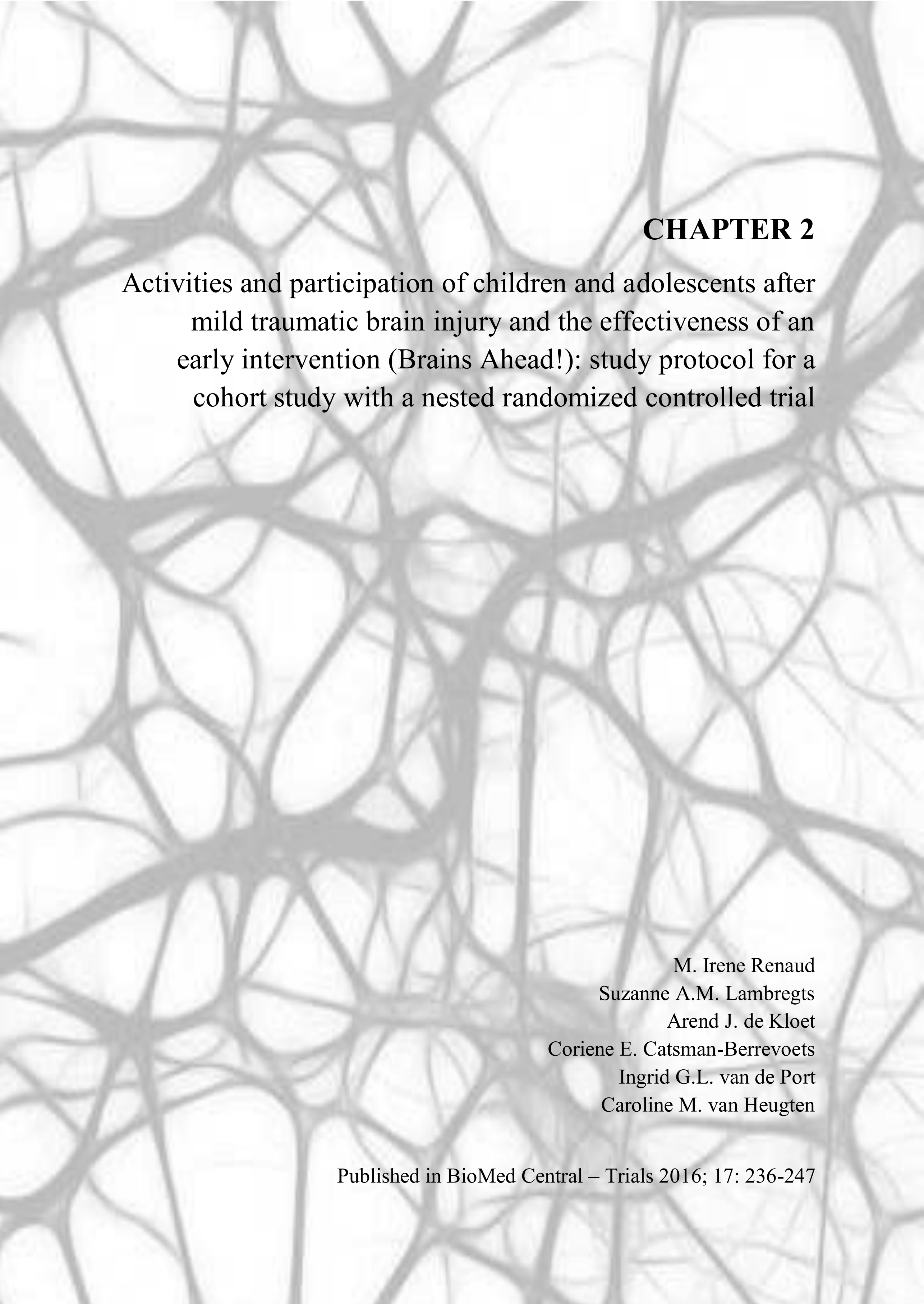

CHAPTER 2

Activities and participation of children and adolescents after mild traumatic brain injury and the effectiveness of an early intervention (Brains Ahead!): study protocol for a cohort study with a nested randomized controlled trial

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Published in BioMed Central – Trials 2016; 17: 236-247

Abstract

Background: Approximately 20% of children and adolescents who have suffered mild traumatic brain injuries may experience long-term consequences, including cognitive problems, posttraumatic stress symptoms and reduced load-bearing capacity. The underestimation and belated recognition of these long-term consequences may lead to chronic and disruptive problems, such as participation problems in school and in social relationships. This study aims to examine the level of activities and participation of children and adolescents up to six months after a mild traumatic brain injury and to identify possible outcome predictors. Furthermore, the study aims to investigate the effectiveness of an early psychoeducational intervention and compares the results to those obtained with usual care.

Methods/Design: This paper presents the Brains Ahead! study design, a randomized controlled trial nested within a multicentre longitudinal prospective cohort study. The eligible participants include children and adolescents between 6 and 18 years who had experienced a mild traumatic brain injury within the last two weeks. The cohort study will include 500 children and adolescents with a mild traumatic brain injury and their caregivers. A subset of 140 participants and their caregivers will be included in the randomized controlled trial. Participants in the randomized controlled trial will be randomly assigned to either the psychoeducational intervention group or the usual care control group. The psychoeducational intervention involves one face-to-face contact and one phone contact with the interventionist, during which the consequences of mild traumatic brain injury and advice for coping with these consequences to prevent long-term problems will be discussed. Information will be provided both verbally and in a booklet. The primary outcome domain is activities and participation, which will be evaluated using the Child and Adolescent Scale of Participation. Participants are evaluated two weeks, three months and six months after the mild traumatic brain injury.

Discussion: The results of this study will provide insight into which children with mild traumatic brain injury are at risk for long-term participation problems and may benefit from a psychoeducational intervention. Trial Register: NTR5153, registered on 17/04/2015.

Introduction

The incidence of traumatic brain injury (TBI) in children between 0 and 18 years is 280-1,373/100,000 but differs by country and region.[1-8] In the Netherlands, the annual estimated incidence of TBI among children and adolescents between 0 and 24 years is 5.86 per 1,000.[9] Therefore, approximately 12,000 – 14,000 cases of TBI occur among children and adolescents aged 0 to 24 years in the Netherlands each year, most (80%) of which are Mild Traumatic Brain Injuries (MTBI).[9-10] Children and adolescents with moderate and severe TBI generally receive follow-up care from a neurologist or rehabilitation physician, but those with MTBI typically do not.[11-12] Notably, however, between 6 and 43% of children and adolescents with MTBI continue to suffer from symptoms 6 months after the injury and beyond.[13-16] MTBI in children and adolescents may lead to physical, cognitive, emotional and behavioural problems.[17-19] Several studies suggest that the post-concussive symptoms and cognitive deficits resulting from an MTBI resolve over time, but there is also evidence suggesting that these consequences persist in some children.[20]

Previous studies of children who had experienced acquired brain injury (ABI) indicate that these children can also be at risk of participation limitations.[21] However, these studies often include heterogeneous groups, making it difficult to identify the participation problems accompanying MTBI more specifically.[21-24] In addition to clarifying the long-term outcomes on the level of activities and participation, more research is needed on the predictors of outcome. The predictors of activity and participation outcomes following a childhood MTBI remain unclear.[25-29] Studies on overall outcome after a childhood MTBI suggest that both injury-related (e.g., Glasgow Coma Scale score, loss of consciousness, posttraumatic amnesia) and non-injury related (e.g., age at injury, socio economic status, family functioning) factors affect outcome.[30-34] To determine which variables predict symptom resolution after an MTBI, well-designed, long-term studies are needed.[20,35]

Early recognition of symptoms and problems after an MTBI is crucial and enables the application of early and focused interventions.[35-36] Long-term symptoms accompanying MTBIs, such as cognitive (e.g., attention) or behavioural symptoms, are often difficult to recognize or to associate with the MTBI.[30] Delayed recognition of these invisible symptoms, underestimation of these problems and delay of diagnosis frequently and unnecessarily lead to chronic and disruptive consequences, such as activity and participation limitations (e.g., in school and social relations).[19,37-38] Several studies indicate that early education, reassurance and even early cognitive behavioural approaches may be effective in preventing long-term problems after an ABI in both children and adults[39-40] and, more specifically, after an MTBI.[41-43]

Although the few available studies on interventions (e.g., psychoeducation) that prevent MTBI symptoms in children and adolescents tend to report positive results, these studies are either retrospective or lack a randomized controlled trial design.[42-45] The Brains Ahead! study is, to the author's knowledge, the first to examine the effect of a psychoeducational intervention on long-term activity and participation outcomes in children and adolescents who have experienced an MTBI using a randomized controlled trial and a large multicentre prospective cohort.

The first aim of the Brains Ahead! study is to examine participation and activity levels in children and adolescents during the first six months after their MTBI and to identify outcome predictors. We expect that 20% of our study population will suffer from activity and participation problems during the first six months after their injury.[13-16,20-24,30,36] Furthermore, we hypothesize that injury-related and non-injury related factors can predict outcomes.[25-34]

The second aim is to investigate the effect of an early psychoeducational intervention on activities and participation. We hypothesize that our intervention will result in an increase in activities and participation during the first six months after an MTBI when compared to usual care.[39-45]

Methods/Design

Study design

The study is a multicentre prospective longitudinal cohort study with a nested single-blind randomized controlled trial (RCT). The RCT is conducted using a subset of participants from the cohort study (Figure 1).[46] The protocol is described according to the SPIRIT checklist for clinical trials (see the additional file SPIRIT checklist). Participants are followed during the first six months post-injury. During this period, there are three measurement points: two weeks (T0), three months (T1) and six months (T2) post-MTBI (Figure 2 and 3). The intervention begins two to four weeks post-injury and ends six months post-injury. The measurements and measurement times are the same for the cohort study and RCT participants. Measurements are performed by the researcher, who is blinded to the RCT group assignment.

Figure 1: Study design.

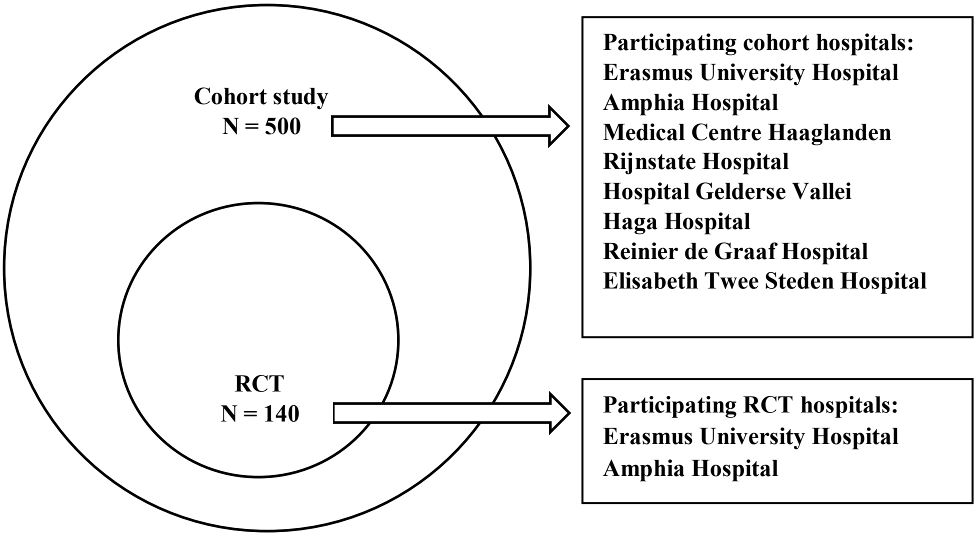
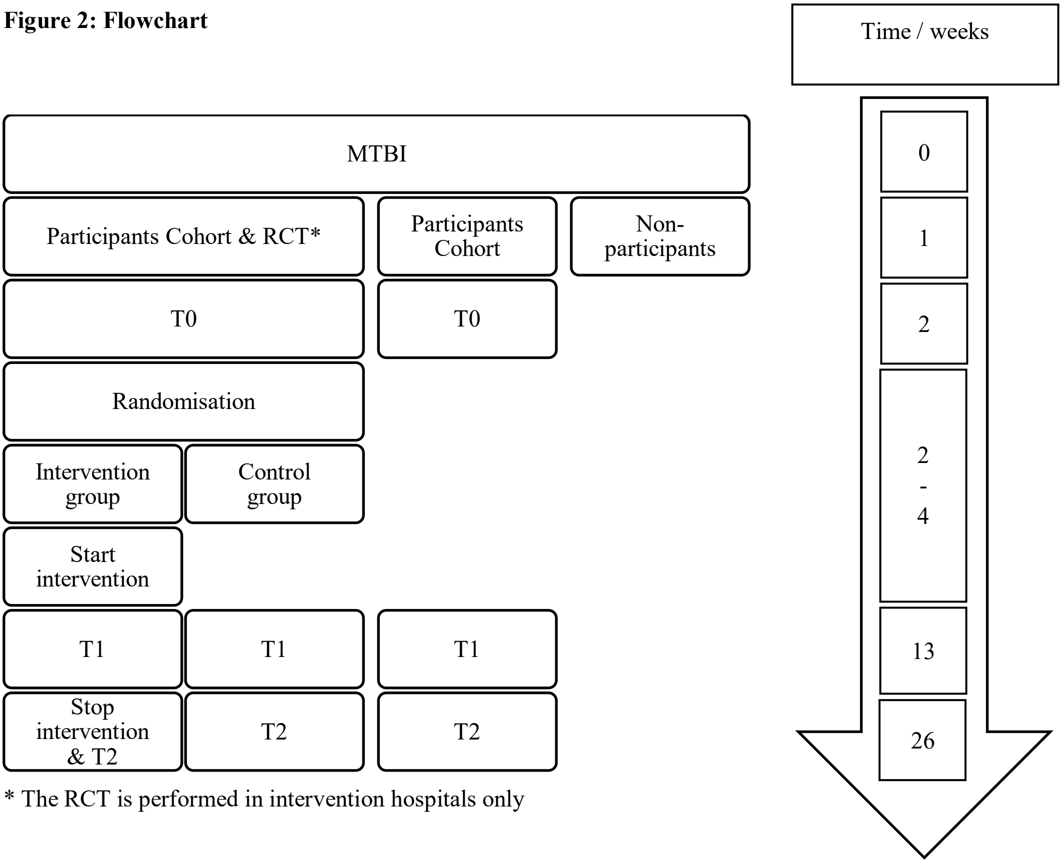


Figure 2: Flowchart



* The RCT is performed in intervention hospitals only

Figure 3: SPIRIT Figure

	Enrolment	Allocation	Post-allocation	Close-out
TIMEPOINT	**$-t_1$**	**0**	**t_1**	**t_2**
ENROLMENT:				
Eligibility screen	X			
Informed consent	X			
Allocation		X		
INTERVENTIONS:				
Brains Ahead Intervention			→	→
ASSESSMENTS:				
Injury and non-injury related variables (listed in table 1)		X		
Outcome variables MTBI patients (listed in table 2)		X	X	X
Outcome variables caregivers (listed in table 3)		X	X	X

Study population

Participants are included at the Emergency Department (ED) of one of the eight participating university and general hospitals in the Netherlands (Erasmus University Hospital, Rotterdam; Amphia Hospital, Breda; Medical Centre Haaglanden and Haga Hospital, The Hague; Rijnstate Hospital, Arnhem; Hospital Gelderse Vallei, Ede; Reinier de Graaf Hospital, Delft; and Elisabeth Twee Steden Hospital, Tilburg). The subset of participants used for the RCT consists of participants from two of these six hospitals only (Figure 1). To avoid selection bias, participants recruited from both a university hospital (Erasmus University Hospital, Rotterdam) and a large general city hospital (Amphia Hospital, Breda) will participate in the RCT. Participants will be recruited between April 2015 and December 2017. The Medical Ethics Committee of Erasmus University Medical Centre, Rotterdam and all of the local committees of the participating hospitals approved the study protocol (see the additional file of local committees) (MEC-2015-047, NL51968.078.14, v03). The study is registered in the Netherlands National Trial Register (NTR5153).

Inclusion and exclusion criteria

Inclusion criteria to participate in the study are: (1) Children and adolescents aged 6-18 years old and their caregivers. In this study, the caregiver is defined as a parent or guardian. (2) Diagnosed with MTBI according to the criteria established by the American Congress of Rehabilitation Medicine (ACRM) and the WHO Collaborating Centre for Neurotrauma Task Force on Mild Traumatic Brain Injury [47] (page number: 266). (3) Given informed consent. All caregivers and all patients aged 12 and older will provide written informed consent to participate in the cohort study and caregivers and patients from the two RCT hospitals (Erasmus University Hospital and Amphia Hospital) will provide this for participation in the RCT as well. For children younger than 12 years, the caregiver will provide written consent.

Exclusion criteria for children include having a previous objectified head trauma or having progressive neurological problems or diseases (based on patient history in the hospitals' electronic patient file), attending a day-care or school for cognitively impaired children and youth, and having insufficient knowledge of Dutch (patient or caregiver).

Patient selection and study procedures

In each of the six participating hospitals, all MTBIs are registered and communicated to the researcher. Within the first week after the MTBI, the researcher will contact the caregivers by phone to ask if they are willing to participate in the study. Subsequently, interested caregivers and patients receive written information about the study. There are two information sheets, one about the cohort study and one about the RCT. The last, is only to be received by interested caregivers and patients from the two RCT hospitals.

The baseline measurement (T0) is scheduled within two weeks post-injury and takes place at the participants' home only after written informed consent is obtained by the researcher. Hereafter, the subset of participants from the two hospitals that participate in the RCT are randomised and the intervention group receives the intervention. Measurements take place at three months and six months post-injury and are equal for participants in the cohort study and in the RCT (see

Figure 2 and 3). The researcher is responsible for data management during the study. After the study is closed, data will be stored with the primary investigator.

Randomisation procedures

Participants who agree to be included in the RCT are randomly assigned to either the intervention or control group. Randomisation is performed after the T0 measurement which takes place within two to four weeks post-injury. It is performed by an independent person who is not involved in the recruitment, intervention or outcome measurements. The randomisation is performed using an online randomisation program that employs computerized block-randomisation, and the randomisation scheme includes stratification based on three variables: age (6 to 12 or 12 to 18 years), gender (male or female) and location (hospital). Caregivers are assigned to the same group as their child. After randomisation, the independent third person informs the interventionist (a professional experienced and educated in child rehabilitation after TBI) about the patients assigned to the intervention group, whereupon appointments for the intervention are scheduled.

Intervention procedures

The intervention period begins two to four weeks post-injury and extends to six months post-injury. Optimally, the intervention is offered during the early phase of recovery to prevent long-term activity and participation problems. Two scheduled sessions occur during the intervention period. The first is a face-to-face session two to four weeks after the injury; the second is a telephone follow-up session six to eight weeks after the injury. During the first one-hour face-to-face session, participants are screened for symptoms or trauma-related problems and receive individualized psychoeducation. The second session—the follow-up telephone call—will last approximately thirty minutes. Patients or caregivers can also consult the interventionist when needed. After participants have received four or more optional follow-up sessions (or fewer, based on the clinical judgement of the interventionist), the patient and caregivers are advised to contact their general practitioner for evaluation or referral.

During the intervention period, there are no restrictions on obtaining care or treatment from other professionals. However, all participants are asked to complete a patient diary every month and record any care received. Information about the sessions, e.g., date, duration, content and whether or not more extensive information on certain topics is given, and the use of additional optional follow-up sessions, e.g., date, duration, content, are recorded during the intervention period by the interventionist. Furthermore, participants, caregivers and patients 12 years and older, are individually asked to evaluate the intervention content and process at the end of the intervention.

Content of the intervention

The intervention consists of the following content:

1) Screening of symptoms and MTBI-related problems: a list of the ten most frequently experienced post-injury symptoms and problems was developed by our research team.

2) Psychoeducation: the information provided during psychoeducation includes general information about symptom occurrence, possible symptoms and practical advice for managing symptoms and developing activities for children and adolescents with MTBI and their caregivers. It also includes more extensive individualized information about specific symptoms (e.g., headaches, dizziness and nausea, attention problems, memory problems). The general information about MTBI is provided verbally and in a written booklet. The booklet is available in three versions: a caregiver version, a version for patients aged 6 to 12 years and a version for patients aged 12 to 18 years. The individualized information is only given to participants who experience MTBI-related symptoms and is provided verbally and in writing.

3) Follow-up: a single follow-up is held via telephone. Optional additional follow-up telephone sessions are scheduled depending on the needs of the patient or caregiver.

The control group receives usual care. Each hospital has a concise standard information brochure that briefly describes the possible consequences of MTBI and what to do if MTBI symptoms persist and increase. This brochure is usually given to patients in the ED.

Outcome measurements

Several injury-related and non-injury related variables are identified. These variables are presented in Table 1 and Figure 3. The instruments used to measure activity and participation after an MTBI and possible outcome predictors are presented in Figure 3, and in Table 2 for patients and in Table 3 for caregivers and are described in more detail hereafter. All instruments described below are completed based on post-injury functioning, unless stated otherwise.

Given the fact that a subset of the cohort sample will receive the intervention, this might influence the outcome data in the cohort study. Therefore, if the intervention is found to be effective, the outcome data of the intervention group will be excluded from all cohort analyses (see statistical analyses).

Table 1: Injury/Non-injury-related variables

Injury-related variables
Glasgow Coma Scale score (first recorded in the ambulance or ED*)
Posttraumatic Amnesia duration in minutes
Loss of consciousness reported in ED
Change in mental functioning: post-acute confusion or disorientation
Other transient neurological abnormalities
CT/MRI/EEG abnormalities
Cause of MTBI
Non-injury-related variables
Location (hospital where MTBI was diagnosed)
Admission to hospital
Age of patient at injury
Gender
Educational level of patient
Pre-injury behavioural and emotional problems of the patient (measured using the CBCL**)
Parental Socio Economic State (SES)
Pre-injury family function (measured using the FAD-GF***)
Family situation (number of family members residing with the patient)

* Emergency Department; ** Child Behaviour Checklist; *** Family Assessment Device – General Functioning

Table 2: Outcome domains, measurement instruments and measurement moments for the MTBI patients

Domain	Measurement instrument	Abbr.	Age (y)	T0	T1	T2
Activities and participation	Children's Assessment of Participation and Enjoyment	CAPE	6-18	X	X	X
	Child and Adolescent Scale of Participation - DLV*	CASP-DLV	10-18	X	X	X
Quality of Life	PedsQL** – Quality of Life Scale	PedsQL-QoL	6-18	X		X
Fatigue	PedsQL – Multidimensional Fatigue Scale	PedsQL-Fatigue	6-18	X		X
Health and behaviour	Health and Behaviour Inventory	HBI	8-18	X		X
Post-traumatic stress	Schokverwerkingslijst (Impact of Events Scale -DLV)	SVL (IES)	8-18	X		X
Sensory processing	Adolescent Adult Sensory Profile – NL***	AASP-NL	12-18	X		X

* Dutch Language Version; ** Paediatric Quality of Life Inventory; *** Netherlands

T0 = two weeks after MTBI; T1 = three months after MTBI; T2 = six months after MTBI

Table 3: Outcome domains, measurement instruments and measurement moments for the caregivers

Domain	Measurement instrument	Abbr.	Age	T0	T1	T2
Activities and participation*	Child and Adolescent Scale of Participation - DLV**	CASP-DLV	All	X	X	X
Quality of Life	PedsQL*** – Quality of Life Scale	PedsQL-QoL	All	X		X
Fatigue	PedsQL – Multidimensional Fatigue Scale	PedsQL-Fatigue	All	X		X
Health and behaviour	Health and Behaviour Inventory	HBI	All	X		X
Post-traumatic stress	Schokverwerkingslijst (Impact of Events Scale -DLV)	SVL (IES)	All	X		X
Family functioning	Family Assessment Device – General Functioning	FAD-GF	All	X		X
Behaviour and emotion	Child Behaviour Checklist	CBCL	All	X		X
Sensory processing	Sensory Profile – NL**** short version	SP-NL	6-11	X		X

T0 = two weeks after MTBI, T1 = three months after MTBI, T2 = six months after MTBI

* Primary outcome measure; ** Dutch Language Version; *** Paediatric Quality of Life Inventory; **** Netherlands

Primary outcome measure

The primary outcome measure, the Child and Adolescent Scale of Participation (CASP), is based on the activity and participation components of the International Classification of Functioning, Disability and Health for Children and Youth (ICF-CY). The CASP-Dutch language version (CASP-DLV) is a 20-item questionnaire designed specifically to measure activities and participation in children who have experienced an ABI.[9] It includes a parent-report and a self-report version for children aged 10 years and older. Our primary outcome will be limited to the results of the parent-reports. The CASP-DLV items are categorized into four domains: (1) participation at home, (2) participation in the district and residence, (3) participation at school, and (4) participation at home and in the environment. The questionnaire has been used in several international studies and has been recommended as an instrument for evaluating participation in children and adolescents after brain injury.[34] The internal consistency (Cronbach's alpha=.95) and test-retest reliability (intraclass correlation coefficient=.90) of the CASP-DLV were found to be good and to have a significant correlation with the Paediatric Quality of Life Inventory (PedsQL) (concurrent validity .45).[48]

Secondary outcome measures

Child and Adolescent Scale of Participation–Dutch language version self-report.

The CASP-DLV self-report questionnaire for children aged 10 to 18 is used as a secondary outcome measure. It evaluates participation after an MTBI from the child's perspective. The self-report version includes the same items and domains as the CASP-DLV parent-report. The self-report (or youth-report) of the original CASP is a psychometrically adequate self-report instrument for measuring activity and participation (internal consistency Cronbach's alpha=.87 and strong internal structure validity). It is used in conjunction with the CASP-DLV parent-version because children and adolescents may have different perceptions about their activity and participation levels than their parents.[49] For children between the ages of 6 and 9, however, only the parent version is used. Information about participation from the child's perspective is obtained using the Children's Assessment of Participation and Enjoyment (CAPE).

Children's Assessment of Participation and Enjoyment

The Children's Assessment of Participation and Enjoyment (CAPE) is a 55-item questionnaire whose items correspond to 55 different activities. It measures children's participation in after-school activities.[50-51] Five domains of participation are included: (1) diversity, (2) intensity, (3) setting/with whom the activity is typically performed, (4) usual location of the activity, and (5) the amount of pleasure the child experiences during the activity. A comparison between the CAPE and the CASP-DLV parent version showed no significant correlation, which may be because of the difference in focus of the two questionnaires: one focuses on activity restriction and the other on diversity and intensity of participation.[48] The CAPE is found to be sensitive over time when measuring functional change in children after an MTBI.[27] Furthermore, the CAPE is also a reliable and valid tool for measuring participation in recreation and leisure activities in Dutch children aged 6 to18 with and without physical disabilities.[51]

Paediatric Quality of Life inventory – Quality of Life Scale

The Paediatric Quality of Life inventory – Quality of Life Scale (PedsQL-QoL) is a 23-item questionnaire that measures health and activities, emotions, peer relations and school-related activities.[52] The questionnaire is internationally recommended for studies of children and adolescents who have experienced an ABI.[25] The psychometric properties of the Dutch PedsQL are found to be adequate, and the questionnaire is appropriate for paediatric research on health-related quality of life in the Netherlands.[52]

Paediatric Quality of Life Inventory – Multidimensional Fatigue Scale

The Paediatric Quality of Life Inventory – Multidimensional Fatigue Scale (PedsQL-Fatigue) is an 18-item questionnaire that measures overall fatigue, problems regarding sleep/rest, and cognitive fatigue.[53] This questionnaire is recommended for studies of children and adolescents after an ABI [25]. The feasibility, reliability and validity of the Dutch version of the PedsQL– Multidimensional Fatigue Scale are adequate, and the scale distinguishes healthy children from children with an impaired health condition.[53]

Health and Behaviour Inventory

The Health and Behaviour Inventory (HBI) is a 50-item questionnaire. It measures (1) physical, (2) emotional, (3) cognitive, and (4) behavioural symptoms. The HBI has sound psychometric properties and is able to distinguish MTBI from other injuries.[25,54] Because a Dutch version of this inventory did not yet exist, we translated the original HBI into Dutch according to the translation guidelines.[55]

Impact of Events Scale

The Dutch version of the Impact of Events Scale (IES-NL) is a 34-item questionnaire that measures possible post-traumatic stress responses.[56] The items are divided into four dimensions: (1) re-experiencing the stressor, (2) avoidance, (3) increased irritability, and (4) child-specific responses. The IES-NL has adequate reliability across various traumatic stressors and reveals a robust structure over various samples.[56] Furthermore, the questionnaire is internationally recommended for studies of children and adolescents who have experienced an ABI.[25]

Family Assessment Device – General Functioning Scale

The Family Assessment Device – General Functioning Scale (FAD-GF) is a 12-item questionnaire used to measure family functioning. It has been used in previous studies on brain injuries in children[31] and is recommended for studies of pre-injury family problems and changes in family functioning associated with the traumatic brain injury.[25,57-58] The psychometric properties of the FAD-GF are sufficient for assessing family functioning.[59] This questionnaire is used to evaluate pre-injury family functioning at T0 and post-injury family functioning at T2.

Child Behaviour Checklist

The Child Behaviour Checklist (CBCL) is a 113-item questionnaire widely used to measure behavioural and emotional problems and skills in children.[60] This questionnaire is recommended for examining these problems in children and adolescents who have experienced an ABI and has sound psychometric properties.[25,60] It is used to assess pre-injury behavioural and emotional problems and skills at T0 and post-injury behavioural and emotional problems and skills at T2.

Sensory Profile – Dutch Short Version and Adolescent/Adult Sensory Profile - NL

The Sensory Profile – Dutch Short Version (SP-NL) is a 38-item questionnaire. In this study, it is completed by the parents of patients between 6 and 11 years old. Patients 12 years and older complete the Adolescent/Adult Sensory Profile (AASP-NL). The questionnaires measure sensory information processing—including several sensory functions, movement abilities, and social-emotional aspects—and assess the child's activity and participation levels.[61] The questionnaire adequately measures sensory information processing in children after a traumatic brain injury.[62]

Sample size

Sample size calculations for the cohort study are based on the available literature about MTBI prevalence and the expected number of participants that may visit the participating hospitals. Based on an inclusion period of 2 years, the aim is to recruit a sample of 500 children and adolescents who have experienced an MTBI. Assuming a 10% dropout rate,[63] our final sample should include 450 participants. Previous research shows that approximately 20% of the population will experience long-term problems[13-16,20-24,30,36] after an MTBI. Therefore, approximately 90 of our participants will suffer long-term problems. When conducting the regression analysis to identify the predictors of the presence of long-term problems, we should include 9 determinants based on the assumption that approximately 10 participants per determinant are needed for a reliable analysis.[64]

Sample size calculations for the RCT are based on the results of studies on paediatric traumatic brain injury patients' participation that relied on the parent-reports of the CASP-DLV. For the CASP-DLV, a standardized difference of 0.5 was expected.[48] Based on an alpha of .05 and a power of .8, a minimum of 63 children per group (control group and intervention group) is required for sufficient statistical power. Assuming a dropout rate of 10%, the aim is to recruit at least 140 children and adolescents for the RCT.

Statistical analyses

To present the data on the participants, number of dropouts, losses during follow-up and the outcome measure scores, descriptive statistics will be used. To determine the sample's representativeness and the generalizability of the results, participants will be compared to non-participants based on the inclusion and exclusion criteria. Furthermore, the baseline characteristics of participants and drops-outs and patients lost during follow-up will be compared. Comparisons will be performed using independent sample t-tests or the non-parametric equivalent.

Cohort study

To determine the results of the primary outcome measure (CASP-DLV parent-reports), descriptive statistics will be used. Continuous variables will be expressed as the means and standard deviations or as medians with interquartile ranges, depending on the distribution values. A repeated-measures ANOVA will be used to determine the difference in activities and participation over time. If a significant difference between the measurement points ($p < .05$) will be found, a post-hoc analysis based on Levene's test will be performed.

Linear regression analysis will be used to identify the outcome predictors of activities and participation at six months post-injury, as measured by the CASP-DLV parent reports. Within two weeks after the injury, both continuous and categorical variables, i.e., injury and non-injury related factors, are measured, as well as pre-injury family functioning (FAD-GF) and behaviour (CBCL), degree of fatigue (PedsQL-fatigue), quality of life (PedsQL-QoL), sensory processing (SP/AASP-NL), physical, cognitive, emotional and behavioural postconcussive symptoms (HBI), post-traumatic stress (SVL) and participation in after-school activities (CAPE). Each variable will first be examined using univariate linear regression analysis to predict activities and participation. Next, variables with values of $p < .2$ in the univariate linear regression analysis will be included in the multivariate linear regression analysis. In the multivariate linear analysis, the significance level will be set at $p < .05$. For more clinically relevant purposes, outcome predictors will also be determined using logistic regression analyses. If the intervention is found to be effective (see statistical analyses of RCT study, below), the data of the intervention group will be excluded from all of the cohort study analyses.

RCT

First, the baseline characteristics of the two groups will be examined using independent sample t-tests or Mann Whitney U-tests (depending on the distribution values). A chi-square test will be used to examine dichotomous variables. Next, the effectiveness of the intervention on the primary outcome measure (CASP-DLV parent-reports) will be assessed using multilevel analysis, i.e., random coefficient analysis, for both short (three months after injury) and long-term (six months after injury) outcomes. Time of measurement, group assignment (control or intervention group), and the interaction between time of measurement and group will be included in the multilevel regression model. The level of significance will be $p < .05$. The random coefficient analysis will be performed with all of the participants using intention-to-treat analyses. For those with incomplete datasets, longitudinal imputation techniques will be used.[65]

Discussion

This paper describes the research protocol of the Brains Ahead! study. The study examines the activities and participation outcomes of children and adolescents during the first six months after experiencing an MTBI and identifies possible outcome predictors. Furthermore, this study investigates the effectiveness of an early psychoeducational intervention on activities and participation when compared to the usual MTBI care received by this population. We chose for a nested design because it is preferred to gain insight into the effect of the intervention on a short term, since it might help to prevent long-term problems after MTBI in children and adolescents In this study a large sample is recruited for the cohort part. Taking a subset of these participants for the RCT along at the same time, enables us to investigate the effectiveness of the intervention faster compared to waiting on results of the cohort study first and setting up a new intervention study afterwards. We believe this is an efficient way of investigating this group of participants from an ethical perspective as well.

In many studies, various types of TBI (mild, moderate, severe) are included. However, this study investigates activities and participation in children and adolescents with a mild TBI only. In a study by Ponsford et al. (2001), the effectiveness of an early intervention in the form of a general information booklet was evaluated in a mild paediatric population only.[42] However, their study measured the impact of the intervention on reported symptoms, cognitive performance and psychological adjustment and not on preventing activity and participation problems. Furthermore, the sample size of their study was small (N=61) compared to the expected sample size of this study, and the outcome was measured at three months post-injury, while this study measures the outcome at three months and six months post-injury. The strength of this study is the substantial RCT sample size extracted from a large cohort. Furthermore, the outcome instruments used in this study are largely based on the ICF-CY.

To the authors' knowledge, this is the first study to examine the effect of an early individualized psychoeducational intervention designed to prevent activity and participation problems in a relatively large group of children and adolescents following an MTBI. All of the participants in the nested RCT design receive usual care, and the intervention group receives an additional intervention. The intervention has a specific theoretical basis, and its design is based on evidence from the literature. Finally, and perhaps most importantly, the intervention is created to suit clinical practice and can be easily and directly applied in the daily practices after its effectiveness has been proven. The results of this study will provide insight into which children with MTBI are at risk for long-term participation problems and may benefit from a psychoeducational intervention.

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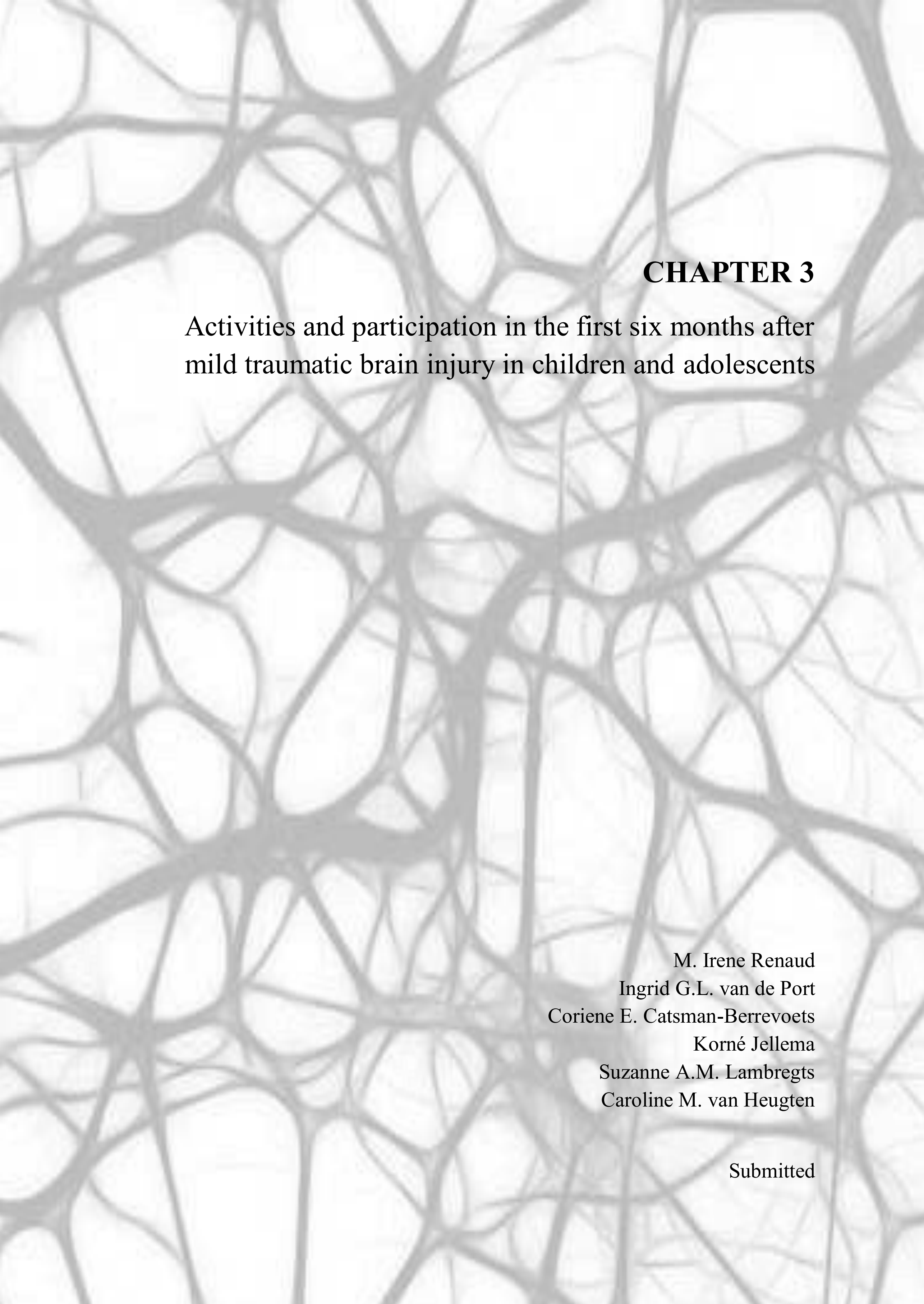

CHAPTER 3

Activities and participation in the first six months after mild traumatic brain injury in children and adolescents

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Abstract

Objective: To investigate the natural course of activities and participation of children up to six months after a mild traumatic brain injury (MTBI).

Methods: A prospective longitudinal cohort study with complete datasets of 231 children diagnosed with MTBI and their caregivers. Outcome measures were activities and participation assessed with the Child and Adolescent Scale of Participation (CASP) and the Children's Assessment of Participation and Enjoyment (CAPE) measured at two weeks, three months and six months post-MTBI. Because of a ceiling effect, the primary outcome measure (CASP) was divided into deviant (not maximum score) or full functioning.

Results: Friendman, Cochran's Q, and MC Nemar's tests (CASP) and Repeated Measures ANOVA's (CAPE) show a significant increase on activities and participation between two weeks and three and six months after MTBI. Based on the parents' perspective, 67% of the children returned to full functioning at six months post-injury, with only 38% of the children themselves.

Discussion: Findings indicate that most children return to maximum level of activities and participation over time after MTBI. In a substantial number of children, however, the level of activities and participation at six months post-injury is evaluated as less in comparison to peers. The importance of investigating predictors for child and caregiver perspectives is emphasized.

Introduction

Traumatic brain injuries (TBI) are considered to be the most common cause of disability or death in children, adolescents and young adults.[1] Emergency departments in the United States triage over nearly half a million children with TBI annually, of which approximately 80% are mild.[2-3] The incidence rate of mild traumatic brain injury (MTBI) in children between 6 and 18 years old in the emergency department of Dutch hospitals is estimated to be 282 per 100,000 /year.[4] In general, children with MTBI recover completely. However, approximately 20% of them suffer from a variety of post-concussion symptoms (PCS) up to six months post-injury or longer.[5-9] It is suggested that these children may experience limitations in daily life activities and societal participation in the long term.[10-11] Daily life activities and participation can be considered in different domains such as social, recreational, and sports and in different settings such as at home, school or in the community. Both terms are common within framework of the International Classification of Functioning (ICF; WHO). Activities and participation can further be considered from different perspectives such as the child by self-report or the parents/caregivers by proxy report.

The course of activities and participation after brain injury is investigated in several studies with mixed samples of TBI and/or samples including children with acquired brain injury (ABI) without differentiating for mild TBI.[12-18] Only two studies investigated the course of activities and participation over time in a sample of children with MTBI.[19-20] In one study, children's activities and participation decreased up to three months, and increased hereafter to full recovery up to three years post-injury.[19] In the other study, participation of children increased up to 12 months in several activity domains such as recreational, active physical, and social activities, but not in skill-based and self-improvement activities.[20] These studies were based on caregiver reports only,[19] or lacked evaluation of participation in different settings such as at home, in school and in the community.[20] Since children with TBI in general seem to evaluate their level of activities and participation higher in comparison to their caregivers, it is important to consider both perspectives[21].

Activities and participation can be measured across settings and for several activity domains, which may reveal different profiles: a child may, for instance, have problems in social activities but not in recreational activities and may participate fully at home but not at school.[22] Activities and participation are very important for the development of a child, since it helps children to acquire different skills and competencies, grow physically and cognitively, develop their own identity and set different life goals[23].

No study has been performed that combines the investigation of the course of activities and participation both in different settings and for several activity domains, with respect to the perception of both the caregivers and the child in a large sample of children with MTBI. Furthermore, it is unknown how the course of activities and participation in different settings and several activity domains are related.

Therefore, the aim of this study was to assess the course of activities and participation after MTBI longitudinally in children in different settings and in several activity domains, using both caregiver- and self-reports. We expected that activities and participation in different settings and for several activity domains is lowest at two weeks after MTBI, increases up to three months and stabilizes at six months post-injury. Furthermore, we expected that children evaluate their own level of activities and participation more positive compared to their caregivers. Finally, we expected that courses of activities and participation in different settings and several activity domains over time after MTBI in children would be positively related.

Methods

Design

This study is part of the larger Brains Ahead! study into activities and participation of children after MTBI,[11] approved by the medical ethics committee of Erasmus University Hospital and by all local committees of the participating hospitals (MEC-2015-047, NL51968.078.14, v08). The Brains Ahead! study consists of a multicenter prospective longitudinal cohort study with a nested randomized controlled trial (RCT); the study design and procedure is published in detail.[11] In the RCT, the effect of an early psychoeducational intervention is evaluated in comparison to care as usual. As the goal of the current analysis is to examine natural recovery after childhood MTBI, participants who were randomized into the intervention group of the RCT are excluded from the current analysis.

Setting

All children aged 6 to 18 years, who presented with MTBI at the Emergency Departments of eight Dutch hospitals between May 2015 and December 2017, and their caregiver(s), were eligible for participation.

Participants

Children were included if they sustained an MTBI according to the criteria of the American Congress of Rehabilitation Medicine and the World Health Organization Collaborating Centre for Neurotrauma Task Force on Mild Traumatic Brain Injury.[24]

Exclusion criteria were 1) having a previous objectified head trauma, 2) having progressive neurological problems or disease, 3) attending a daycare center or school for cognitively impaired children, and 4) having insufficient knowledge of the Dutch language (child or caregivers). The caregivers were defined as parents or guardians. There were no further exclusion criteria for caregivers.

Procedure

The full study procedure is described in the Brains Ahead! study design.[11] After written informed consent, the baseline measurement (T0) was scheduled at two weeks post-injury. Further measurements took place at three (T1) and six (T2) months post-injury. All measurements were conducted at the participant's home in the presence of the researcher who gave instructions, prevented missing data as much as possible by checking the filled out questionnaires, and prevented false respondent bias by ensuring the child and the caregiver filled out the questionnaires independently.

Measures

All instruments have sound psychometric properties and are recommended for evaluating activities and participation after childhood brain injury.[22,25-26,28-30]

Several demographic (e.g. child's gender, age of the child at injury, parental socioeconomic status (SES), and pre-injury behavioral functioning of the child) and injury-related (e.g. Glasgow Coma Scale score (GCS), loss of consciousness (LOC), posttraumatic amnesia (PTA), and cause of injury) variables were collected from the patient files and at T0. The Child Behavior Checklist (CBCL) was filled out on pre-injury functioning at baseline (T0). The CBCL is a 113-item questionnaire to measure cognitive and behavioral problems and skills in children on a three-point scale (0) never, (1) sometimes, or (2) often.[25] The CBCL provides a Total Behavior Problem Score (T=50, SD=15). For the Total Scale, a score >60 can be considered impaired (61-69 mildly impaired, >70 severely impaired).[25]

CASP

Level of activities and participation was measured in different settings with the Child and Adolescent Scale of Participation (CASP Caregiver and CASP self-report). The CASP is a 20-item questionnaire designed specifically to measure participation in children with ABI, according to the components of the International Classification of Functioning, Disability and Health for Children and Youth (ICF-CY).[22,26-27] The CASP can be filled out by caregivers for children aged 6-18 years old, and the self-report can be filled out by children aged 10-18 years old. The CASP items are added to obtain a total score.

Additionally, the items are categorized to obtain sub scores for the following settings: at home, in the community, at school, and in the environment. The CASP is scored on a four point scale (1) age appropriate, (2) slightly impaired, (3) heavily impaired, (4) not capable. Summary scores are created by summing the item responses, dividing this number by the maximum possible score and multiplying this number by 100 to conform to a 100-point scale. The total score range is therefore 25 - 100, with a higher score representing better outcome. Missing and 'not applicable' scores were not included in the scoring.

CAPE

Level of activities and participation was measured for several domains of activities with the Children's Assessment of Participation and Enjoyment (CAPE self-report). The CAPE is a 55-item questionnaire, which can be filled out by children aged 6-18 years old. It measures diversity in recreational (12 items), active physical (13 items), social (10 items), skill-based (10 items) and self-improvement activity (10 items) domains and can be scored binary as (0) the activity was not performed, or (1) the activity was performed.[28-29] The total score range is 0-55, with higher scores indicating more participation in activities. The range per activity domain differs: recreational (0-12), physical activity (0-13) and social, skill-based and self-improvement (0-10). Diversity in activity domains measured with the CAPE differs based on the child's age, with certain CAPE items being more age-appropriate for younger children (e.g. playing with toys) and other items more being more age-appropriate for older children (e.g. having a paid job). Therefore, participants are not expected to score a maximum of 55 on the CAPE.[29] In this study, the CAPE was filled out about the performed activities from the time since injury up to T0, and at T1 and T2 it was filled out about the performed activities in the month prior to the measurement.

Statistical Analysis

Descriptive statistics were used to describe baseline variables and outcomes. Means (SD's) or medians (ranges) were reported depending on the distribution of the data.

Since outcome data on activities and participation for the CASP caregiver and CASP self-report were not normally distributed, Friedman tests were used to investigate the course of activities and participation in different settings over time post-injury (i.e. two weeks, three, and six months after MTBI). Since a ceiling effect on the CASP can be suspected, and because scores on the CASP are given based on the child's functioning with regard to the injury and in comparison with age-related peers, we dichotomized the total and setting-scores of the CASP into:

(0) deviant functioning (any score below 100), and (1) full functioning in comparison to their healthy/non-injured age-related peers.[15,22,26]
The dichotomized scores were examined over time with Cochran's Q tests and McNemar's tests (significant level set at p <.05). Outcome data on activities and participation in several activity domains over time post-injury, measured with the CAPE were normally distributed, and therefore analyzed with Repeated Measures ANOVA. In case a significant difference (*p* <.05) was found between the three moments in time, Wilcoxon signed-rank test (significant level set at p <.05) for CASP scores, and Levene's test with Bonferonni correction (LSD *p*-value for significance <.0167) for CAPE scores was used to determine changes over time.[11,31]

To examine if children evaluate their own level of activities and participation more positive than their caregivers, comparisons between caregivers and children were made for CASP reports of children aged 10-18 with Wilcoxon signed-rank tests, and with McNemar's tests for the dichotomized data.

The relation between the course of activities and participation in different settings (CASP) and the course of domains (CAPE) over time after MTBI, was examined with correlation coefficients (Spearman's ρ) at T0, T1, T2, and for the change score between T0 and T2 for the CASP and the CAPE. Because the CAPE was filled out by children and not by caregivers, and the self-report of the CASP was filled out by children aged 10-18 years old and not by younger children, we used the datasets of children aged 10-18 years old only to examine this relationship. We considered correlation coefficients to be weak if <0.3, moderate between 0.3 and 0.5, and strong >0.5 (significant level set at p <.05).[32]

Since there was a low number of only ten participants with incomplete data (e.g. dropped out the study, or skipped a measurement due to holiday), we decided to work with complete datasets only. Statistical analyses were performed using IBM SPSS Statistics for Windows, version 24.0.

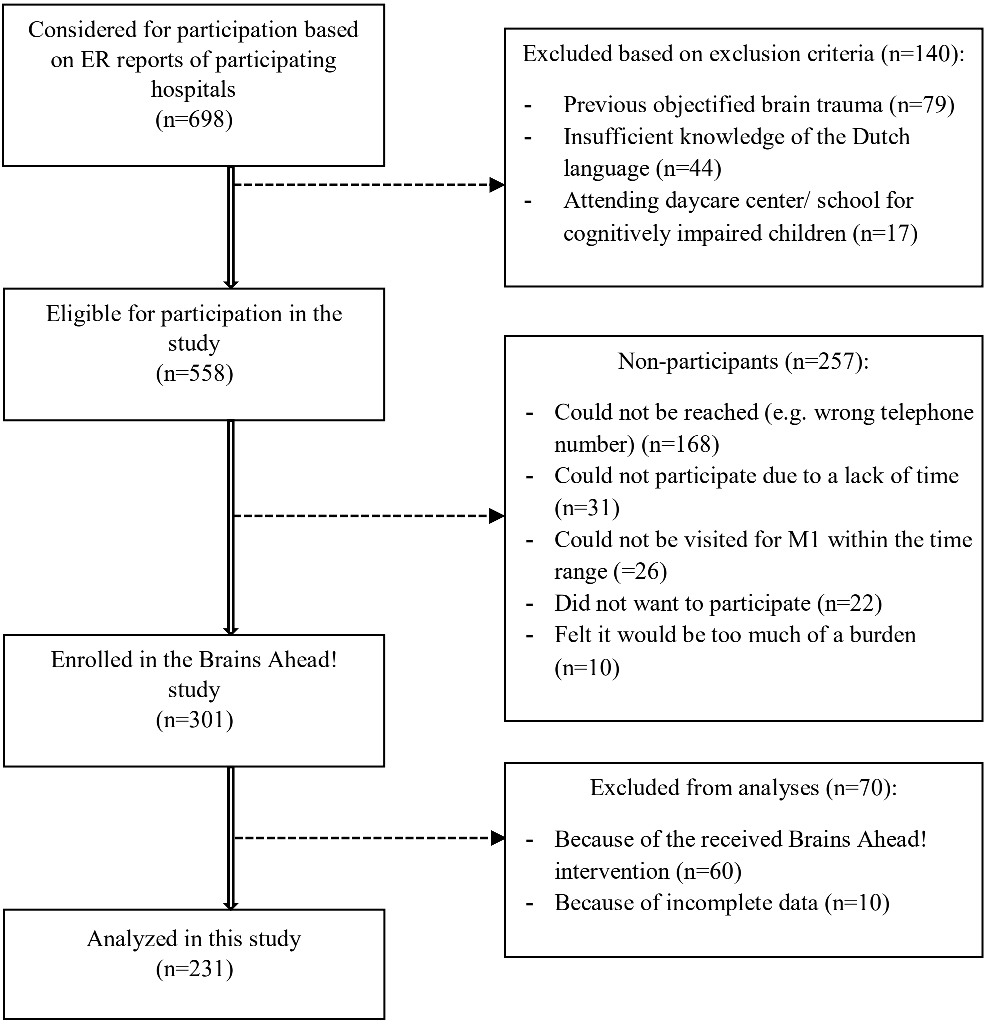
Results

Sample characteristics

In total 698 children with MTBI were considered for participation in the study, of whom 140 were excluded based on the exclusion criteria (see Figure 1). Furthermore, a total of 257 persons did not participate, from which the vast majority (168) could not be reached. Finally, 60 participants received the Brains Ahead! Intervention, and were excluded from the analyses. Complete datasets were available for 231 children.

Sociodemographic, injury-related and pre-injury characteristics showed that the sample consisted of more boys than girls and the mean age was 11.4 years (Table 1). The vast majority of the sample presented a high SES and normal pre-injury behavioral functioning. Most children sustained MTBI due to sports- and traffic-accidents, scored a GCS of 15 and a PTA of less than one hour, and about half of the sample experienced LOC.

Figure 1. Flow of participants



Considered for participation based on ER reports of participating hospitals
(n=698)

Excluded based on exclusion criteria (n=140):

- Previous objectified brain trauma (n=79)
- Insufficient knowledge of the Dutch language (n=44)
- Attending daycare center/ school for cognitively impaired children (n=17)

Eligible for participation in the study
(n=558)

Non-participants (n=257):

- Could not be reached (e.g. wrong telephone number) (n=168)
- Could not participate due to a lack of time (n=31)
- Could not be visited for M1 within the time range (=26)
- Did not want to participate (n=22)
- Felt it would be too much of a burden (n=10)

Enrolled in the Brains Ahead! study
(n=301)

Excluded from analyses (n=70):

- Because of the received Brains Ahead! intervention (n=60)
- Because of incomplete data (n=10)

Analyzed in this study
(n=231)

Table 1. Sociodemographic and injury-related characteristics (N=231)

	Characteristics	***N (%)***	***M* (SD)**
Demographics	Child gender: male	151 (65.4)	
	Child age at injury in years	231 (100)	11.4 (3.3)
	(Min – Max, Range)	(6-17)	
	SES:		
	Low	53 (22.9)	
	Average	41 (17.7)	
	High	137 (59.3)	
	Pre-injury Behavioral functioning*		50 (10)
	Normal score	192 (83.1)	
	Mild impaired	29 (12.6)	
	Severe impaired	10 (4.3)	
Injury-related	GCS:		
	13	8 (3.5)	
	14	37 (16.0)	
	15	186 (80.5)	
	LOC duration:		
	None	117 (50.6)	
	<2 minutes	69 (29.9)	
	2-5 minutes	33 (14.3)	
	>5 minutes	12 (5.2)	
	PTA duration:		
	None	50 (21.6)	
	<1 hour	120 (51.9)	
	1-2 hours	18 (7.8)	
	2-6 hours	30 (13.0)	
	6-12 hours	5 (2.2)	
	12-18 hours	1 (.4)	
	18-24 hours	7 (3.0)	
	Cause of injury:		
	Sports accident	72 (31.2)	
	Traffic accident	68 (29.4)	
	Outdoor play accident	48 (20.8)	
	Accident at school/work	22 (9.5)	
	Accident at home	13 (5.6)	
	Physical abuse	5 (2.2)	
	Other	2 (.9)	

GCS = Glasgow Coma Scale score, LOC = Loss of Consciousness, PTA= Posttraumatic amnesia, SES = Caregiver's Socioeconomic State,

*Measured at baseline; Behavioral functioning with the Child Behavior Checklist T-scores

The course of activities and participation over time post-MTBI in different settings

Descriptive results indicated that the scores on the CASP increased for total and domain scores over time post-injury (see Table 2). Friedman tests showed that the increase of scores on the CASP between T0 and T2 was significant (*p*<.000) for total and all domain scores. Wilcoxon signed-rank tests showed that total and all domain CASP scores increased significantly (*p*<.000) between T0 and T1, and T0 and T2, but not between T1 and T2 except for total activities based on CASP caregiver results for ages 6-18 years old (*p*=.049), and for activities at home based on CASP caregiver results for ages 6-18 years old (*p*=.001) and for ages 10-18 years old (*p*=.023) (Appendix 1).

Analyses of the dichotomized CASP scores showed that at T0 between 5.2%-25.5% (depending on the perspective chosen) of the participants scored a maximum total CASP score (see Table 3). At T1 between 39.4% and 61.9% and at T2 between 36.1% and 66.2% scored maximum. Cochran's Q tests showed that the number of children with full functioning scores on the CASP increased significantly (*p*<.000) over time post-injury for all total and domain scores (Table 4). McNemar's tests showed that the number of children with full functioning scores on the CASP increased significantly (*p*<.000) for all total and domain CASP scores between T0 and T1, and T0 and T2, but not between T1 and T2 except for activities at home (*p*=.001) and in the community (*p*=.024) according to CASP caregiver results for ages 6-18 years old (Table 4).

The course of activities and participation in several activity domains over time post-MTBI

Descriptive results indicate that the scores on the CAPE increase for total and domain scores over time post-injury (see Table 5). Repeated Measures ANOVA's showed a significant increase of the CAPE over time between T0 and T2 for all total and domain scores (Table 6). Post-hoc analyses showed that all total and domain CAPE scores increased significantly (*p*<.000) between T0 and T1, and T0 and T2, but not between T1 and T2 except for recreational activities, where a significant (*p*=.005) decrease was reported.

Table 2. Outcome on activities and participation in different settings over time post-MTBI

	CASP Setting	T0 Median (Range)	T1 Median (Range)	T2 Median (Range)	Friedman X^2 *p*
Caregiver report 6-18 ***N*=231**	Total	93.75 (82.50-100.00)	100.00 (97.50-100.00)	100.00 (98.68-100.00)	182.16 <.000
	At home	95.83 (87.50-100.00)	100.00 (100.00-100.00)	100.00 (100.00-100.00)	126.86 <.000
	In the community	93.75 (75.00-100.00)	100.00 (100.00-100.00)	100.00 (100.00-100.00)	140.09 <.000
	At school	95.00 (85.00-100.00)	100.00 (100.00-100.00)	100.00 (100.00-100.00)	148.36 <.000
	In the environment	95.00 (80.00-100.00)	100.00 (95.00-100.00)	100.00 (95.00-100.00)	121.44 <.000
Caregiver report 10-18 ***N*=155**	Total	91.25 (81.25-98.75)	100.00 (97.50-100.00)	100.00 (97.50-100.00)	129.87 <.000
	At home	95.83 (87.50-100.00)	100.00 (100.00-100.00)	100.00 (100.00-100.00)	96.51 <.000
	In the community	87.50 (75.00-100.00)	100.00 (100.00-100.00)	100.00 (100.00-100.00)	101.01 <.000
	At school	95.00 (80.00-100.00)	100.00 (100.00-100.00)	100.00 (100.00-100.00)	107.03 <.000
	In the environment	90.00 (75.00-100.00)	100.00 (95.00-100.00)	100.00 (95.00-100.00)	96.39 <.000
Self-report 10-18 ***N*=155**	Total	87.50 (75.00-93.75)	97.50 (92.50-100.00)	97.50 (93.75-100.00)	116.11 <.000
	At home	87.50 (79.17-95.83)	100.00 (91.67-100.00)	100.00 (95.83-100.00)	92.99 <.000
	In the community	81.25 (66.67-93.75)	100.00 (93.75-100.00)	100.00 (93.75-100.00)	95.12 <.000
	At school	90.00 (75.00-100.00)	100.00 (95.00-100.00)	100.00 (100.00-100.00)	122.53 <.000
	In the environment	85.00 (70.00-95.00)	100.00 (90.00-100.00)	95.00 (90.00-100.00)	80.73 <.000

CASP = Child and Adolescent Scale of Participation
T0=two weeks post-MTBI, T1=3 months post-MTBI, T2=6 months post-MTBI

Comparisons between caregiver reports and children's self-reports on activities and participation in different settings

Table 3 shows that, with regard to caregivers reports for children aged 10 to 18 years, 99 (63.9%) followed a course with complete recovery at T2, while with regard to the CASP self-report, only 56 (36.1%) did. Wilcoxon signed-rank tests for continuous data, and McNemar's tests for dichotomized data showed that caregivers tend to score their child's total activities and participation level more positive than the children themselves at T0 (z=-3.84, p<.000, and χ^2(155)=16.69, p<.000), at T1 (z=-5.36, p<.000), and T1 χ^2(155)=17.65, p<.000), and at T2 (z=-6.34, p<.000, and χ^2(155)=32.07, p<.000).

Table 3. Full or deviant outcome on activities and participation in different settings over time post-MTBI

	CASP Setting	T0		T1		T2	
		Deviant *N (%)*	Full *N (%)*	Deviant *N (%)*	Full *N (%)*	Deviant *N (%)*	Full *N (%)*
Caregiver report 6-18 *N*=231	Total	172 (74.5)	59 (25.5)	88 (38.1)	143 (61.9)	78 (33.8)	153 (66.2)
	At home	118 (51.1)	113 (48.9)	51 (22.1)	180 (77.9)	28 (12.1)	203 (87.9)
	In the community	129 (55.8)	102 (44.2)	50 (21.6)	181 (78.4)	34 (14.7)	197 (85.3)
	At school	122 (52.8)	109 (47.2)	38 (16.5)	193 (83.5)	30 (13.0)	201 (87.0)
	In the environment	135 (58.4)	96 (41.6)	62 (26.8)	169 (73.2)	60 (26.0)	171 (74.0)
Caregiver report 10-18 *N*=155	Total	124 (80.0)	31 (20.0)	63 (40.6)	92 (59.4)	56 (36.1)	99 (63.9)
	At home	88 (56.8)	67 (43.2)	34 (21.9)	121 (78.1)	22 (14.2)	133 (85.8)
	In the community	96 (61.9)	59 (38.1)	37 (23.9)	118 (76.1)	29 (18.7)	126 (81.3)
	At school	90 (58.1)	65 (41.9)	27 (17.4)	128 (82.6)	22 (14.2)	133 (85.8)
	In the environment	98 (63.2)	57 (36.8)	42 (27.1)	113 (72.9)	43 (27.7)	112 (72.3)
Self-report 10-18 *N*=155	Total	147 (94.8)	8 (5.2)	94 (60.6)	61 (39.4)	99 (63.9)	56 (36.1)
	At home	123 (79.4)	32 (20.6)	58 (37.4)	97 (62.6)	59 (38.1)	96 (61.9)
	In the community	123 (79.4)	32 (20.6)	62 (40.0)	93 (60.0)	53 (34.2)	102 (65.8)
	At school	105 (67.7)	50 (32.3)	41 (26.5)	114 (73.5)	31 (20.0)	124 (80.0)
	In the environment	123 (79.4)	32 (20.6)	74 (47.7)	81 (52.3)	80 (51.6)	75 (48.4)

CASP = Child and Adolescent Scale of Participation
1=maximum score (100.00) on CASP representing full recovery; 0=score <100.00 on CASP representing deviant functioning
T0=two weeks post-MTBI, T1=3 months post-MTBI, T2=6 months post-MTBI

The relation of the course of activities and participation in different settings with the course of activities and participation in activity domains

Activities and participation in different settings (CASP) and several activity domains (CAPE) for children aged 10 to 18 years old were measured at three measurement points. Results showed a significant moderate positive correlation (r_s=.345, p<.000) at T0, a non-significant weak positive correlation (r_s=.156, p=.052) at T1, and a non-significant weak positive correlation (r_s=.116, p=.151) at T2. Change scores showed a mean difference of 11.81 (*SD* 16.46, Range -58.75-61.25) for scores on the CASP self-report for children aged 10 to 18 years between T0 and T2, and a mean difference of 5.89 (*SD* 5.78, Range -13.00-26.00) for scores on the CAPE for children aged 10-18 years between T0 and T2.

Correlation coefficients (Spearman's ρ) of these change scores showed a significant weak positive correlation between the change score of activities and participation in different settings and the change score of activities and participation in activity domains ($r_s=.287$, $p<.000$).

Table 4. Cochran's Q tests and McNemar's tests for outcome on activities and participation in different settings over time post-MTBI

	CASP Setting	Cochran's Q *p*	T0 vs. T1 χ^2 *p*	T1 vs. T2 χ^2 *p*	T0 vs T2 χ^2 *p*
Caregiver report 6-18 *N*=231	Total	116.73	68.89	1.35	75.87
		<.000	<.000	.245	<.000
	At home	101.69	41.49	10.30	74.73
		<.000	<.000	.001	<.000
	In the community	114.98	56.86	5.11	74.15
		<.000	<.000	.024	<.000
	At school	123.68	71.76	1.11	73.94
		<.000	<.000	.292	<.000
	In the environment	88.37	55.74	.02	54.22
		<.000	<.000	.892	<.000
Caregiver report 10-18 *N*=142	Total	83.11	49.32	.80	53.44
		<.000	<.000	.371	<.000
	At home	78.89	35.11	3.78	55.59
		<.000	<.000	.052	<.000
	In the community	81.98	42.58	1.53	51.25
		<.000	<.000	.216	<.000
	At school	92.67	51.25	.552	54.74
		<.000	<.000	.458	<.000
	In the environment	66.26	44.49	.00	37.87
		<.000	<.000	1.000	<.000
Self-report 10-18 *N*=142	Total	59.06	47.44	.28	36.82
		<.000	<.000	.596	<.000
	At home	80.80	50.57	.00	49.61
		<.000	<.000	1.000	<.000
	In the community	81.33	44.44	1.56	51.75
		<.000	<.000	.212	<.000
	At school	93.90	49.61	2.13	60.56
		<.000	<.000	.144	<.000
	In the environment	43.29	32.45	.46	24.16
		<.000	<.000	.496	<.000

*Exact sig. (2-tailed)

CASP = Child and Adolescent Scale of Participation

T0=two weeks post-MTBI, T1=3 months post-MTBI, T2=6 months post-MTBI

Table 5: Outcome on activities and participation for several activity domains over time post-MTBI (*N*=231)

CAPE Domain	T0 M *(SD)*	T1 M *(SD)*	T2 M *(SD)*
Total	15.93 (5.45)	22.77 (5.27)	21.92 (5.03)
Recreational	5.50 (2.27)	6.74 (2.50)	6.39 (2.45)
Active physical	1.55 (1.27)	2.55 (1.07)	2.61(1.16)
Social	3.54 (1.74)	5.67 (1.61)	5.50 (1.83)
Skill-based	.98 (1.15)	1.87 (1.29)	1.68 (1.28)
Self-improvement	3.23 (1.50)	4.25 (1.63)	4.13 (1.63)

CAPE = Children's Assessment of Participation and Enjoyment
T0=two weeks post-MTBI, T1=3 months post-MTBI, T2=6 months post-MTBI

Table 6: Repeated Measures ANOVA and post-hoc analyses for outcome on activities and participation for several activity domains over time post-MTBI (*N*=231)

CAPE Domain	RMA				Post-hoc test (Bonferroni correction)		
	df_M	df_R	*F*	*p*	T0 vs. T1 *p*	T1 vs. T2 *p*	T0 vs T2 *p*
Total	1.82	417.50	218.06	<.000	<.000	.054	<.000
Recreational	1.97	451.95	56.21	<.000	<.000	.005	<.000
Active physical	1.85	425.60	98.15	<.000	<.000	1.000	<.000
Social	1.87	429.43	191.71	<.000	<.000	.295	<.000
Skill-based	1.95	447.81	54.44	<.000	<.000	.075	<.000
Self-improvement	1.98	455.48	47.27	<.000	<.000	.862	<.000

CAPE = Children's Assessment of Participation and Enjoyment, RMA = Repeated Measures ANOVA
T0=two weeks post-MTBI, T1=3 months post-MTBI, T2=6 months post-MTBI

Discussion

The present study showed a general improvement of activities and participation in different settings and for several activity domains during the first six months after childhood MTBI. In accordance with our expectations, the level of activities and participation was lowest at two weeks post-injury, increased up to three months post-injury, and stabilized up to six months post-injury in most settings and activity domains. Strikingly, caregivers evaluated their child's level of activities and participation in different settings more positive compared to the evaluation of the children themselves.

The course of activities and participation over time after MTBI in different settings and on several activity domains were, in accordance with our expectations, positively correlated.

The finding that activities and participation improves over time after MTBI is largely in agreement with previous findings.[12-13] We found that in most settings the level of activities and participation stabilized between three and six months post-injury. Caregivers, however, reported that the level of activities and participation of their child at home had increased significantly between two weeks and three months, as well as between three and six months post-injury. The idea that caregivers may set higher priorities at returning to school (i.e. following classes) and pick up on activities in the community (i.e. returning to sports) in comparison to picking up on activities at home (i.e. cleaning their room), may be an explanation for the further improvement in this setting after three months post-injury. Although activities and participation improve over time, it was found that between 33.8% and 63.9% of the children with MTBI still participate less in comparison to their peers at six months post-injury. The difference in percentages was explained by the chosen perspective, resulting in a more positive evaluation of the child's level of activities and participation from the caregivers' perspective in comparison to the children's perspective for children aged 10 to 18 years. This finding was not in accordance with findings from another study, in which children seem to evaluate their level of activities and participation higher in comparison to their caregivers,[21] but this mixed sample study did not differentiate for mild TBI. An explanation for the more positive evaluation of the parents could be that they mostly observe their children in the home situation while the more complex activities are performed at school. It could be possible that MTBI affects the more complex activities to a greater extent.

Concerning child motivation, we observed that high school aged children seemed less motivated and used the injury more often as an excuse, in comparison to pre-school aged children, who preferred to return to activities and participation as soon as possible after the injury. Child motivation is one of the facilitating factors for good participation after traumatic brain injury.[33] Our observation is in line with the general behavior in puberty, during which less motivation for things that have to be done (i.e. homework, dishes) is more common than in younger children. Another explanation may be that younger children spend more time with their parents in comparison to older children. For younger children, caregivers may therefore have a more complete view on their child's functioning in comparison to their view on older children who commonly spend more time without their parents' interference. Caregivers may assume that their older child has successfully returned to activities and participation in all settings, because it is doing so at home, while the child may experience that, for example at school, participation is more difficult due to for example problems with concentrating.

This study has several strengths. First, this study had a large population of children with MTBI only, and assessed both children of all school ages (6-18) as well as their caregivers. Second, the outcome instruments used in this study are based largely on the International Classification of Functioning, Disability and Health for Children and Youth (ICF-CY) and are recommended by the inter-agency Pediatric Outcome workgroup.[30]

This study also had some limitations. First, children and adolescents with MTBI were recruited from emergency departments, and may therefore not be representative of the larger population as this excludes those who do not receive acute medical care. Population research is needed to find out how these children function on the level of activities and participation. Second, a relatively large number of children who were eligible for participation in the study could not be reached, which influences the external validity. From the number of eligible participants who were reached however, almost 80% chose to participate. We checked whether the children in the intervention group (n=60) differed in terms of baseline characteristics from the control group in our intervention study; no significant differences were found. Our ethics regulations do not permit to collect data on excluded participants and therefore we cannot test differences for this group.

This study adds to the literature on the ceiling effect of the CASP. For a better understanding, we recommend using dichotomized scores to interpret results. The CASP seems a reliable instrument to assess activities and participation in children with more severe head injuries, but may not be the most sensitive measure for children with MTBI. Recently it was shown that the CASP is responsive to change over time, particularly in more severe TBI.[19] Additionally, we were the first to use the CAPE in children with MTBI specifically and therefore, reference material is currently lacking; our detailed description of data in a large sample adds to the existing knowledge base. To the best of our knowledge, though, a better instrument to assess activities and participation in children after MTBI at this point does not yet exist. We emphasize the importance of developing an instrument that is more sensitive in distinguishing levels of activities and participation among children with mild brain injuries.

Conclusion

This is the first large sample prospective longitudinal study on a homogeneous sample of children with only mild TBI. Activities and participation increase over time in different settings and for several activity domains after MTBI in children. For a substantial number of children, however, the level of activities and participation at six months post-MTBI is evaluated as less in comparison to peers. Future studies should investigate predictors for activities and participation, in order to provide insight into those children who are at risk for long term problems and who may benefit from early interventions. Furthermore population research is needed, because at this point we only have information on those children with MTBI who were admitted to the emergency departments of hospitals. Since outcome on activities and participation differs between the perspective of the caregiver and the child, and across domains and settings, we emphasize the importance of investigating predictors for all perspectives.

Appendix 1. Wilcoxon signed-rank test for outcome on activities and participation in different settings over time post-MTBI

	CASP Setting	T0 vs. T1 *Z* *p*	T1 vs. T2 *Z* *p*	T0 vs T2 *Z* *p*
Caregiver report 6-18	Total	-10.09 <.000	-1.969 .049	-10.303 <.000
***N*=231**	At home	-7.858 <.000	-3.412 .001	-8.940 <.000
	In the community	-8.854 <.000	-.489 .625	-8.806 <.000
	At school	-8.589 <.000	-1.709 .088	-8.964 <.000
	In the environment	-8.720 <.000	-.732 .464	-8.591 <.000
Caregiver report 10-18	Total	-8.474 <.000	-1.396 .163	-8.743 <.000
***N*=155**	At home	-6.785 <.000	-2.269 .023	-7.632 <.000
	In the community	-7.420 <.000	-.157 .876	-7.584 <.000
	At school	-7.318 <.000	-1.617 .106	-7.661 <.000
	In the environment	-7.683 <.000	-.718 .473	-7.606 <.000
Self-report 10-18	Total	-8.838 <.000	-.020 .984	-8.635 <.000
***N*=155**	At home	-7.612 <.000	-.140 .889	-7.358 <.000
	In the community	-8.004 <.000	-.179 .858	-7.459 <.000
	At school	-7.859 <.000	-1.618 .106	-7.841 <.000
	In the environment	-7.245 <.000	-.014 .989	-7.037 <.000

CASP = Child and Adolescent Scale of Participation

T0=two weeks post-MTBI, T1=3 months post-MTBI, T2=6 months post-MTBI

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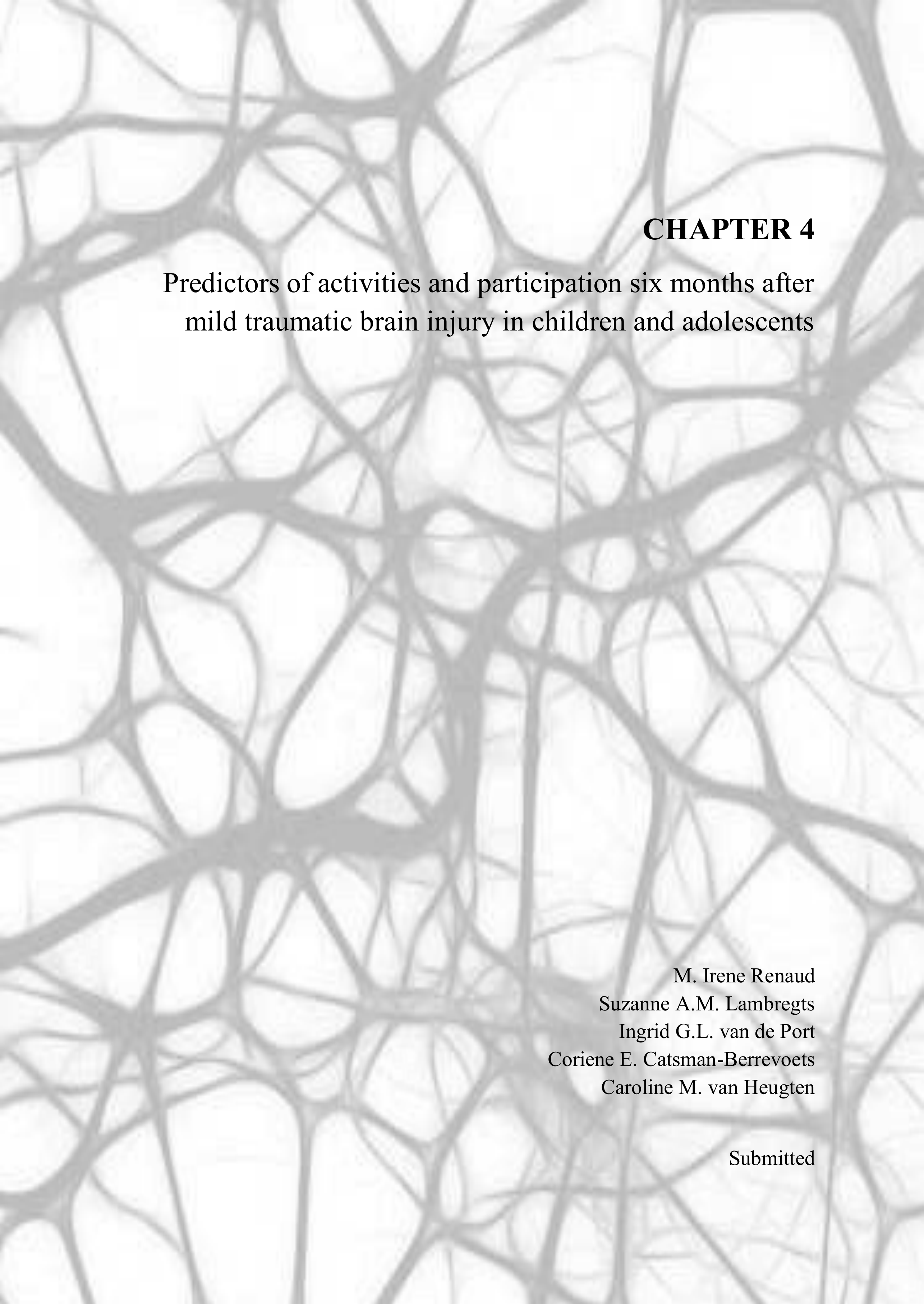

CHAPTER 4

Predictors of activities and participation six months after mild traumatic brain injury in children and adolescents

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Submitted

Abstract

Objective: This study aimed to identify predictors for a risk of decreased level of activities and participation in children at long term after mild traumatic brain injury (MTBI).

Methods: We conducted a multicentre prospective longitudinal cohort study. The primary outcome measure was activities and participation measured with the Child and Adolescent Scale of Participation – CASP, which was filled out by children and caregivers (N=301) at six months after MTBI. CASP items were categorized into home, community, school, and environment. Predictors were categorized according to the International Classification of Functioning, Disability and Health for Children and Youth and included injury-related factors, symptoms, and resumption of activities in the first two weeks after MTBI, (pre-injury) personal- and environmental factors. Univariate and multivariate logistic regression analyses were used to determine the predictive value of these factors.

Results: Results show that predictors for children who are at risk of long-term consequences on activities and participation differ per setting and per chosen perspective (child or caregiver). Adverse pre-injury behavioral functioning of the child (p<.000 – p=.038), adverse pre-injury family functioning (p=.001), lower parental SES (p=.038), more stress symptoms post-injury (p=.017 – p=.032), more post-concussive symptoms (p=.016 – p=.028) and less resumption of activities (p=.006 – p=.045) predict decreased activities and participation after pediatric MTBI.

Discussion: Not injury-related factors but pre-injury factors, more symptoms post-injury and less resumption of activities should be considered when children are screened for unfavorable outcome. Additional factors may add to the prediction. We recommend future research to focus on psychosocial factors, such as coping styles, emotion-regulation, personality traits, social support, and other comorbid problems of both children and caregivers.

Introduction

Traumatic brain injuries (TBI) are considered the most common cause of disability or death in children, adolescents and young adults.[1] Although most children recover well from mild TBI (MTBI), approximately 20% of them suffer from a variety of post-concussion symptoms (PCS)[2-6] and it is suggested that these children may experience limitations in activities and participation in the long term for which support may be needed but is often not offered.[7-8] Outcome on activities and participation may differ depending on the perspective of either the caregivers or the children themselves[9] and may differ per setting (e.g. at home, in the community, at school, and in the environment).[10] Because many children recover well from MTBI, overtreatment should be avoided. Knowledge of predictive factors can help to identify the children and adolescents that are at risk of problems on activities and participation after MTBI, enables application of early and focused interventions and may help prevent such long-term problems.

Several studies have examined predictors for outcome after MTBI in children.[11-24] The majority of these studies, however, focus on predictors of PCS.[18-24] There are no studies on predictors for outcome on activities and participation after MTBI specifically in children. Earlier outcome studies on the level of activities and participation included heterogeneous groups of children with brain injury, such as acquired brain injury and/or mixed samples of severity, their sample sizes not permitting subgroup analyses of MTBI,[11-16] or were restricted to sport-related concussions only.[17] They show that a less severe injury (e.g. moderate vs. severe TBI, higher Glasgow Coma Scale (GCS) score),[11-13,16] better pre-injury functioning of the child,[14] better family functioning,[11-13] higher socioeconomic state (SES),[11,13,16] and less cognitive-, behavioral-, and emotional symptoms early after injury[11,17] predict better outcome on the level of activities and participation. Age was found to be a predictor in some studies[12], but not in others.[11,15] Cause of injury is not found to predict outcome on activities and participation after pediatric TBI.[11,13,16]

These results suggest that not only injury-related, but also personal and environmental factors influence outcome after pediatric brain injury. In order to predict which children are at risk of long-term consequences after MTBI on activities and participation, it is therefore important to study relevant factors from a biopsychosocial perspective in a comprehensive model. Categories of the International Classification of Functioning, Disability and Health for Children and Youth (ICF-CY) may be useful for this purpose.[25] The abovementioned studies[11-17] did not differentiate for perspectives (i.e. child or caregiver/teacher) or for activities and participation per setting.

The present study is the first to examine multiple predictors for activities and participation at six months after MTBI in children and adolescents from a biopsychosocial perspective following the relevant ICF-CY categories[25] for activities and participation in different settings in one model, from both the perspective of the caregiver and the child. Knowledge of the predictive factors of activities and participation, should result in a better identification of children who are at risk of long-term limitations and might benefit from early interventions.

Materials and Methods

Design

This study was part of the larger Brains Ahead! study on the natural course of activities and participation of children after MTBI. The Brains Ahead! study protocol is described in detail elsewhere[7] and was approved by the medical ethics committee of Erasmus University Hospital in Rotterdam and by all local committees of the participating hospitals (MEC-2015-047, NL51968.078.14, v08). The Brains Ahead! study consists of a multicenter prospective longitudinal cohort study with a nested randomized controlled trial (RCT). In the RCT, the effect of an early psychoeducational intervention is evaluated in comparison to care as usual.[26] We excluded patients who were randomized into the intervention group of the RCT from the current analysis in order to follow a natural occurring cohort receiving usual care.

Setting

All children aged 6 to 18 years, who presented with MTBI at the Emergency Departments of eight Dutch hospitals (Erasmus University Hospital, Rotterdam; Amphia Hospital, Breda; Haaglanden Medical Centre and Haga Hospital, The Hague; Rijnstate Hospital, Arnhem; Hospital Gelderse Vallei, Ede; Reinier de Graaf Hospital, Delft; and Elisabeth-Twee Steden Hospital, Tilburg) between May 2015 and April 2018, and their caregiver(s), were eligible for participation.

Participants

Children were included if they sustained a MTBI according to the criteria established by the American Congress of Rehabilitation Medicine and the World Health Organization Collaborating Centre for Neurotrauma Task Force on Mild Traumatic Brain Injury.[27] Exclusion criteria were 1) having a previous objectified head trauma, 2) having progressive neurological problems or disease (based on patient history in the hospitals' electronic patient files), 3) attending a daycare center or school for cognitively impaired children and youth, and 4) having insufficient knowledge of the Dutch language (child or caregivers). The caregivers were defined as parents or guardians. There were no further exclusion criteria for caregivers.

Procedure

The full study procedure is described in the Brains Ahead! study design.[7] After written informed consent, obtained by the researcher, the baseline measurement was scheduled at two weeks (T0) post-injury at home. The final measurement took place at six months (T1) post-injury, also at the participant’s home. No procedural differences between the participating hospitals existed.

Materials

All instruments have been used in several international studies, have sound psychometric properties, and are recommended as instruments for evaluating predictors[28] in terms of function level (e.g. fatigue, post-concussive symptoms (PCS,) and posttraumatic stress symptoms (PTSS)[29-31], environmental factors (e.g. family functioning)[32-33], personal factors (e.g. behavioral functioning)[34], and outcome in terms of activities and participation in children and adolescents after brain injury.[35-38] All measurements took place in the presence of the researcher who gave the instructions, could check the filled out questionnaires and prevent missing data as much as possible. False respondent bias was prevented by the researcher ensuring the child filled out the self-report questionnaires and the caregiver filled out the caregiver-report questionnaires.

Outcome measure

Level of activities and participation was measured in different settings with the Child and Adolescent Scale of Participation (CASP). The CASP is a 20-item questionnaire designed specifically to measure participation in different activity settings in children with ABI, according to the components of the International Classification of Functioning, Disability and Health for Children and Youth (ICF-CY).[9,25,35-36] The CASP can be filled out by caregivers for children aged 6-18 years old, and the self-report can be filled out by children aged 10-18 years old. Since it was found that caregivers and children report differently on activities and participation outcome after TBI[9], we decided to use both reports filled out at T1.

The CASP items are categorized into the following settings: at home, in the community, at school, and in the environment, and can be scored on a four point scale (1) age appropriate, (2) slightly impaired, (3) heavily impaired, (4) not capable. Summary scores are created by summing the item responses, dividing this number by the maximum possible score and multiplying this number by 100 to conform to a 100-point scale.

The total score range is therefore 25 - 100, with a higher score representing better outcome. Missing and ‘not applicable’ scores are not included in the scoring. In case of missing and not applicable scores, the sum of the item responses is divided by the amount of applicable scores. Since scores on the CASP are well-known for their ceiling effect we dichotomized the scores resulting in a full score of 100 being evaluated as full functioning and any score below 100 as deviant functioning.[9,13,35-36]

Predictors

The predictors were categorized according to the ICF-CY[25] in health condition, function, activities, environmental and personal factors (see Figure 1). These variables were identified and collected from the patient files and at the initial assessment two weeks post-injury (T0) and are described in more detail below.

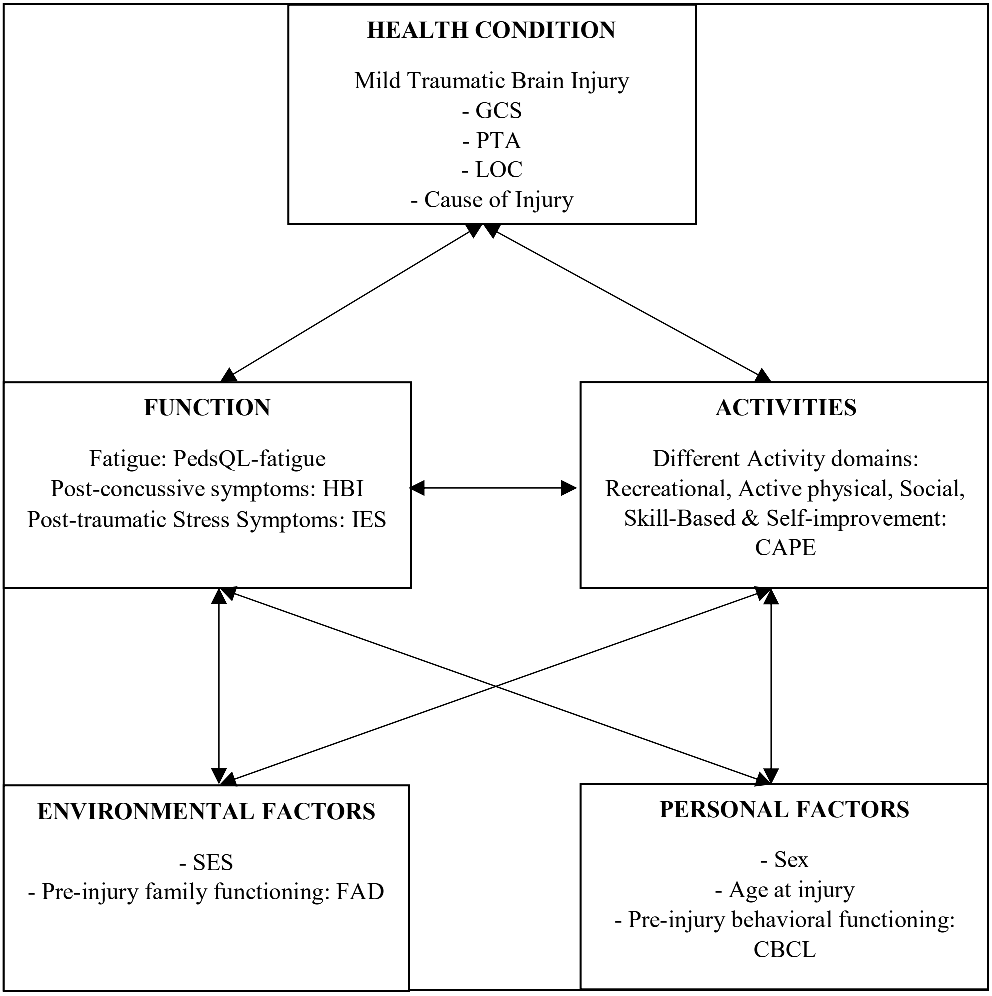
Health condition

With the health condition being MTBI, the injury-related characteristics in this study are GCS (13-15), posttraumatic amnesia (PTA) (<24h), loss of consciousness (LOC) (<30min.) and cause of injury divided into traffic accident, sports accident, outdoor play accident, accident at school/work, accident at home, physical abuse, and other.

Function

Predictors on function level in this study are fatigue, measured with the Pediatric Quality of Life Inventory-fatigue scale (PedsQL-fatigue), post-concussive symptoms, measured with the Health and Behavior Inventory (HBI), and posttraumatic stress symptoms, measured with the Impact of Events Scale (IES). These questionnaires were filled out by caregivers about the experience of symptoms at T0.The PedsQL-Fatigue is an 18-item questionnaire that measures overall fatigue, problems regarding sleep/rest, and cognitive fatigue. A higher score indicates fewer symptoms of fatigue.[29] The HBI is a 50-item questionnaire that measures physical, emotional, cognitive, and behavioral post-concussive symptoms. A lower total score represents fewer PCS. [30] The IES is a 34-item questionnaire measuring possible post-traumatic stress responses. A lower score represents less symptoms.[31]

Figure 1. Relevant predictors based on the categories from the ICF-CY model



ICF-CY model and predictors used for outcome on Activities and Participation.[22]
Abbreviations: GCS, Glasgow Coma Scale score; PTA, Posttraumatic Amnesia; LOC, Loss of Consciousness; PedsQL-fatigue, Pediatric Quality of Life Inventory-fatigue scale; HBI, Health and Behavior Inventory; IES, Impact of Events Scale; SES, Socioeconomic Status; CAPE, Children's Assessment of Participation and Enjoyment; FAD, Family Assessment Device; CBCL, Child Behavior Checklist.

Activities

In this study, engagement in different domains of activities was measured with the Children's Assessment of Participation and Enjoyment (CAPE). The CAPE is a 55-item self-report questionnaire, whose items correspond to engagement in 55 different activities, filled out by children aged 6-18 years old. It measures diversity in recreational, active physical, social, skill-based and self-improvement activity domains and can be scored binary; 0 if the activity was not performed, 1 if the activity was performed. The total score range is therefore 0-55, with higher scores indicating more participation in activities.[37-38] In this study, the CAPE was filled out about the performed activities from the time since injury up to T0.

Environmental Factors

Physical, social, and attitudinal environment was measured with the parental Socioeconomic Status (SES), and pre-injury family functioning, measured with the Family Assessment Device (FAD) filled out by caregivers at T0 about the pre-injury family functioning. The FAD-GF is a 12-item questionnaire to measure the general family functioning, of which half (six) of the items need to reversely scored to fit the four-point Likert scale (1) strongly disagree, (2) disagree, (3) agree, and (4) strongly agree. The item scores are averaged to yield a possible total score range from 1.00 (healthy family functioning) to 4.00 (unhealthy family functioning). The cut-off score for healthy family functioning is 2.00).[32-33]

Personal Factors

Individual background characteristics in this study are sex, age at the time of injury, and pre-injury behavioral functioning, measured with the Child Behavior Checklist (CBCL), filled out by caregivers at T0 on the child's pre-injury behavioral functioning. The CBCL is a 113-item questionnaire to measure cognitive and behavioral problems and skills in children. The CBCL provides a Total Behavior Problem Score (T=50, SD=15). For the Total Scale, a score >60 can be considered impaired (61-69 mild impairment, >70 severe impairment).[34]

Statistical Analysis

Descriptive statistics were used to describe baseline health condition, function, activities, environmental, and personal characteristics. Means (SD's) or medians (ranges) were reported depending on the distribution of the data.

The predictive value of health condition, function, activities, environmental, and personal characteristics for the dichotomized (either full or deviant functioning) CASP outcome in different settings of activities and participation six months after MTBI was first investigated by univariate binomial logistic regression analyses for each factor. When statistical significance at an alpha level of .10 or less[39] was reached, the factor was entered into multivariate binomial logistic regression (backward LR) analyses per setting of activities and participation.

The abovementioned analyses were performed both for the perspective of the caregivers and of the children themselves. The statistical significance for the multivariate binomial logistic regression analyses was set at an alpha level of .05. The regression models were checked for independence of error and absence of co-linearity (Box-Tidwell) and outliers. Nagelkerke R^2 was used to describe the proportion of variance of the CASP associated by the predictor(s) in the final multivariate model. Goodness of fit of the multivariate models were tested with the Hosmer-Lemeshow test, with *p*-values higher than .05 representing a good fit. Statistical analyses were performed using IBM SPSS Statistics for Windows, version 25.0.

Results

Sample characteristics

In total 698 children with MTBI were considered for participation in the study, of whom 140 were excluded based on the exclusion criteria (see Figure 2). Furthermore, a total of 257 persons did not participate in the study, from which the vast majority (168) could not be reached. Finally, 60 participants received the Brains Ahead! Intervention, and were, therefore, excluded from the analyses in this study. Since we decided to work with complete datasets, the incomplete datasets of 10 participants were left out of further analyses. In total 231 participants were included in the analyses for the perspective of the caregivers. Since the CASP self-report could be filled out by children aged 10-18 years only, data of 156 participants were included in the analyses for the perspective of the children.

Children's characteristics show that the sample consisted of more boys (65.4%) the mean age at injury was 11.4 (*sd* 3.3) (Table 1). The majority of the participants had a high parental SES (59.3%) and normal pre-injury behavioral functioning of the child (83.1%). Most children sustained MTBI due to sports (31.2%) or traffic accidents (29.4%), showed a GCS of 15 (80.5%) and a PTA of less than one hour (73.5%), and about half of the children experienced LOC (49.4%).

Figure 2. Flow of participants

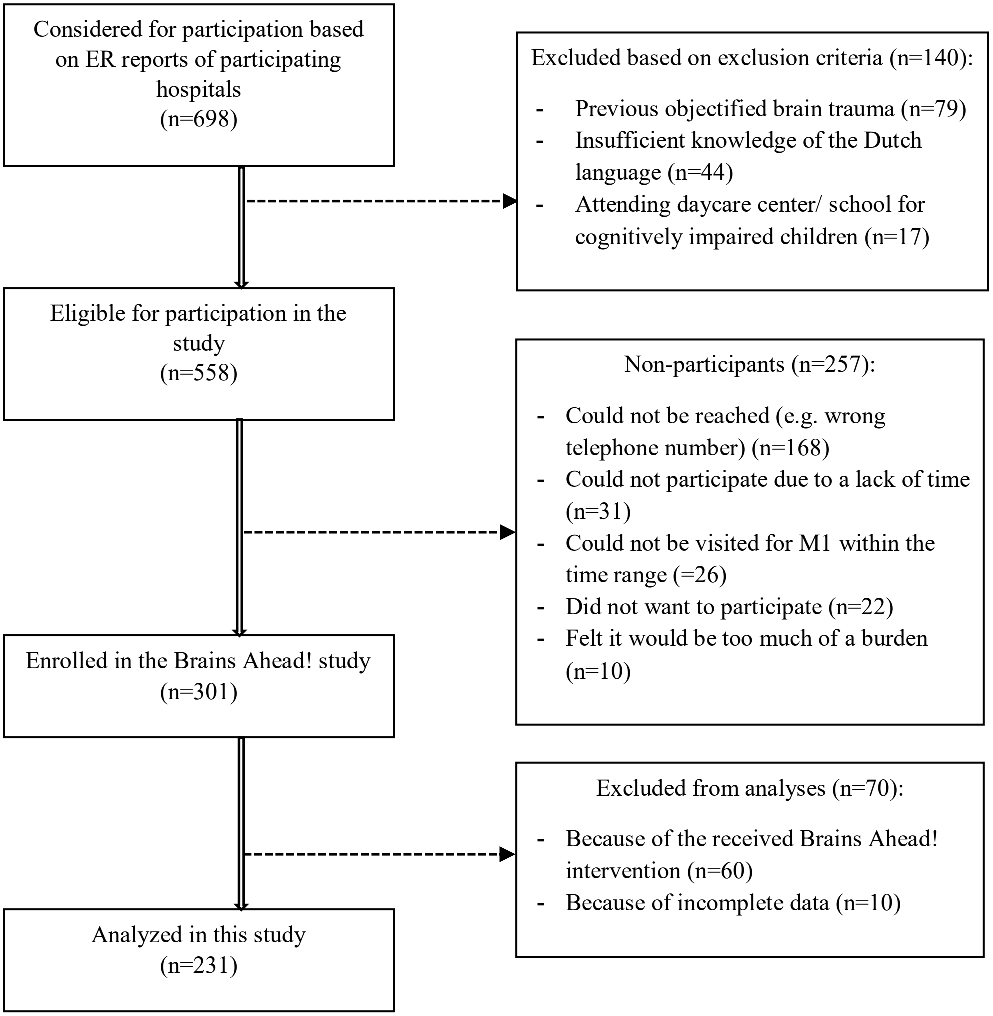


Table 1. Predictor characteristics (N=231)

	Characteristics	*N (%)*	*M* (SD)
Health condition	GCS:		
	13	8 (3.5)	
	14	37 (16.0)	
	15	186 (80.5)	
	PTA duration:		
	None	50 (21.6)	
	<1 hour	120 (51.9)	
	1-2 hours	18 (7.8)	
	2-6 hours	30 (13.0)	
	6-12 hours	5 (2.2)	
	12-18 hours	1 (.4)	
	18-24 hours	7 (3.0)	
	LOC duration:		
	None	117 (50.6)	
	<2 minutes	69 (29.9)	
	2-5 minutes	33 (14.3)	
	>5 minutes	12 (5.2)	
	Cause of injury:		
	Sports accident	72 (31.2)	
	Traffic accident	68 (29.4)	
	Outdoor play accident	48 (20.8)	
	Accident at school/work	22 (9.5)	
	Accident at home	13 (5.6)	
	Physical abuse	5 (2.2)	
	Other	2 (.9)	
Function	Fatigue [A]		63.8 (19.5)
	PCS [B]		94.0 (22.3)
	PTSS [C]		59.0 (14.5)
Activities	Engagement in Activity domain [D]:		
	Total		15.9 (5.4)
	Recreational		5.5 (2.3)
	Active physical		1.6 (1.3)
	Social		3.5 (1.7)
	Skill-based		1.0 (1.2)
	Self-improvement		3.2 (1.5)
Environmental Factors	SES:		
	Low	53 (22.9)	
	Average	41 (17.7)	
	High	137 (59.3)	
	Pre-injury family functioning [E]		1.5 (.4)
	Healthy score	200 (86.6)	
	Unhealthy score	31 (13.4)	
Personal Factors	Child sex: male	151 (65.4)	
	Child age at injury in years	231 (100)	11.4 (3.3)
	(Min – Max, Range)	(6-17)	
	Pre-injury Behavioral functioning [F]		50.0 (10.0)
	Normal score	192 (83.1)	
	Mild impaired	29 (12.6)	
	Severe impaired	10 (4.3)	

GCS = Glasgow Coma Scale score, PTA= Posttraumatic amnesia, LOC = Loss of Consciousness, SES = Caregiver's Socioeconomic State,

[A], Measured with the PedsQL-Fatigue; [B], Post-concussive symptoms measured with the HBI; [C], Posttraumatic Stress Symptoms measured with the IES; [D], measured with the CAPE; [E], measured with the FAD-GF; [F], measured with the CBCL

Activities and participation in different settings at six months post-MTBI.

With regard to the perspective of the caregivers, 87.9% scored full functioning on activities and participation at home, 85.3% in the community, 87.0% at school, and 74.0% scored full functioning in the environment at six months post-MTBI. With regard to the perspective of the children, 61.9% scored full functioning on activities and participation at home, 65.8% in the community, 80.0% at school, and 48.4% scored full functioning in the environment at six months post-MTBI.

Univariate binomial logistic regression analyses

Results of the univariate binomial logistic regression analyses are shown in Tables 2 and 3. It was found that fewer symptoms on the PedsQL-Fatigue, HBI and IES, lower scores on (all) CAPE activities, low SES, higher scores on the FAD, and higher scores on the CBCL significantly predicted outcome, and injury-related factors did not. Predictive factors differ across settings and per perspective.

Multivariate binomial logistic regression analyses

The results of the multivariate binomial logistic regression analyses are shown in Tables 4 and 5. From the perspective of the caregivers, higher scores on the CBCL significantly predicted a higher chance of deviant functioning on the level of activities and participation in all settings (*p*<.000). For activities and participation in the community, lower scores on CAPE recreational activities (*p*=.006) significantly added to the model, as did lower scores on CAPE total activities (*p*=.045) for activities and participation at school.

From the perspective of the children, higher scores on the CBCL and higher scores on the IES significantly predicted a higher chance of deviant functioning on the level of activities and participation at home (CBCL: *p*=.001; IES: *p*=.017) as well as in the community (CBCL: *p*=.038; IES: *p*=.032). Higher scores on the HBI significantly predicted a higher chance of deviant functioning on the level of activities and participation at school (*p*=.016) and in the environment (*p*=.028). For activities and participation at school, lower SES (*p*=.038) significantly added to a higher chance of deviant functioning, as did higher scores on the FAD (*p*=.001) for activities and participation in the environment.

Nagelkerke R^2 and goodness of fit (Hosmer-Lemeshow) test results from the final models of the multivariate binomial logistic regression analyses are shown in Table 6. All Nagelkerke R^2 scores were <.23 and all Hosmer Lemeshow tests showed a good final model fit, except for the caregivers perspective at school.

Table 2. Univariate binomial logistic regression analyses (*N*=231) – Perspective of Caregiver

		CASP Setting											
		Home			Community			School			Environment		
ICF-CY Category	**Characteristics**	**β**	***p***	**Odds (95% CI)**	**β**	***p***	**Odds (95% CI)**	**β**	***p***	**Odds (95% CI**	**β**	***p***	**Odds (95% CI)**
Health condition	GCS:	.07	.863	1.08 (.47 - 2.44)	- .16	.654	.85 (.43 - 1.71)	.56	.264	1.76 (.65 - 4.72)	- .02	.944	.98 (.54 - 1.77)
	PTA duration:	.17	.218	1.18 (.91 - 1.55)	.09	.485	1.10 (.85 - 1.43)	.03	.840	1.03 (.77 - 1.37)	.01	.936	1.01 (.81 - 1.26)
	LOC duration:	.19	.355	1.22 (.80 - 1.84)	.26	.172	1.30 (.89 - 1.89)	.33	.100	1.39 (.94 - 2.05)	.14	.377	1.15 (.84 - 1.59)
	Cause of injury**:		.521			.672			.878			.870	
Function	Fatigue ^{A}	- .03	.017*	.98 (.96 - 1.00)	- .02	.063*	.98 (.96 - 1.00)	- .02	.050*	.98 (.96 - 1.00)	- .02	.038*	.98 (.97 - 1.00)
	PCS ^{B}	.03	.001*	1.03 (1.01 – 1.05)	.02	.020*	1.02 (1.00 - 1.04)	.02	.008*	1.02 (1.01 – 1.04)	.03	<.000*	1.03 (1.02 – 1.05)
	PTSS ^{C}	.03	.016*	1.03 (1.01 – 1.06)	.02	.088*	1.02 (1.00 - 1.05)	.03	.017*	1.03 (1.01 - 1.06)	.02	.030*	1.02 (1.00 - 1.04)
Activities ^{D}	Total	- .05	.236	.96 (.89 - 1.03)	- .10	.007*	.90 (.84 - .97)	- .08	.046*	.93 (.86 - 1.00)	- .03	.323	.97 (.92 - 1.03)
	Recreational	- .01	.933	.99 (.83 - 1.18)	- .21	.020*	.81 (.68 - .97)	.00	.996	1.00 (.84 - 1.18)	- .01	.902	.99 (.87 – 1.13)
	Active physical	- .27	.135	.77 (.54 - 1.09)	- .34	.046*	.71 (.51 - .99)	- .20	.243	.82 (.59 - 1.14)	- .03	.791	.97 (.77 - 1.22)
	Social	- .07	.550	.93 (.74 - 1.18)	- .11	.316	.89 (.72 - 1.11)	- .17	.170	.85 (.67 - 1.07)	- .03	.700	.97 (.82 - 1.15)
	Skill-based	- .12	.539	.89 (.61 - 1.29)	.04	.798	1.04 (.77 - 1.42)	- .30	.153	.74 (.49 - 1.12)	- .11	.438	.90 (.69 - 1.18)
	Self-improvement	- .16	.259	.86 (.65 - 1.12)	- .20	.115	.82 (.64 - 1.05)	- .23	.095*	.80 (.61 - 1.04)	- .23	.031*	.80 (.65 - .98)
Environmental Factors	SES	- .39	.085*	.67 (.43 – 1.06)	- .21	.331	.81 (.53 - 1.24)	- .10	.653	.90 (.57 - 1.742	- .19	.294	.83 (.59 - 1.18)
	Pre-injury family functioning ^{E}	1.07	.056*	2.90 (.97 – 8.65)	.84	.103	2.31 (.85 – 6.28)	.85	.115	2.34 (.81 - 6.72)	.26	.528	1.30 (.68 – 2.93)
Personal Factors	Child sex	.13	.768	1.14 (.49 – 2.64)	.12	.762	1.13 (.52 - 2.45)	- .58	.141	.56 (.26 - 1.21)	- 22	.484	.80 (.44 - 1.48)
	Child age at injury	.08	.208	1.08 (.96 – 1.22)	.09	.100	1.10 (.98 - 1.23)	.04	.513	1.04 (.93 - 1.17)	.03	.521	1.03 (.94 - 1.13)
	Pre-injury Behavioral functioning ^{F}	.08	<.000*	1.08 (1.04 – 1.12)	.05	.001*	1.06 (1.02 - 1.09)	.08	<.000*	1.08 (1.05 - 1.12)	.08	<.000*	1.08 (1.05 – 1.11)

CASP = Child and Adolescent Scale of Participation, measured at T1, GCS = Glasgow Coma Scale score, PTA= Posttraumatic amnesia, LOC = Loss of Consciousness, SES = Caregiver's Socioeconomic State.

^{A}, Measured with the PedsQL-Fatigue; ^{B}, Post-concussive symptoms measured with the HBI; ^{C}, Posttraumatic Stress Symptoms measured with the IES; ^{D}, measured with the CAPE; ^{E}, measured with the FAD-GF; ^{F}, measured with the CBCL

* Factor entered into multivariate binomial logistic regression analyses** For cause of injury, β and Odds (95% CI) could not be calculated

Table 3. Univariate binomial logistic regression analyses (N=156) – Perspective of Child

		CASP Setting											
		Home			Community			School			Environment		
ICF-CY Category	**Characteristics**	**β**	***p***	**Odds (95% CI)**	**β**	***p***	**Odds (95% CI)**	**β**	***p***	**Odds (95% CI)**	**β**	***p***	**Odds (95% CI)**
Health condition	GCS:	- .37	.238	.69 (.38 - 1.27)	- .25	.432	.78 (.42 - 1.45)	.05	.892	1.06 (.49 - 2.28)	-.09	.752	.91 (.50 - 1.66)
	PTA duration:	- .02	.899	.98 (.77 - 1.26)	- .09	.507	.91 (.70 - 1.19)	-.10	.544	.90 (.65 - 1.25)	-.08	.509	.92 (.72 - 1.18)
	LOC duration:	.18	.302	1.19 (.85 - 1.67)	.15	.392	1.16 (.82 - 1.64)	.34	.090*	1.40 (.95 – 2.07)	.15	.371	1.16 (.83 - 1.62)
	Cause of injury**:		.656			.742			.986			.838	
Function	Fatigue ^{A}	- .02	.017*	.98 (.96 - 1.00)	-.02	.096*	.99 (.97 - 1.00)	-.02	.102	.98 (.96 - 1.00)	-.02	.060*	.98 (.97 - 1.00)
	PCS ^{B}	.03	<.000*	1.03 (1.02 - 1.05)	.02	.010*	1.02 (1.01 - 1.04)	.03	.007*	1.03 (1.01 – 1.04)	.02	.001*	1.03 (1.01 - 1.04)
	PTSS ^{C}	.04	.001*	1.04 (1.02 - 1.07)	.04	.006*	1.04 (1.01 - 1.06)	.02	.143	1.02 (.99 - 1.05)	.02	.106	1.02 (1.00 - 1.04)
Activities ^{D}	Total	.01	.656	1.01 (.96 - 1.07)	- .02	.434	.98 (.92 - 1.04)	-.10	.017*	.91 (.84 - .98)	-.04	.137	.96 (.91 - 1.01)
	Recreational	.10	.235	1.10 (.93 - 1.30)	.01	.889	1.01 (.85 - 1.20)	-.10	.330	.90 (.73 - 1.11)	-.11	.190	.90 (.76 - 1.06)
	Active physical	.08	.500	1.08 (.86 - 1.37)	- .14	.286	.87 (.68 - 1.12)	-.16	.316	.86 (.63 - 1.16)	.10	.404	1.10 (.88 - 1.39)
	Social	- .01	.914	.99 (.82 - 1.19)	- .04	.687	.96 (.80 - 1.16)	-.34	.013*	.71 (.54 - .93)	-.07	.455	.93 (.78 - 1.12)
	Skill-based	.07	.583	1.08 (.83 - 1.40)	- .07	.649	.94 (.71 - 1.24)	-.46	.046*	.63 (.40 - .99)	-.23	.096	.80 (.61 - 1.04)
	Self-improvement	- .09	.431	.92 (.74 - 1.14)	- .05	.681	.96 (.77 - 1.19)	-.17	.205	.84 (.65 - 1.10)	-.24	.030*	.79 (.64 - .98)
Environmental Factors	SES	- .19	.327	.82 (.56 - 1.21)	- .10	.628	.91 (.61 - 1.35)	-.52	.026*	.60 (.38 - .94)	-.31	.112	.73 (.50 - 1.08)
	Pre-injury family functioning ^{E}	1.30	.006*	3.661 (1.44 - 9.29)	.57	.229	1.76 (.70 - 4.44)	.84	.133	2.31 (.78 - 6.90)	1.98	<.000*	7.23 (2.72 - 19.22)
Personal Factors	Child sex	.14	.691	1.15 (.58 - 2.26)	- .41	.242	.66 (.34 - 1.32)	-.19	.653	.83 (.37 - 1.87)	.25	.460	1.28 (.66 - 2.48)
	Child age at injury	- .01	.874	.99 (.86 - 1.14)	- .01	.889	.99 (.85 - 1.15)	.13	.148	1.14 (.96 - 1.36)	.12	.099*	1.13 (.98 - 1.30)
	Pre-injury Behavioral functioning ^{F}	.08	<.000*	1.08 (1.04 - 1.13)	.05	.008*	1.05 (1.01 - 1.08)	.02	.280	1.02 (.98 - 1.06)	.06	.003*	1.06 (1.02 - 1.10)

CASP: Child and Adolescent Scale of Participation, measured at T1

GCS = Glasgow Coma Scale score, PTA= Posttraumatic amnesia, LOC = Loss of Consciousness, SES = Caregiver's Socioeconomic State.

^{A}, Measured with the PedsQL-Fatigue; ^{B}, Post-concussive symptoms measured with the HBI; ^{C}, Posttraumatic Stress Symptoms measured with the IES; ^{D}, measured with the CAPE; ^{E}, measured with the FAD-GF; ^{F}, measured with the CBCL

* Factor entered into multivariate binomial logistic regression analyses

** For cause of injury, β and Odds (95% CI) could not be calculated

Table 4. Multivariate binomial logistic regression analyses (N=231) – Perspective of Caregiver

		CASP Setting											
		Home			Community			School			Environment		
ICF-CY Category	**Characteristics**	**β**	***p***	**Odds (95% CI)**	**β**	***p***	**Odds (95% CI)**	**β**	***p***	**Odds (95% CI)**	**β**	***p***	**Odds (95% CI)**
Health condition	GCS:												
	PTA duration:												
	LOC duration:												
	Cause of injury:												
Function	Fatigue ^{A}	N.I.	.096	N.I.	N.I.	.551	N.I.	N.I.	.541	N.I.	N.I.	.223	N.I.
	PCS ^{B}	N.I.	.291	N.I.	N.I.	.638	N.I.	N.I.	.645	N.I.	N.I.	.074	N.I.
	PTSS ^{C}	N.I.	.370	N.I.	N.I.	.499	N,I	N.I.	.640	N.I.	N.I.	.605	N.I.
Activities ^{D}	Total				N.I.	.227	N.I.	- .08	.045*	.92 (.85 - 1.00)			
	Recreational				- .26	.006*	.77 (.64 - .93)						
	Active physical				N.I.	.073	N.I.						
	Social												
	Skill-based												
	Self-improvement							N.I.	.600	N.I.	N.I.	.126	N.I.
Environmental Factors	SES	N.I.	.247	N.I.									
	Pre-injury family functioning ^{E}	N.I.	.554	N.I.									
Personal Factors	Child sex												
	Child age at injury												
	Pre-injury Behavioral functioning ^{F}	.08	<.000*	1.08 (1.04 – 1.12)	.06	<.000*	1.07 (1.03 - 1.10)	.08	<.000*	1.08 (1.05 - 1.12)	.08	<.000*	1.08 (1.05 – 1.11)

CASP = Child and Adolescent Scale of Participation, measured at T1, GCS = Glasgow Coma Scale score, PTA= Posttraumatic amnesia, LOC = Loss of Consciousness, SES = Caregiver's Socioeconomic State.

^{A}, Measured with the PedsQL-Fatigue; ^{B}, Post-concussive symptoms measured with the HBI; ^{C}, Posttraumatic Stress Symptoms measured with the IES; ^{D}, measured with the CAPE; ^{E}, measured with the FAD-GF; ^{F}, measured with the CBCL

* Significant in the final model (p<.05)

N.I. = Factor not included in the final model

NB: No β and Odds (95% CI) could be calculated for the factors that were not included in the final model (p>.05)

Table 5. Multivariate binomial logistic regression analyses (*N*=156) – Perspective of Child

		CASP Setting											
		Home			Community			School			Environment		
ICF-CY Category	**Characteristics**	**β**	***p***	**Odds (95% CI)**	**β**	***p***	**Odds (95% CI)**	**β**	***p***	**Odds (95% CI)**	**β**	***p***	**Odds (95% CI)**
Health condition	GCS:												
	PTA duration:												
	LOC duration:							N.I.	.278	N.I.			
	Cause of injury:												
Function	Fatigue [A]	N.I.	.656	N.I.	N.I.	.962	N.I.				N.I.	.775	N.I.
	PCS [B]	N.I.	.428	N.I.	N.I.	.953	N.I.	.02	.016*	1.02 (1.00 – 1.04)	.02	.028*	1.02 (1.00 - 1.03)
	PTSS [C]	.03	.017*	1.03 (1.01 - 1.06)	.03	.032*	1.03 (1.00 - 1.06)						
Activities [D]	Total							N.I.	.594	N.I.			
	Recreational												
	Active physical												
	Social							N.I.	.052	N.I.			
	Skill-based							N.I.	.401	N.I.			
	Self-improvement										N.I.	.053	N.I.
Environmental Factors	SES							-.51	.038*	.60 (.37 - .97)			
	Pre-injury family functioning [E]	N.I.	.241	N.I.							1.83	.001*	6.25 (2.24 - 17.45)
Personal Factors	Child sex												
	Child age at injury										N.I.	.197	N.I.
	Pre-injury Behavioral functioning [F]	.07	.001*	1.07 (1.03 - 1.12)	.04	.038*	1.04 (1.00 - 1.08)				N.I.	.467	N.I.

CASP = Child and Adolescent Scale of Participation, measured at T1, GCS = Glasgow Coma Scale score, PTA= Posttraumatic amnesia, LOC = Loss of Consciousness, SES = Caregiver's Socioeconomic State.

[A], Measured with the PedsQL-Fatigue; [B], Post-concussive symptoms measured with the HBI; [C], Posttraumatic Stress Symptoms measured with the IES; [D], measured with the CAPE; [E], measured with the FAD-GF; [F], measured with the CBCL

* Significant in the final model ($p<.05$)

N.I. = Factor not included in the final model

NB: No β and Odds (95% CI) could be calculated for the factors that were not included in the final model ($p>.05$)

Table 6. Final model test results of the multivariate binomial logistic regression analyses

	Caregivers' perspective		Children's perspective	
CASP setting	Nagelkerke R^2	Hosmer-Lemeshow*	Nagelkerke R^2	Hosmer-Lemeshow*
Home	.147	.311	.203	.657
Community	.138	.797	.105	.219
School	.190	.044	.166	.550
Environment	.150	.711	.221	.115

CASP = Child and Adolescent Scale of Participation, measured at T1
* Hosmer-Lemeshow *p*-values

Discussion

The results of this prospective cohort study show that predictors for children who are at risk of long-term consequences on activities and participation differ per setting and per chosen perspective. Child function factors (pre-injury and post-injury), personal factors, and environmental factors play a role in predicting consequences on activities and participation.

The present study adds to the literature that injury-related factors do not play an important role in predicting long-term functioning on activities and participation in children with MTBI. This is in accordance with previous mixed sample studies[11,13,16-17] for the predictive value of cause of injury, and in contrast to the same and more previous studies[11-13,16-17] for the predictive value of GCS on the level of activities and participation in samples of children with mixed TBI-severity. A previous study on long-term functional outcomes post-TBI in adults found that GCS was significantly related to mobility, but not to cognitive and physical independence or occupation and social integration.[40] Since mobility is more often affected in patients with lower GCS scores, possibly, the predictive value of GCS is more prominent in the more severe TBI's in comparison to MTBI. Furthermore, the results of our study add to the literature that psychosocial (personal and environmental) factors are predominant for the prediction of unfavorable outcome after pediatric MTBI. These findings are in agreement with findings in adult in MTBI, in which predictors were also found in psychosocial categories, and not injury-related.[41-42]

More specifically, based on our findings, pre-injury behavioral functioning of the child should be taken into account when considering children at risk of unfavorable long term outcome on activities and participation.

This finding is in accordance with the results of previous studies in children with mixed TBI-severity[14], and comparable to the predictive value of pre-injury mental health (e.g. physical, emotional and social-behavioral functioning) on outcome in studies after adult MTBI.[42]

Furthermore, we found that factors within the categories activities, function, and the environment should be taken into account as well. Children are expected to be more at risk of decreased functioning on activities and participation when they experience more symptoms such as PTSS and PCS, grow up in a family with low parental SES and have a less healthy pre-injury family functioning, and participate in less activities. These findings are highly in accordance with results of previous pediatric mixed TBI-sample studies, in which it was indicated that levels of PTSS and PCS are important predictors for activities and participation[11], A previous study emphasized that psychological resilience plays an important role in recovery from concussion in adolescents, and this relationship may be negatively influenced by anxiety and depressive symptoms[24]. Therefore, emotional distress and maladaptive coping may be considered both as important predictors for outcome on activities and participation, as well as important components of interventions aimed at preventing long-term problems after pediatric MTBI, which is also previously proposed in an adult study on outcome after MTBI.[42]

Furthermore, SES[11,13,16], and family functioning[11-13] were found to be predictors for activities and participation in earlier mixed sample studies, also in accordance with our current findings. In a study on extra-curricular physical activity in Italian adolescents, a positive relationship between participation in these activities and their families high SES was found.[43] Family relationship quality was found to indirectly affect activity involvement in a study on predicting organized activity involvement in adolescents.[44] These studies also emphasized the importance of the interplay between family- and individual factors in predicting activity involvement during high-school, regardless of the presence of an injury.[43-44]

Factors within the category activities were not previously studied on their predictive value for activities and participation. In a previous study in which the relation between children's self-efficacy and physical activity performance after MTBI were explored, it appeared that children lack confidence in their abilities to perform such activities as compared to before the injury.[45] The results of our study show that participating in less activities in comparison to healthy peers increases the risk for decreased activities and participation in several settings. Our finding supports the idea that resilience, individualized advice and information on returning to activities is a warranted element for early interventions after MTBI.[45-46] Furthermore, social support from caregivers, but also from peers may help children to regain their confidence in returning to activities.[47]

Fatigue was not previously investigated as a predictor for activities and participation either, despite its common occurrence in children after TBI and often an obstruction for daily functioning. In this study, we did not find that fatigue adds to the prediction of outcome on activities and participation when combined with other predictive factors (such as pre-injury behavioral functioning) in one model. Possibly, children after MTBI suffer less from fatigue in comparison to children with more severe types of TBI, making its predictive value less prominent. From a methodological view, however, another explanation could be that fatigue in this study was investigated as one overall concept. In an adult study, it was found that mental fatigue could last for several years after MTBI, profoundly affecting work capacity as well as social activities.[48] Therefore, in future pediatric MTBI studies focusing on prediction of activities and participation, fatigue may be measured on more specific domains, such as physical fatigue, problems regarding sleep/rest, and mental or cognitive fatigue in order to obtain a more complete view of the possible predictive value.

This study has several strengths. First, this study had a large population of children with MTBI only, and assessed both children of all school ages (6-18) as well as their caregivers. Second, this study examined multiple injury-related, functional and psychosocial factors based largely on the relevant ICF-CY categories in one model on their predictive value for activities and participation in various settings and from different perspectives. This provides us with a more complete overview of predictors for children who are at risk of long-term problems on activities and participation after pediatric MTBI. Furthermore, this study used face-to-face assessments, preventing bias caused by missing values.

This study also had some limitations. First, admission to hospital emergency departments was part of the inclusion criteria. As a consequence, the study sample may not be representative of the larger MTBI population as this excludes those who do not receive acute medical care. Second, concerning external validity, a relatively large number of children who were eligible for participation in the study could not be reached. From the number of reached eligible participants, however, almost 80% chose to participate.

In conclusion, this study showed that not injury-related factors, but pre-injury factors (pre-injury behavioral and family functioning, parental SES), more symptoms two weeks post-injury (PTSS, PCS) and less resumption of activities predict decreased activities and participation after pediatric MTBI. This knowledge can be used to select those children who are at risk and may benefit from interventions at an early stage after injury. Although the results of our study are very useful for this purpose, our final model only declared a small proportion of the variance in outcome on activities and participation after MTBI. There are more factors which may further add to the prediction and could be investigated in future studies. For example resilience[24] and motivation for returning to activities and participation[45-46], coping styles of children and caregivers[42], the child's self-efficacy and emotion-regulation[41], the child's and caregivers personality traits[41], the level of social support from caregivers and peers[47], and other comorbid problems, such as chronic pain, substance abuse, life stress and protracted litigation.[49]

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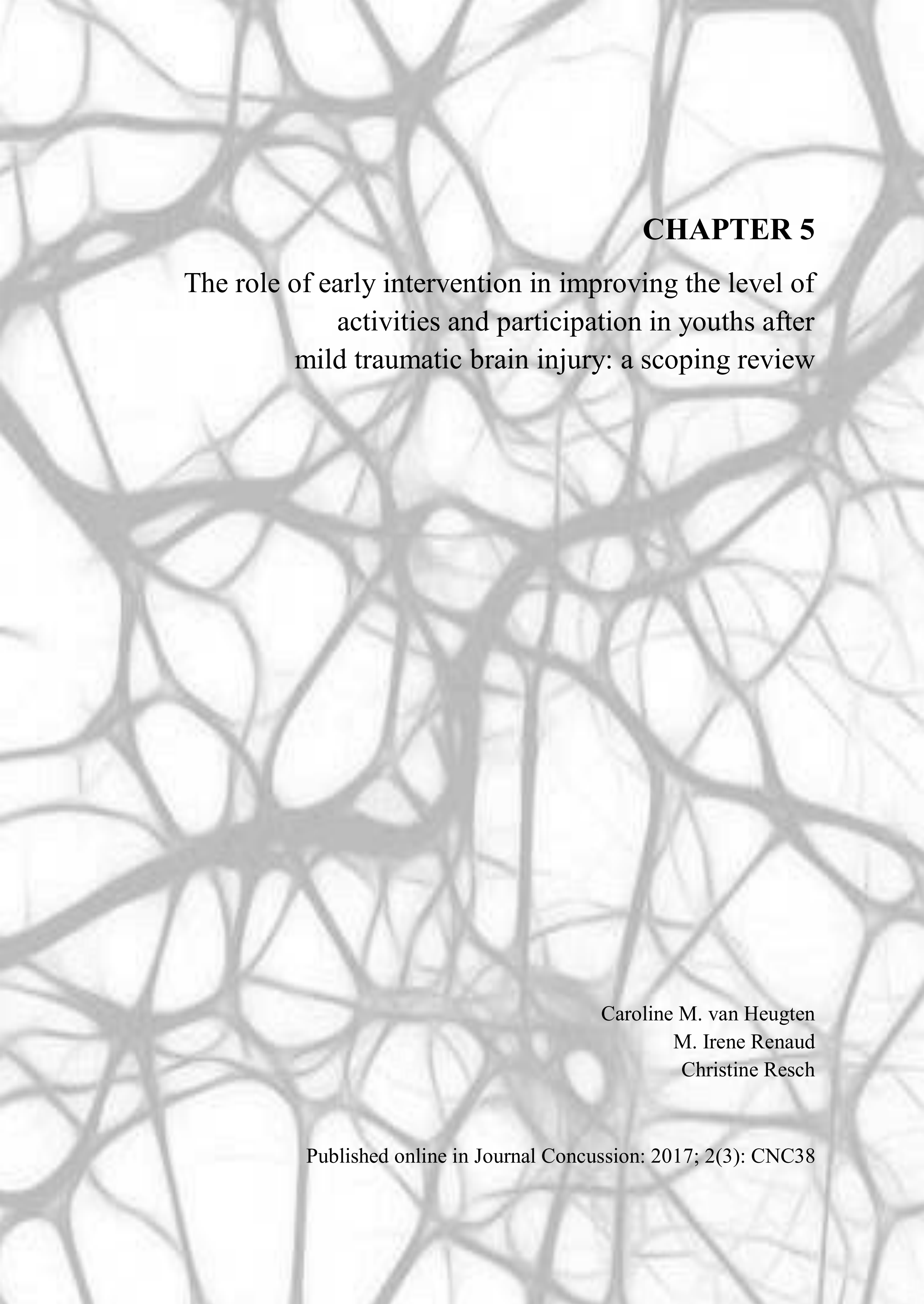

CHAPTER 5

The role of early intervention in improving the level of activities and participation in youths after mild traumatic brain injury: a scoping review

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Published online in Journal Concussion: 2017; 2(3): CNC38

Abstract

Mild traumatic brain injury (MTBI) in children can lead to persistent cognitive and physical symptoms which can have a negative impact on activities and participation in school and at play. Preventive treatment strategies are preferred because these symptoms are often not recognized and therefore not treated adequately. In this review clinical studies investigating interventions directed at pediatric MTBI are summarized, and clinical recommendations and directions for the future are provided. Results show that the literature is scarce and more high quality studies are needed. Information and education about the injury and its consequences are recommended, with additional follow-up consultation, including individualized advice and reassurance. The interventions should be family-centered and, ideally, the return to activity and participation should be graded and done step-by-step.

Introduction

Accidents can happen. Children and adolescents are often involved in accidents leading to traumatic brain injuries (TBI). The incidence of traumatic brain injury (TBI) in children between 0 and 18 years is 280-1,373 per 100,000, but there is a large variation between studies and countries; most of these injuries are mild (MTBI).[1-8] Most children recover completely after an MTBI, but 6 to 43% of children experience post-concussive symptoms (PCS) up to 6 months after the injury and beyond.[9-12] Persistent symptoms are found in the areas of physical, cognitive, emotional and behavioral functioning.[13-16] These consequences can lead to limitations in activities and participation such as returning to school and play.[17-20] Pediatric MTBI can also affect health-related quality of life (HRQOL).[21] Children with PCS had significantly lower HRQOL scores at 4, 8 and 12 weeks post-injury than children without PCS and normal controls. Children without PCS had lower HRQOL scores than the norms at 4 and 8 weeks post-injury. School functioning scores were lower at all time points, regardless of the presence of PCS.

In general, children suffering the more severe forms of TBI (i.e., moderate and severe) are followed and receive rehabilitation treatment, but children with MTBI do not.[22] Both for professionals and for parents, the cognitive, emotional and behavioral problems are difficult to recognize and are therefore underestimated, underdiagnosed and not treated adequately.[23] Delayed recognition may, however, lead to unnecessary chronic and disruptive problems in activities and participation.[13,24-25]

Several intervention strategies can be considered. First, all children and their parents can be given information and education on the possible consequences of an MTBI in order to prevent long-term problems. Second, children at risk of long-term problems can be identified at an early stage and information and education can be directed specifically towards this group. Early recognition and interventions are essential for children at risk of long-term problems.[26-27] It is, however, difficult to identify those at risk because the prognostic factors are not yet fully known. Third, information provision can be combined with routine follow-up aimed at detecting possible consequences. If disabling consequences are found, referral for treatment can be arranged. Finally, patients or parents who report consequences themselves, for instance to their general practitioner, can be referred for treatment. However, often this does not occur as these consequences are not recognized, either by the patients and parents themselves or by professionals. Accordingly, strategies for preventing long-term problems have been suggested to be the best treatment option.[28-29]

In this paper we will review the available literature on early interventions for improving the level of activities and participation in children and adolescents with MTBI. On the basis of this overview we will formulate recommendations for clinical practice and suggest directions for future research.

Review of the literature

We did not perform a systematic review with a predefined search strategy because of the limited resources on this topic. Instead we performed a scoping review which uses a more broad research question: inclusion and exclusion criteria can be developed post hoc, study quality is not a priority, the review may or may not involve data extraction and offers a more qualitative than quantitative synthesis of evidence.[30] However, we did make some decisions concerning the inclusion of studies and we did extract data. To begin, we used the definition of MTBI as defined by the American Congress of Rehabilitation Medicine, that is: 'a Glasgow Coma Scale (GSC) score of 13-15 and at least one of the following: (1) loss of consciousness of no more than 30 minutes, (2), Post Traumatic Amnesia (PTA) no longer than 24 hours, (3) any alteration in mental state at the time of the injury, (4) focal neurological deficit(s) that may or may not be transient'. We searched studies using the terms 'mild brain injury', 'mild traumatic brain injury', 'mild head injury' and 'concussion' in combination with 'children'/'childhood', 'youth', 'adolescents'/'adolescence', 'pediatric'/'paediatric' and 'interventions', 'activities' and participation'.

We selected clinical studies in which an intervention for children with MTBI was evaluated in the domains of activities and participation according to the framework of the International Classification of Functioning (ICF, World Health Organization). Activities can be activities of daily life such as self-care, school, sports, hobby and play. Participation refers to the involvement of the children in life situations such as in domestic, community, social and civic life. We also considered family functioning or parent-child interaction as outcome domains. We did not include studies measuring outcome solely in terms of functioning such as motor functioning or cognitive functioning. We also did not include studies on interventions aiming at biochemical and neurochemical changes such as oxidative stress, inflammation and the neurometabolic cascade because these are mostly experimental and involve animal models, and outcome is measured mostly on the level of physiological and neurological functioning. Since pharmacological interventions are not primarily directed at improving the level of activities and participation, we excluded medication studies as well. If, however, medication was part of a more comprehensive program we did include the study.

Second, since the literature is still rather scarce in this area, we also considered studies in which children with MTBI were part of larger studies on moderate and severe pediatric TBI. Furthermore, studies that did not measure the level of activities and participation, but nevertheless investigated interventions for children with MTBI that might also be suitable for preventing problems with or improving the level of activities and participation, were included. Last, we discuss some potentially effective interventions from the literature on adult brain injury.

In addition to research papers, we considered reviews on interventions for children with (M)TBI[30-37] and searched for relevant references in these reviews. We extracted only studies in which interventions were evaluated. Papers describing treatment programs without an outcome evaluation were not considered; if these papers contained relevant recommendations for future research or clinical practice these are taken into account in our discussion section. If the review considered adults and children, we selected only the studies investigating children. If multiple papers were published about the same study, these are discussed separately only when they concern a different sample.

Summary of the evidence on (early) interventions in pediatric (M)TBI

The following paragraphs describe the various identified types of intervention (e.g., information and education, online family problem-solving interventions, cognitive and physical rest), separating interventions that are primarily aimed at all children with (M)TBI from interventions that target specific complaints in a subgroup of children who experience negative symptoms and/or are at risk of experiencing them in the future.

Table 1 provides an overview of studies investigating the effectiveness of interventions for activities and participation of children with MTBI. It also shows studies where children with MTBI were part of a larger group of children with moderate and/or severe TBI. Table 1 is the main table in which conclusions are drawn. The online appendix displays studies of interventions for children with MTBI that are not directed at activities and participation, but nevertheless might be suitable for achieving improvement in these domains. These studies and studies on adults with mild forms of brain injury are described in the text only as 'additional information'.

It has to be noted that the definitions of TBI severity (i.e., mild, complicated mild, moderate or severe) were not consistent over the studies. Furthermore, the terms 'mild brain injury', 'mild traumatic brain injury', 'mild head injury' and 'concussion' may be used interchangeably.[38-39] The general clinical medical literature now uses MTBI.[40] The definitions used by the studies in this review vary.

Table 1. Overview of studies into interventions for improving the level of activities and participation for children with (M)TBI

Study and participants		**Intervention**		**Outcomes**
Authors, year, country	Study design, participants (*n*, injury, age)	Type	Start, duration and frequency	Measurement time points, measures and results[12]
Casey et al. [58], 1987, USA	Prospective, randomized controlled trial *n*=321 (intervention *n*=153, control *n*=168) **Injury:** MTBI **Age:** 6m-14y	**Information and education / follow-up consultancy** Content: discharge interview, take-home booklet, follow-up telephone call Control intervention: care as usual	Start: Directly at discharge Duration/frequency: Interview and phone-call once, consult booklet when needed	Time points: 1 m post-injury (by telephone, *n*=204) Physical (e.g., general health, resistance) - no effect **Social limitations in daily activities: Role activity index** - no effect Behavior (e.g., behavioral screening, mental health survey) - no effect
Ponsford et al. [41], 2001, Australia	Non-randomized, controlled study *n*=119 (intervention *n*=61, control *n*=58) **Injury:** MTBI **Age:** 6-15 years	**Information and education** Content: neuropsychological assessment, symptom booklet, coping strategies Control intervention: care as usual	Start: Within 1 week post-injury Duration/frequency: One-time early face-to-face assessment. Information booklet could be consulted whenever needed.	Time points: 3 m post-injury Post-concussion symptoms (PCSC) + Less overall symptoms, less headaches, less irritability, better judgement. Irritability, inattentiveness and conduct (Rowe BRI) + Fewer behavioral problems. - No effects on restlessness and sleep. Behavior (CBCL) + Less problems with somatic symptoms, anxiety, social, thought, attention, delinquency, aggression, total problems and internalizing. - No effects on externalizing problems. **Behavior in daily activities (VABS)** - No effect of the intervention Neuropsychological measures - No intervention effects
Narad et al. [50], 2015; Wade et al. [52, 54], 2015/2014, USA	Randomized controlled trial *n*=132 (intervention *n*=65, control *n*=67) **Injury:** Complicated mild/moderate TBI (*n*=40 in CAPS, *n*=41 in IRC) and severe TBI. All participants had been hospitalized overnight. **Age:** 12-17 years	**Online family problem-solving training** Content: CAPS Control intervention: IRC	Start: 1-7 m after hospitalization for TBI (M=3.54) Duration/frequency: CAPS: 6 m, 7-11 sessions IRC: ≥1h per week	Time points: Baseline, 6 m, 12 m, 18 m **Parent-reported and teen-reported conflicts (PSDRS)** + Decreased conflicts in the CAPS group at 6 m for adolescents with complicated mild/moderate TBI, but not after 6 m **Effective communication/observed parent-teen interactions (IFIRS)** - No change over time for adolescents with complicated mild/moderate TBI in the CAPS group. **Parent-rated problem-solving (FAD)** + Improved at 6 m, independent of group or TBI severity. **Child and adolescent functioning (CAFAS)** + Everyday functioning in school and the community improved

				more over time (18 m) for the CAPS group than for the IRC group. - The CAPS had no effects on home functioning, behavior, mood or thinking. Externalizing and internalizing adolescent behavior (CBCL) + Older adolescents in the CAPS group had less externalizing problems than adolescents in the IRC group. No group differences in effects on internalizing behaviors.
Wade et al. [57], 2005, USA	Quasi-experimental pre-test/post-test design *n*=6 **Injury:** Complicated mild/moderate (*n*=2) and severe (*n*=4) TBI **Age**: 5 to 16 years	**Online family problem-solving training** Content: Online FPS	Start: >15 m post-injury (M=18.67m, SD=4.93) Duration/frequency: 8 core sessions and 4 supplementary sessions.	Time points: Baseline, post-intervention Child social competence and anti-social behavior problems (HCSBS) + Reduced parent-reported antisocial behaviors. - No effects on social competence. **Parent-child conflict (IBQ-C/P, PARQ).** + Reduced adolescent-reported conflicts about school - No effects on global conflict ratings and parent-reported school conflict **Family functioning (FAD)** - No effects. Executive function skills behavior (BRIEF-GEC). - No effects.
Wade et al. [53], 2006, USA	Randomized controlled trial *n*=32 (intervention *n*=16, control *n*=16) **Injury:** Complicated mild/moderate (67.6%) and severe (32.4%) TBI. **Age:** 5-16 years	**Family problem-solving training** Content: FPS *Note.* Participants in the FPS group additionally received care as usual. (n=16) Control intervention: care as usual = standard medical care. (n=16)	Start: Until 18 m after injury (M=8.78, SD=4.53) Duration/frequency: 7 core-sessions, 4 supplementary sessions (M=8.31 sessions completed, range 3-11)	Time points: baseline, post-intervention Child adjustment (CBCL) + Reduced behavioral problems at post-test for FPS group. Parental psychological distress (BSI) - No effects **Parent-child interaction (CBQ)** - No effects + In addition, parents of the FPS group reported improvements in knowledge of problem-solving strategies and understanding their child better.
Wade et al. [51], 2006, USA	Randomized controlled trial *n*=39 (intervention *n*=19, control *n*=20) **Injury:** Complicated mild/moderate (65% in IRC and 75% in FPS group) and severe TBI. **Age:** 5 to 16 years	**Online family problem-solving training** Content: Adapted online FPS Control intervention: IRC	Start: Between 1 and 24 m after injury (M=13.73, SD=3.16) Duration/frequency: 14 self-guided sessions: 8 core session and 6 supplementary sessions	Time points: baseline, post-intervention **Family functioning (FAD problem-solving and communication subscales)** - No effects Child adjustment (CBCL) - No effects Social competence and antisocial behavior (HCSBS) + Improvement in self-management for the FPS group - No improvement on total score or peer relations
Wade et al. [56], 2008 USA	Quasi-experimental pre-test/post-test design *n*=9	**Online family problem-solving training** TOPS	Start: 24 m after injury Duration/frequency: 10 self-guided core sessions	Time points: baseline, post-intervention Child behavior problems (CBCL) + Less internalizing symptoms.

	Injury: Complicated mild, moderate and severe TBI **Age:** 11-18 years	Two conditions were compared: TOPS-audio (*n*=5), where families could have the text on the web-site read out loud to them, and TOPS-no-audio (*n*=4).	and up to 4 out of 6 additional sessions.	- No effects on externalizing symptoms or total score. Daily executive functioning (BRIEF) - No effects Depression (CDI) + Lower levels of depression post-intervention. Parental distress (SCL-90-R) + Decline in parental depressive symptoms. **Parent-adolescent communication and conflict behavior (CBQ, Issues Checklist, Issues Severity Scales)** + Reduced parent-reported conflicts. - No change in intensity of conflicts.
Wade et al. [55], 2011, USA	Randomized controlled trial *n*=41 **Injury:** Complicated mild/ moderate and severe TBI (GCS M=9.58, SD=4.56) **Age:** 11-18 years	**Online family problem-solving training** TOPS (see Wade et al., 2008) (*n*=20) Control intervention: IRC (*n*=21)	Start: 8-10 m post-injury Duration/frequency: See Wade et al., 2008)	Time points: baseline, 8 m Child behavior problems (CBCL, YSR) + Participants with severe TBI in the TOPS group showed improved parent-reported internalizing symptoms. - No effects for complicated mild/moderate TBI. **Parent-adolescent communication and conflict behavior (IBQ-C/P)** + Decreased parent-reported conflict in TOPS group. - No effect on adolescent reported parent-teen conflict after TOPS
Thomas et al. [42], 2015, USA	Randomized controlled trial *n*=88 (intervention *n*=45, control *n*=43) **Injury:** MTBI **Age:** 11-22 years	**Cognitive and physical rest** Intervention group: 5-day rest, then step-by-step return to activity Control group: 1-2 day rest, then return to school and step-by-step return to physical activity	Start: Within 24 hours of MTBI Duration: 1-5 days	Time points: Day 0, day 1-3, day 3, day 4-10 and day 10 Balance (BESS) - No group differences Neurocognition (ImPACT, Ancillary Neuropsychiatric) - No group differences Post-concussive symptoms (PCSS) + More post-concussive symptoms during follow-up period in intervention group. **Physical and mental activity** + The strict rest group reported less school and mental activity than controls. No group differences in physical activities.

[1] Outcomes printed in **bold** are measures of activities and participation as categorized by the authors of the present review.

[2] '+' indicates a significant intervention effect. '-' indicates no significant effect.

Abbreviations: h = hour(s), m = month(s), y= year(s), d=day(s), wk= week(s), M = mean, SD = standard deviation, Md = median, IQR = Inter-quartile range

Abbreviations interventions: CAPS = Counsellor Assisted Problem Solving, FPS = Family Problem-Solving, IRC = Internet Resource Comparison, TOPS = Teen Online Problem Solving

Abbreviations neuropsychological measures: BESS = Balance Error Scoring System, BRIEF = Behavioural Rating Inventory of Executive functioning (GEC = General Executive Compound, MI = Metacognition Index), BSI = Brief Symptom Inventory, CAFAS = Child and Adolescent Functional Assessment Scale, CBCL = Child Behaviour Checklist, CBQ = Conflict Behaviour Questionnaire, CDI = Children's Depression Inventory, FAD = Family Assessment Device, HBI = Health Behaviour Inventory, HCSBS = Home and Community Social Behaviour Scale (HCSCBS-AB = Antisocial Behaviour, HCSBS-SC = Social Competence), IBQ = Interaction Behaviour Questionnaire (IBQ-C = Child-report, IBQ-P = Parent-report), IFIRS = Iowa Family Interaction Rating Scale, ImPACT = Immediate Post-Concussion Assessment and Cognitive Testing, PARQ = Parent-Adolescent Relationship Questionnaire, PCSC = Post Concussion Symptoms Checklist, PCSS = Post Concussion Symptoms Scale, PSDRS = Problem-Solving Discussion Rating Scale, Rowe BRI = Rowe Behavioral Inventory, SCL-90-R = Symptom Checklist-90 – Revised, VABS = Vineland Adaptive Behaviour Scales, YSR = Youth Self-Report, ESS = Balance Error Scoring System.

One study used the definition of the American Congress of Rehabilitation Medicine.[41] One study[42] made use of the Acute Concussion Evaluation form.[43] In two studies[44-45] the International Consensus on Concussion in Sport[46-47] was used. Other studies defined MTBI based on Glasgow Coma Scale scores (i.e., >12) and/or duration of loss of consciousness, duration of post-traumatic amnesia and presence/absence of focal neurological deficits.[48-57] For three studies[58-60], the definition of MTBI was described as, i.e., ‘minor head injury’, or ‘diagnosed by a sports or rehabilitation medicine specialist’. Complicated MTBI was defined as a GCS score of greater than 12 with evidence of significant findings on clinical imaging[48,50-57]. Moderate TBI was defined as a GCS score of 9 to 12[50-57]. Some studies combined complicated MTBI and moderate TBI and defined this group as moderate.[50-57] Severe TBI was defined as a GCS score of less than 9.[50-57]

Information and education

Information about MTBI and education on signs and symptoms can be provided with the intention of improving the outcome of patients or their caregivers or both. Casey et al.[58] were the first to study the effectiveness of an information and education protocol after childhood MTBI in reducing physical, social and/or behavioral problems post-injury. Their intervention, consisting of a discharge interview during which the nurse explained a take-home booklet of symptoms that could be expected, instructions to follow at discharge, and a follow-up telephone call 24h after discharge, was found to be no more effective than the routine discharge sheet (i.e., a list of symptoms requiring reassessment at the hospital). However, in general, reporting of symptoms one month post-injury was low. A closer look at the data seemed to indicate that most symptoms at the one-month follow-up occurred in children who had anxious parents, although this finding did not reach significance. Based on these findings, Casey et al.[58] emphasize the importance of reassurance and education for parents about the signs and symptoms of minor head trauma (i.e., emphasizing that the symptoms are common and that they can be dealt with). This might aid children in returning to their daily activities and routines. Ponsford et al.[41] developed just such an early education and reassurance intervention for children post MTBI. This study was the first to provide evidence that children who received a booklet describing symptoms and coping strategies within one week post-injury reported fewer post-concussive symptoms at 3 months post-injury, in comparison with those that did not receive this information. The intervention, however, had no direct effect on behavior in daily activities. However, the amount of difficulties that the study sample experienced in daily behavior before the interventions was already low. This low rate of symptoms might explain the lack of effect of the intervention in improving the functioning of children with MTBI.

Taken together, these studies seem to indicate that information and education interventions are useful in decreasing post-concussive symptoms in children with MTBI. These types of interventions could also be used to improve the level activities and participation of children with MTBI who report a decrease in or are at risk for problems in activities and participation (e.g., by preventing unnecessary absenteeism from school), but more research is necessary.

Problem-solving interventions for families

Four different but very similar interventions, two offline and two online, were identified in the literature for improving family and adolescent problem-solving skills following childhood TBI. The Counsellor Assisted Problem Solving (CAPS) intervention, the Family Problem-Solving (FPS) intervention, the online FPS intervention, and the Teen Online Problem Solving (TOPS) intervention all provide therapist-guided problem-solving training to adolescents with TBI and their families. In six to eight core sessions and, depending on the families' needs, up to four additional sessions, self-guided online learning of problem-solving skills, communication, self-management and self-regulation, as well as video-counseling with a therapist are offered. The (non-online) FPS intervention differs slightly, since the therapist and the families met at the families' homes or at the clinic for the therapy sessions, instead of participating in video-counseling. In most of the studies in the CAPS, (online) FPS or TOPS intervention, Internet Resource Comparison (IRC) was used as a control intervention. Participants in the control group, if present, were provided with access to a website with links to other websites about childhood brain injury and various brain-injury associations.

The different (online) family problem-solving interventions were investigated in six different studies, resulting in eight published articles. More specifically, one study investigated the CAPS,[50,52,54] two studies examined the TOPS,[55-56] one study investigated the non-online FPS,[53] one study looked into an online version of the FPS,[57] and one examined an adapted version of the FPS.[51] The design method of all of these studies varied (i.e., randomized controlled trials and quasi-experimental pre-test/post-test experiments), and outcome measures varied as well (e.g., parent-child conflict is measured in three of the six studies, with two different measures). This makes it difficult to compare the interventions. Overall, the (online) family problem-solving interventions seem to have potential to improve child and family functioning, and therefore the level of activities and participation, of children with (M)TBI. More specifically, the CAPS intervention decreased parent- and teen-reported family conflict and improved everyday functioning in school and in the community of adolescents with complicated mild/moderate TBI.

Communication and parent-teen interactions as well as home functioning, behavior, mood or thinking did not change with CAPS.[50,52,54] The TOPS intervention led to reduced parent-adolescent communication and conflict behavior and decreased parent-reported, but not adolescent-reported, conflict.[55-56] The online FPS intervention seems to be the least effective in improving the level of activities and participation of children with (M)TBI: no effects on parent-child interaction, global-parent-child conflict or family functioning were found,[53] although improvement was shown for adolescent-reported conflicts regarding school.[57]

Several factors influencing effectiveness were identified in the studies investigating the CAPS, the (online) FPS and the TOPS interventions. For one, more improvement in child and adolescent functioning as well as in teen-reported family problem-solving skills and parent- and adolescent-reported child behavior after the (CAPS or adapted online FPS) intervention is related to lower parental education.[50-52] This seems to indicate that especially children with MTBI and lower-educated parents can benefit from a problem-solving intervention. Second, in contrast to younger adolescents, older adolescents showed positive behavioral changes and improvements in self-management after the CAPS and online FPS interventions.[50-51,54] Furthermore, the CAPS intervention was especially effective in improving school, work and community functioning, rather than other domains of functioning (e.g., home functioning, behavior, and thinking). Last, parent-reported teen internalizing symptoms improved after the TOPS intervention, but only for participants with severe TBI. Taken together, these results indicate that factors such as parental education, age of the child, domain of functioning to be improved, and severity of the injury can influence intervention effectiveness.

The effectiveness of the CAPS, the (online) FPS and the TOPS interventions was investigated in groups of children with complicated mild, moderate and severe TBI who were not selected based on their complaints and/or being at risk for these complaints. These interventions should therefore be categorized as interventions for the prevention of long-term symptoms. The effectiveness of these interventions in a more selected group of children with TBI remains unknown. Furthermore, since children with complicated MTBI were always analyzed together with children with moderate TBI, it remains unclear what effect these interventions would have on the level of activities and participation and other outcomes in a group solely of children with (complicated) MTBI.

Cognitive and physical rest

Rest during the acute stage of recovery, reduction of physical and cognitive activities, monitoring symptoms in collaboration with their parents, taking rest breaks after returning to school, spending fewer hours at school, being allowed more time to take exams, having help with schoolwork, gradually returning to sports, and reducing time spent with the computer, reading, and writing are among the recommendations for managing symptoms after MTBI in children.[45-47,59,61] Cognitive and physical rest recommendation is often part of the care as usual for children with MTBI and is also described in protocols such as the Return to Learn and the Return to Play protocols.[62] However, in reviewing the literature, we encountered only one study investigating the effects of cognitive and physical rest on the level of activities and participation for children with MTBI.[42] To determine if strict cognitive and physical rest was beneficial with regard to post-injury recovery, patients were divided into two groups: one group was recommended to have 1-2 days of rest, while the other group was advised to have strict rest for 5 days. Both groups were recommended to return to activity step by step after the days of rest. Results showed that strict rest caused children with MTBI to report more post-concussive symptoms. Furthermore, in comparison with children who had only 1-2 days of rest, the more rested children experienced a decrease in the level of activities and participation. This is not surprising, since per definition cognitive and physical rest entails restricted level of activities and participation. The effects of cognitive and physical rest on the level of activities and participation over the long term still have to be determined.

Additional information

Information and education

Kirkwood et al.[48] performed a pilot study investigating a one-time neuropsychological consultation consisting of interviews with parents and children and a standardized battery of tests. Feedback on the results was provided to the families by a neuropsychologist, including general education about concussion, information about injury and non-injury related factors contributing to the child's specific symptoms and recommendations for addressing any concerns. They found that post-concussive symptoms decreased significantly following the consultation. Unlike the two studies reported above, the study by Kirkwood et al.[48] was focused on children with MTBI who were already reporting problems for some time. The finding that the intervention was effective in decreasing post-concussive symptoms in these children is promising, indicating that interventions consisting of information and/or education are suited not only for the prevention of symptoms but also for more specific treatment.

Follow-up consultancies

In a study of Bell et al.[63], follow-up contact by telephone was found to be effective in reducing symptoms after MTBI. This study, however, was performed with children aged 16 years and older and with adults after MTBI and the effect on younger children is unknown (and therefore not in Table 1). Furthermore, the effect on the level of activities and participation was not measured.

Cognitive and physical rest

From the studies we reviewed for the present article, no consensus can be derived regarding the benefits of cognitive and physical rest for children with MTBI. One study supports rest as an effective form of care after MTBI in children. Independent of when a minimum of one week of cognitive and physical rest was described (i.e., 1-7 days, 8-30 days or more than 31 days post-injury), post-concussive symptoms were reduced, and cognitive functioning was improved.[45] Another study found no association between the prescription of cognitive rest and the duration of symptoms.[44]

While these results seem contradictory, methodological differences between the studies have to be taken into account when interpreting the results. While the first study[45], finding benefits of cognitive and physical rest, examined only the presence of post-concussive symptoms at one time point, the other study[44], failing to find an association between rest and post-concussive symptoms, investigated the duration of symptoms over time. Furthermore, while the first study examined a period of cognitive and physical rest of approximately one week, the duration of rest used in the second study is not clear. This should be taken into account, since, as described above, increasing the duration of cognitive and physical rest from 1-2 days to 5 days was found to have negative effects for children with MTBI.[42] The relation between the duration of post-concussive symptoms and the duration of cognitive and physical rest needs further research.

Combined interventions

Some interventions in children with MTBI are comprised of a combination of components. For example, Gagnon et al.[59] used graded guided rehabilitation as their primary intervention. The intervention stops when children are symptom-free. Children who do not remain symptom-free receive a return appointment for re-evaluation, education and a weekly follow-up. This combination continues until the child remains symptom-free. The results of this study suggest that involvement in controlled and closely monitored rehabilitation in the post-acute period may promote recovery in children and adolescents who present with slow recovery after MTBI.

Another combined intervention consisted of education and advice on avoiding analgesic overuse, avoiding any opiate medications, and encouraging light exercise when post-concussive symptoms persisted for three months or longer post-injury.[49] Furthermore, prophylactic medications were selected based on comorbidities by a neurologist with expertise in acquired brain injury and headache disorders. A marked reduction in the frequency of headaches was reported in half of the cases after the intervention, while 45 percent reported complete resolution of headaches.

A combined collaborative care intervention, consisting of care management, CBT, and possible psychopharmacological consultation, was examined by McCarty et al.[60] They found that efforts to systematically implement collaborative care treatment approaches for slow-to-recover adolescents may be useful given the reductions in post-concussive and co-occurring psychological symptoms in addition to improved quality of life.

All of the above-mentioned combined interventions were conducted with children and adolescents who experienced symptoms after MTBI. Although the results are promising, the influence of such interventions on preventing symptoms in the first place was not studied, nor was the influence on activities and participation.

Evidence from literature on mild forms of brain injury in adults

Interventions designed to reduce symptoms after MTBI in adults have been investigated by several researchers. Providing information with educational brochures or sessions about common symptoms after MTBI, including reassurance of recovery, the likely time course of recovery and information on how to cope with symptoms are among the intervention strategies,[64-67] as are neuropsychological assessments and follow-up contact by telephone.

More specifically, for adults with MTBI, Paniak et al.[68] showed that an education-oriented single session and a more extensive assessment, education, and treatment-as-needed intervention showed similar results on symptom-related, functional, and vocational variables 3-4 months after the initial assessment. These results were maintained at the 12-month follow-up, while most improvements in both groups were seen in the first three months.[65] Recently similar results were found in a study where a high risk MTBI group received a doctor's visit in addition to written information, in comparison with a control group receiving only written information.[69] The high risk group was defined as patients having three or more post-concussive symptoms at 10 days post-injury. The groups did not differ in terms of symptoms, anxiety or depression at the 3-month follow-up. Ponsford et al.[66] studied the effectiveness of an extra follow-up moment in which an information booklet on MTBI was given to adults one week after visiting the emergency department.

The information booklet contained information about MTBI, the possible consequences and time course and coping strategies to deal with these consequences. In comparison with a control group receiving no information booklet, the patients in the intervention reported significantly fewer symptoms and were less stressed at the 3-month follow-up. Nygren-de Boussard et al.[70] conducted a systematic review on the evidence of nonsurgical interventions for persistent symptoms after MTBI and also showed the beneficial effects of early, reassuring educational interventions.

Based on the effectiveness of these education interventions, Moulaert et al.[71] developed an early neurologically-focused intervention for patients with hypoxic brain injury due to a cardiac arrest. Cardiac arrest can lead to hypoxic brain injury which can be comparable to the diffuse damage seen in MTBI. The intervention consists of screening for cognitive and emotional problems, provision of information and support, promotion of self-management strategies and referral to further specialized care if indicated. This intervention was found to be feasible in clinical practice[72] and both clinically effective[73] and cost-effective[74] in comparison with care as usual. Patients in the intervention group had a better quality of life, a better overall emotional state and fewer symptoms of anxiety one year post-cardiac arrest. Moreover, more people returned to work three months post-injury.

Nelson, Sheese and Hammeke[75] propose treatment strategies both on the basis of clinical consensus and the limited evidence base. In addition to education about MTBI, possible persistent symptoms and the natural course of recovery, and reassurance of a good outcome, they suggest reducing activity levels and refraining from hazardous behaviors during the acute phase and a gradual return to lifestyle activities as symptoms permit. Professionals should carefully monitor and offer early intervention for adverse emotional responses, offer symptom-specific treatment when needed, and enable ready access to providers during the first weeks of recovery. Al Sayegh, Sandford, and Carson[76] also suggest that information, education and reassurance alone may not be sufficient in reducing post-concussive symptoms. They suggest that cognitive behavioral therapy with psychotherapeutic elements or mindfulness or relaxation techniques may lead to increased improvements. These interventions are directed mainly towards the reduction of post-concussive symptoms and to a lesser extent toward improving the level of activities and participation.

Conclusions from the literature

Most interventions for children with MTBI are designed to reduce symptoms, such as headaches, cognitive problems or other post-concussive symptoms, and are not specifically designed to improve the level of activities and participation. Interventions consisting of information and education seem effective in preventing symptoms when reassurance is combined with information. Reassurance can be optimized by including a follow-up consultation by telephone, during which individual concerns can be addressed. Family problem-solving interventions are effective in improving child and family functioning but have not been investigated for a group of children with only MTBI. There is no consensus on the benefits of cognitive and/or physical rest, but graded activity procedures seem effective in supporting return to school, sports and play. Combined interventions including medication have not been offered as a preventive strategy and the effects of such interventions on the level of activities and participation are unknown.

In addition to studies investigating the effectiveness of interventions for children with MTBI, several protocols and recommendations have been published on returning to activity and returning to school, for which no studies have been made regarding their effectiveness. Protocols on returning to activity can be divided into graded, or step-by-step protocols, and severity-oriented guidelines on how to build levels of activity. The protocols with a graded approach reported the following six steps: (1) no activity, (2) light aerobic exercise, (3) sport-specific exercise, (4) non-contact training drills, (5) full contact practice, and (6) return to play.[77-79] Guidelines that are severity-oriented focus on the severity of symptoms or the numbers of previous concussions. For example, when a child's first concussion is considered to be mild, the guideline would recommend returning to play after being symptom-free for one week. For a concussion that is considered severe, the child should be symptom-free for a month.[80] Furthermore, severity-oriented guidelines focused on injury-related factors such as confusion, loss of consciousness and post-traumatic amnesia.[81-82] A protocol on returning to school was provided by Master et al.[62]. Their step-by-step protocol consisted of the following steps: (1) no activity, (2) gradual reintroduction of cognitive activity, (3) homework at home before schoolwork at school, (4) school re-entry, (5) gradual reintegration into school, and (6) full return to school and cognitive workload. Sady et al.[83] recommend a graduated accommodation-based education plan with similar steps. Furthermore, several other recommendations on returning to school can be found in the literature, such as monitoring and support, removal of distractions, excused or absence from class or activity, and increased time to complete tests and tasks.[84] Unfortunately, most of these protocols focused on sports concussions in school athletes and the effects of these protocols were not examined. Studies on interventions that are set up in order to directly prevent long-term restrictions on participation in activities for children and adolescents after MTBI are, to our knowledge, unknown.

In conclusion, evidence suggests that information and education should always be offered, ideally followed by a consultation in which personalized reassurance is given. The family should be involved and problem-solving interventions seem effective. In addition, clinical recommendations suggest a step-by-step return to cognitive and physical activities, not only restricted to sports.

Future perspective

This review shows that the literature on early interventions to improve the level of activities and participation in is scarce regard to pediatric MTBI. There are not many high quality studies available and the comparability of studies is limited because of variation in population (i.e. separate studies on MTBI), definitions (i.e. the definition of TBI), the aim of the intervention (i.e. prevention or treatment) and outcome domains (i.e. symptoms or activities and participation) and outcome measures. Ideally the first step should be to identify children at risk of long-term problems by conducting longitudinal prospective cohort studies, followed by high quality randomized controlled trials in which targeted interventions are investigated. Given the current economic pressures in health care these evaluation studies should include analyses of both clinical effectiveness and cost effectiveness, and consider potential implementation in clinical practice at an early stage. Research studies investigating preventive strategies are challenging because of recruitment (i.e. can we detect all cases), selection bias (i.e. will all cases participate or only those having complaints or fearing consequences) and follow-up (i.e. will all cases remain in the study).

Currently we are conducting a randomized controlled trial (RCT) in which the early intervention Brains ahead! is being evaluated in terms of effectiveness on participation in activities in comparison with standard care.[85] The Brains ahead! intervention is a combination of screening for MTBI symptoms, psycho-education and follow-up. Outcome is measured three and six months post-injury. The primary outcome measure is the Child and Adolescent Scale of Participation (CASP)[86]; in addition, other measures of activities, participation, quality of life and child behavior are performed. We hope to have recruited 140 children by the end of 2017.

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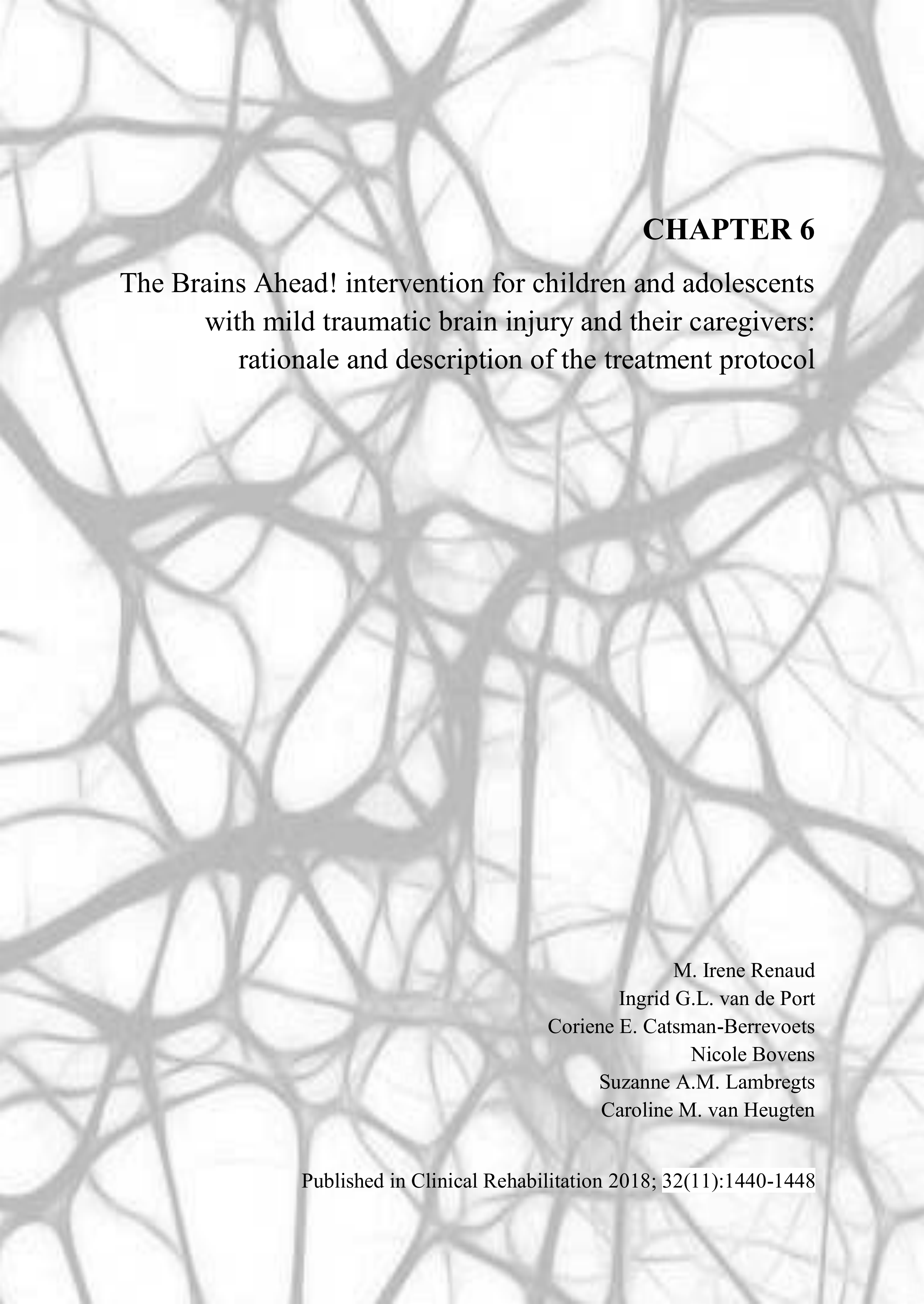

CHAPTER 6

The Brains Ahead! intervention for children and adolescents with mild traumatic brain injury and their caregivers: rationale and description of the treatment protocol

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Published in Clinical Rehabilitation 2018; 32(11):1440-1448

Abstract

Purpose: Approximately twenty percent of the children and adolescents after mild traumatic brain injury will not fully recover. They suffer long-term postconcussive symptoms and may experience limitations in activities and participation. Research suggests that early psychoeducational interventions may prevent long-term post-concussive symptoms. The Brains Ahead! Intervention was developed to prevent long-term symptoms and, furthermore, to establish a more successful return to activities and participation after mild traumatic brain injury in children and adolescents. The intervention is currently being evaluated in a multicenter randomized controlled trial.

Rationale: Providing individualized information and personal advice in addition to standardized information about the injury and possible consequences early after the injury may enable patients and caregivers to recognize and anticipate on relevant symptoms at an early stage and to prevent problems in activities and participation.

Theory into practice: The Brains Ahead! Intervention is a psychoeducational intervention for children and adolescents who sustained a mild traumatic brain injury and for their caregivers. The patients will receive a partially standardized and partially individualized psychoeducational session and a telephone follow-up within the first 2-8 weeks after the injury.

Clinical Message

The Brains Ahead intervention combines an inventory of symptoms, standardised and personalised psychoeducation, and follow-up, and involves the child's caregiver in the process.

Introduction

Mild traumatic brain injury is the most common cause of acquired brain injury among children and adolescents. There is no international consensus on structural follow-up by a (paediatric) neurologist or rehabilitation physician for this group of patients, despite the fact that approximately 20% of them suffer at long term from a variety of symptoms in the physical, cognitive, emotional or behavioural domains.[1-4] As a consequence of these post-concussive symptoms, children may develop limitations in activities and participation, e.g., in school and social relations on the long term.[5-7]

Several studies indicate that early education, reassurance and even early cognitive behavioural approaches may be effective in preventing long-term problems after traumatic brain injury in both children and adults[8-10] and, more specifically, after mild traumatic brain injury.[11-12] The few available studies including interventions (e.g., psychoeducation) intended to prevent post-concussive symptoms in children and adolescents report positive results. However, these studies are either retrospective or lack a randomized controlled trial design.[12-15]

We have recently developed the Brains Ahead! psychoeducational intervention. To the authors' knowledge, this is the first intervention that prospectively intends to prevent long-term problems related to activities and participation in children and adolescents aged 6 to 18 years old following mild traumatic brain injury.[15] The Brains Ahead! psychoeducational intervention combines an inventory of symptoms, psychoeducation, and follow-up, and involves the child's family in the process.

The Brains Ahead! intervention study is part of a larger cohort study with a nested randomized controlled trial.[16] The medial ethics committee of Erasmus University Medical Centre, Rotterdam, and all of the local committees of the participating hospitals approved the study protocol (MEC-2015-047, NL51968.078.14). The study is registered in the Netherlands Trial Register (NTR5153). In this paper, the theoretical basis and content of the Brains Ahead! treatment protocol for children and adolescents after mild traumatic brain injury and their primary caregivers is described. The TIDieR checklist for describing interventions was used to structure the paper (see online Appendix 1). Also, a patient case is described to illustrate the intervention (Table 1). Results of this intervention study will be published when the trial is finished.

Table 1. Illustration of the intervention by case description

Description of the incident

The 15-year old JD fell off his bike and fell on his head on his way to school, wearing no helmet, as is customary in the Netherlands. There was no loss of consciousness, but there was a period of posttraumatic amnesia of two hours. At the emergency room he was disoriented in time and place. A CT-scan showed no abnormalities. JD was admitted for a 12-hour observation, after which he was sent home. JD is in high school, has lots of friends and plays volleyball.

Inventory of complaints

JD and his parents receive the intervention at three weeks post-injury. Both JD and his parents say JD still suffers from headaches and fatigue. Furthermore, JD has trouble concentrating in class and when doing his homework. Bright light increases headaches. JD has not yet fully returned to school, but aims to join his class three hours a day now. A week of school holiday is coming up, and JD's parents planned to start full days of school after the holidays. JD says he wants to return to volleyball as soon as possible; he misses his team. His headaches and fatigue are keeping him from returning to volleyball at this moment.

Psychoeducation – standardized and personalized

JD and his parents received the standardized information on mild traumatic brain injury and specific information on headaches, fatigue, attention and concentration, and on sensory visual information processing. Advice on taking (planned) moments of rest was given. JD said he likes to rest by playing games on a tablet. The interventionist explained it is better to avoid screens (i.e. television, tablet) while taking a moment of rest. Considering his sensitivity to bright light, he was advised to wear sunglasses outside and to dim the lights indoors if possible. Furthermore, advice was given on the stepwise way of getting back into school, instead of starting full days right away after a holiday. This was important, especially considering the fact that JD was experiencing quite some symptoms at this late stage after the injury. Finally, a gradual return to participation in volleyball was advised as well, for example by starting with just a part of the training and building up based on that experience.

Follow-up

At the telephone follow-up, four weeks after the inventory of symptoms and psychoeducation, JD's father said he is very satisfied with the recovery his son has made since the psychoeducational session. JD and his mom confirmed this. The headaches have resolved completely and barely any symptoms of fatigue were still present. However, learning new words in another language, for example, was taking more time and effort compared to before the injury. School grades, nevertheless, were good. JD said that bright light was not bothering him anymore and that he got back to a full return to school in stages. Joining volleyball was being gradually increased as well. Next week he planned to join a match again. This was the last step in returning fully to this activity as well.

Rationale

Evidence suggests that information and education should always be offered following mild traumatic brain injury in general. Ideally, it should be followed by consultation in which personalized reassurance is given.[15] Therefore, the Brains Ahead! intervention consists of the following three components: (1) inventory of symptoms, (2) psychoeducation, and (3) follow-up. Hereafter is explained why these three components were chosen.

After mild traumatic brain injury most children and their primary caregivers leave the emergency department or the general doctor's office at best with a leaflet explaining what post-concussive symptoms are in general terms and that these may persist for some time. Structural individual follow-up is almost never offered. Because of the high prevalence of mild traumatic brain injury, a general follow-up guideline for all children could lead to overtreatment, considering that 80% has no persistent post-concussive complaints or symptoms.[1-4] However, a not to be neglected 20% of children and adolescents do have lasting and often debilitating post-concussive complaints or symptoms.[1-4] For this reason, a stepwise approach in order to identify the children and adolescents that need treatment is urgently needed.[15] The first step in this approach is to explore the symptoms a child may experience after mild traumatic brain injury, for example by using an inventory of symptoms containing the most common symptoms after mild traumatic brain injury, based on the literature.[17-24]

With regard to treatment, previous intervention studies[12,14-15,25-30] consisting of psychoeducation were found to be effective in preventing long-term post-concussive symptoms and functional problems after mild traumatic brain injury in adults and children. A study on long-term problems after mild traumatic brain injury in adults demonstrated that the effect of the education was most profound when administered at the earliest possible stage.[31] The studies that apply these interventions to children have been performed with other patient groups, e.g. children with only sports-related concussions,[32-33] or more severe brain injuries,[24] or they were limited to case reports.[33] Also, some interventions were focused on preventing long-term post-concussive symptoms and resolving existing post-concussive symptoms and not on preventing problems in activities and participation for children with mild traumatic brain injury.[12,15,29-30,35] Despite these limitations, the results of these psychoeducational intervention studies are very promising with respect to decreasing post-concussive symptoms in children with mild traumatic brain injury.[9-12,30]

The World Health Organisation Collaborating Centre for Neurotrauma Task Force on Mild Traumatic Brain Injury developed guidelines for the content of psychoeducational interventions, such as standardized information about diagnosis, incidence, risk factors, prevention, prognosis and treatment. In addition, they advise that the intervention should also contain individualized information. However, an overload of information makes it difficult to determine what is specifically important.[36] Furthermore, misunderstanding of information may result in anxiety and keeping the child off activities, while a stepwise return to activities in the first days after mild traumatic brain injury was found to have positive effects on participation in the long term.[37] For this reason, information should be relevant to the child's injury and symptoms and appropriate for the child's age and situation.[36] Information that is provided verbally, on the day of the injury and in the first days after, is often less well absorbed by caregivers.[12] For this reason verbal information should be given two or three weeks after the injury, and written information and instructions should be provided additionally.[12,36]

Caskey and Nance (2014) describe a study in which children with mild traumatic brain injury were routinely scheduled for an outpatient follow-up two weeks after the injury. During that visit, post-concussive symptoms were assessed and patients were referred to specialists if needed. The authors describe that patients and their caregivers often were noncompliant with the scheduled follow-up, despite the experience of ongoing persistent symptoms.[38] Possibly, an outpatient follow-up is too time-consuming and less flexible, in comparison with telephone counselling. A follow-up contact by telephone during the first three months post-injury was found to be effective in reducing symptoms in children aged 16 years and older and in adults after mild traumatic brain injury.[39] More recently, Nowacki et al. (2016) also found effective results after such a follow-up six weeks after mild traumatic brain injury, in children aged 4 to 18 years old.[40]

In summary, all described interventions are mostly directed towards the reduction of post-concussive symptoms and to a lesser extent to improvement in activities and participation. The psychoeducational part of the Brains Ahead! intervention provides standardized and personalized information on how to deal with symptoms after mild traumatic brain injury and advice on the stepwise return to participation in activities is provided. We expect that our approach prevents post-concussive symptoms over the long term and will have a positive effect on improvement of activities and participation after mild traumatic brain injury.[15]

Procedures

In order to illustrate the use of the intervention in practice, we described the case of JD and his parents who underwent the intervention as part of the randomized controlled trial (Table 1). Signed informed consent for participation in the intervention study was received as well as additional consent for this anonymized use of the description of their experiences throughout the intervention procedure. The characteristics of the Brains Ahead! intervention, including timeline, components, content and duration per component are presented in Table 2. Further details on the study design and procedures are published elsewhere.[16]

Target group

The intervention is designed for children and adolescents from 6 to 18 years, diagnosed with mild traumatic brain injury at the emergency room, and their caregivers. In this study, the intervention was offered to patients from two participating centres (Erasmus University Hospital, Rotterdam; and Amphia Hospital, Breda). The caregiver was defined as a parent or guardian. Diagnosis of mild traumatic brain injury is based on the criteria established by the American Congress of Rehabilitation Medicine and the World Health Organisation Collaborating Centre for Neurotrauma Task Force on Mild Traumatic Brain Injury (p. 266).[41]

Materials

The psychoeducation is administered using a presentation on a laptop and a standardized booklet containing information to take home. There is a booklet for parents, a booklet for children aged 6-12 years old, and a booklet for children aged 12-18 years old.

Location and therapist

The inventory of complaints and psychoeducational session takes place in the hospital where the child was seen on the emergency department at the time of the injury. The intervention is administered by a professional, experienced and educated in paediatric rehabilitation after mild traumatic brain injury in children and adolescents.

Table 2. Characteristics of the Brains Ahead! intervention

Target group	Children and adolescents (6-18y) with mild traumatic brain injury and their caregivers
Interventionist	Professional, experienced and educated in child rehabilitation after mild traumatic brain injury in children and adolescents

Intervention	When and where	Component	Content	Duration
	Face-to-face at the hospital 2-4 weeks after hospital discharge	**Inventory of symptoms**	- introduction	5 min*
			- fill out list of complaints	10 min
		Psycho-education Standardized	- verbal explanation of standardized information and individualized advice	25 min
			- provision of standardized information take-home booklets	3 min
		Additional	- additional verbal information on specific symptoms experienced based on inventory of symptoms	15 min
			- provision of take-home hand-outs per specific experienced symptom	2 min
	Telephone 6-8 weeks after hospital discharge	**Follow-up** Standardized	- questions about inventory of symptoms, psychoeducation and booklets	5 min
			- checking up on the experienced symptoms (if any) after mild traumatic brain injury	5-10 min
			- any new symptoms after mild traumatic brain injury that they did not experience before	5-10 min
			- indicate additional follow-up and provide contact information	5 min
	Telephone Available on demand by the participant until 6 months after the mild traumatic brain injury	Additional contact(s)	- any of the above-mentioned	5-15 min per contact

Y= years, Min = minutes

* The described time periods, durations and frequencies are referred to as guidelines. The interventionist is allowed to modify these guidelines, for example if participants experience many symptoms after the mild traumatic brain injury and more time for explanation is needed.

Treatment sessions

Session 1: Inventory of complaints and psychoeducation

The goal of the inventory of symptoms is to enable focused psychoeducation with additional information on post-concussive symptoms that the patient may experience. A list of common symptoms after mild traumatic brain injury, based on the most common symptoms after mild traumatic brain injury according to the literature,[17-24] is discussed with the child and his/her caregivers in order to discover what is relevant (e.g. does the child experience this symptom or not) for the child's personal situation. The list contains the following symptoms: (1) headache, mental fatigue, sleep, tension and stress; (2) difficulties with attention and concentration; (3) impaired efficiency and speed of information processing; (4) difficulties learning new information; (5) impaired memory; (6) difficulties with movement (motor skills and balance); (7) difficulties with executive skills (planning, impulsivity); (8) changes in personal and social skills; (9) changes in language and speech; and (10) impaired use of senses (seeing, hearing, feeling, smelling and tasting).

The aim of the psychoeducation is to provide information and advice about mild traumatic brain injury as well as to prevent long-term problems in activities and participation. Psychoeducation contains standardized information on causes, incidence, and possible consequences of mild traumatic brain injury, information and advice about returning to activities and participation, sensory sensitivity, and load-bearing capacity after mild traumatic brain injury, and is based on the literature.[1,9,11-12,15,29,36,39] The information is administered verbally by the interventionist and is the same for every participant. This standardized information is also given to the participants in a booklet to take home. There are three versions of the booklet: one for the caregivers, one for children aged 6-12 years, and one for children aged 12-18 years. To individualise the treatment, customised information is provided by the interventionist. In case the child experiences symptoms after the mild traumatic brain injury - based on the inventory of symptoms - additional information, specific to these symptoms, is given, both verbally and on paper. For every individual symptom, standardized information is available. Furthermore, individualized advice can be provided on returning to activities and participation, based on the individuals' daily life and goals, such as returning to school, sports and hobbies or work.

Session 2: Follow-up

The aim of the follow-up is to provide customized treatment, based on the individual questions of participants and possible symptoms the patient may be experiencing after mild traumatic brain injury, without overloading them with excessive information.

During the standardized follow-up by telephone, the interventionist asks participants whether there are any questions about the inventory of symptoms and information that was given during the psychoeducation. Furthermore, the interventionist inquires about specific symptoms experienced (if any) after the mild traumatic brain injury. In case new common post-concussive symptoms have occurred, participants receive a short explanation on these symptoms by telephone and are sent extra standardized information about these specific symptoms. In cases where there was doubt about the relation between the mild traumatic brain injury and the new occurring symptoms, participants were advised to consult their general practitioner.

Additional session(s)

The additional follow-up can be used by participants on their own initiative. Based on the fact that 20% suffer from long-term symptoms after mild traumatic brain injury, this follow-up was offered as an option for avoiding overtreatment. The interventionist can be contacted by e-mail for this additional follow-up, for example, in case new symptoms occur, or if questions about the consequences of mild traumatic brain injury arise at a later stage after the standardized follow-up. The interventionist responds within two workdays after receiving the e-mail. The interventionist registers the number and content of the additional follow-up contacts. There is no limit on the number of additional follow-up contacts. However, the interventionist advises the participant and caregivers to contact their general practitioner when four additional follow-up contacts occur – or earlier, based on professional, clinical opinion.

Practical issues

The intervention has been developed in such a way that - if the intervention is proven to be effective - it can easily be implemented in hospital discharge routines and also in general practices. However, time-consuming and cost-effectiveness issues may affect the implementation of the intervention, especially in the emergency room.

Discussion

To our knowledge, the Brains Ahead! intervention is the first standardized psychoeducational intervention combined with an individual approach and follow-up for children and their caregivers, provided at an early stage after mild traumatic brain injury in order to help prevent long-term problems concerning activities and participation.

The early stage after injury at which the intervention is administered, may help answer questions about what patients and their caregivers may expect after a mild traumatic brain injury and prevent the patient from experiencing long-term symptoms after the injury and from making steady progress towards a full return to school and other activities, and is, therefore, considered a strength of the intervention.[42-44] Another strength of the intervention is that it is designed to meet patients' individual needs. Patients and their caregivers are protected from an information overload, and receive enough individualized information to guide them in the first period after mild traumatic brain injury.

The usual care in many countries for children with mild traumatic brain injury consists of short hospitalisation or immediate discharge.[45] At discharge they often receive a concise information brochure to take home, with recommendations to return to the general practitioner or hospital in case of frequent vomiting, increasing drowsiness, and/ or an increase in other complaints during the following days.[16] In comparison with this usual care, the Brains Ahead! intervention is more time-consuming and labour-intensive. However, if this approach proves to be effective, a web-based psychoeducational intervention with optional features in order to meet the child's personalized needs may provide a solution for this in the future. The age of the target group of the Brains Ahead! intervention was set at 6-18 years, because one of the main purposes of our study was to examine the effects of the intervention on activities and participation both from the parental perspective and from the child's perspective.[16] If we would have included younger children, we could not use our selected outcome measures. This may be considered a limitation since it reduces generalisability for the use of it in younger children. One might want to examine the effects of the intervention for children aged 0-6, which seems quite possible when administering the intervention to the caregiver only and measuring outcome in the caregivers only considering the level of understanding of the child itself.

We recognize that some patients may not need an intervention after mild traumatic brain injury, because approximately 80% may not experience any symptoms at all. However, around 20% may suffer from symptoms at six months post-injury and beyond, related to reduced activities and participation.[1-4] Therefore, another part of the Brains Ahead! study is to investigate possible predictive factors for outcome after mild traumatic brain injury and to identify which patients are at risk for long-term problems. The results of the Brains Ahead! study on possible predictive factors for outcome after mild traumatic brain injury, the effectiveness of the intervention, and the evaluation of the intervention process will be presented in ensuing papers.

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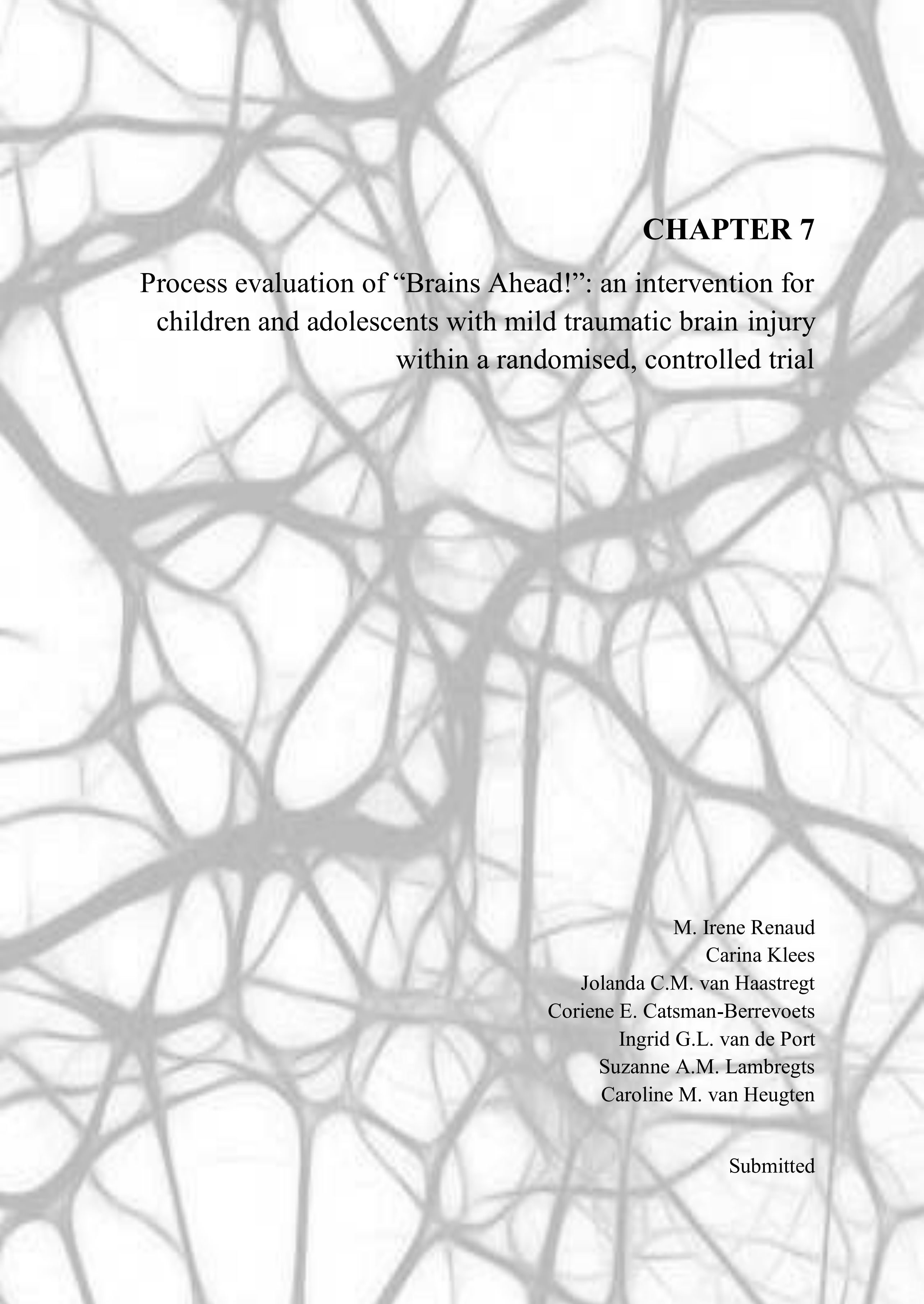

CHAPTER 7

Process evaluation of “Brains Ahead!”: an intervention for children and adolescents with mild traumatic brain injury within a randomised, controlled trial

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Abstract

Objective: To investigate whether the Brains Ahead! Intervention for children and adolescents with mild traumatic brain injury was implemented as intended. Additionally, involvement in and satisfaction with the intervention among patients, caregivers, and professionals delivering the intervention was studied.

Design: Mixed methods, prospective study.

Participants: Children with mild traumatic brain injury and their caregivers, allocated to the intervention group of the randomized controlled trial in the Brains Ahead! study, and the two professionals providing the intervention.

Intervention: The intervention consists of a standardized and individualized psychoeducational session with written take-home information, and follow-up telephone call(s).

Main measures: Registration forms, evaluation questionnaires for patients and caregivers, and semi-structured interviews for professionals.

Data analysis: Qualitative data were categorized based on content. Quantitative data were reported as descriptive statistics.

Results: Fifty-five patients and caregivers out of 60 study-participants attended both sessions. All elements of the intervention were delivered to 53 study-participants. Evaluation questionnaires were completed by 21 of the 31 patients aged 12 years and older, and by 41 caregivers. Overall, the sessions were considered useful by 19 patients, 40 caregivers and both professionals. Reassurance, creating a better understanding and recognition of symptoms were rated as important aspects. On a scale from 1 to 10, the intervention was rated by children, caregivers, and professionals with 7.6 (SD 1.2), 8.1 (SD .9) and 8.0 (SD .0) respectively.

Conclusion: The Brains Ahead! intervention was largely implemented as intended and the process evaluation revealed that it is considered feasible according to patients, caregivers and professionals.

Clinical messages

(1) The “Brains Ahead!” intervention is a feasible intervention according to participants and interventionists; (2) One session containing individualized information and reassurance within 1-2 weeks after the injury seems the most appropriate; (3) For implementation in clinical settings, timing, location and distribution of the content of the intervention needs adjustments.

Introduction

In this study, we present the outcomes of the process evaluation of the "Brains Ahead!" intervention,[1] which was performed alongside a randomized controlled trial (Netherlands National Trial Register; NTR5153), among the participants allocated to the intervention group of the trial.[2] The effectiveness of the "Brains ahead!" intervention is evaluated in the randomized controlled trial and results will be presented elsewhere. This process evaluation aimed to examine the feasibility of the "Brains Ahead!" intervention and to evaluates the extent to which the intervention was implemented according to protocol within the context of the trial.

From guidelines on how to manage mild traumatic brain injury in children and adolescents and conclusions from a recent review, it was indicated that early interventions aimed at preventing problems on activities and participation should contain information and education on mild traumatic brain injury, with additional follow-up consultation, including individualized advice on step-by-step resumption of activities and participation, and personalized reassurance.[3-4] In addition, it should be offered to child/adolescent and family.[3-4] An evidence-based intervention does, however, not yet exist. Therefore, we have developed the "Brains Ahead!" intervention for children and adolescents with mild traumatic brain injury (hereafter: patients) and their parent(s) or legal guardian(s) (hereafter: caregivers).[1] The "Brains Ahead!" intervention focuses on increasing the patients' and caregivers' knowledge about mild traumatic brain injury and possible consequences of the injury, and enabling them to recognize and anticipate on relevant symptoms in an early stage. It was expected that the intervention would prevent limitations in activities and participation in the long term.

The process evaluation is based on the framework of Saunders et al.[5] and assesses the attendance and adherence of patients and their caregivers (reach and dose received exposure), the extent to which the intervention was performed according to protocol (fidelity and dose delivered), and the opinion of patients, caregivers, and interventionists about the intervention (dose received satisfaction). The results of this study may be used to optimize the intervention, to facilitate a correct interpretation of the results of the randomized controlled trial, and eventually help to facilitate implementation of the intervention in health care.

Method

The intervention was delivered between May 2015 and April 2018, at two hospitals in The Netherlands (Erasmus University Hospital, Rotterdam and Amphia Hospital, Breda) and was offered to patients and their caregivers (when referred to patient and his/her caregiver together, hereafter; participants).[1-2] Two professionals experienced and educated in child rehabilitation after traumatic brain injury (here after; the interventionists) delivered the intervention to participants.[1] The medical ethics committee of Erasmus University Medical Centre, Rotterdam, and the local committees of the two participating hospitals approved the study (MEC-2015-047, NL51968.078.14).[2] The study was funded by the Johanna Kinderfonds (Award Number 2012/0040-1552) and Handicap.nl (previously the Revalidatiefonds) (Award Number R2012175).

The intervention consisted of two sessions, provided within the first two to eight weeks after the injury. It was ensured that each participant received both sessions from the same interventionist. The first session involved a face-to-face contact approximately two weeks after the injury with participants, during which the consequences of mild traumatic brain injury and advice for coping with these consequences to prevent long-term problems were discussed. The second session took place approximately four weeks after the first session and involved a telephone follow-up with the caregiver, during which was checked if the patient's individual consequences of mild traumatic brain injury had been resolved, remained, or worsened. Moreover, additional information was provided in case of specific complaints. The sessions are described in more detail in Table 1 and in the intervention protocol.[1]

For the process evaluation, information was gathered about the attendance and adherence of patients and their caregivers (reach and dose received exposure), the extent to which the intervention was performed according to protocol (fidelity and dose delivered), and the opinion of patients, caregivers, and interventionists about the intervention (dose received satisfaction). Table 2 presents an overview of the measurement instruments (questionnaire, registration form, and interview) used to collect this information.

Table 1. Characteristics of the "Brains Ahead!" Intervention

Target group	Children and adolescents (6-18y) with mild traumatic brain injury and their caregivers			
Interventionist	Professional, experienced and educated in child rehabilitation after mild traumatic brain injury in children and adolescents			
Intervention	**When and where**	**Component**	**Content**	**Duration**
	Face-to-face at the hospital 2-4 weeks after hospital discharge	**Inventory of symptoms**	- introduction	5 min*
			- fill out the list of complaints	10 min
		Psycho-education Standardized	- a verbal explanation of standardized information and individualized advice	25 min
			- provision of standardized information take-home booklets	3 min
		Additional	- additional verbal information on specific symptoms experienced based on the inventory of symptoms	15 min
			- provision of take-home hand-outs per specific experienced symptom	2 min
	Telephone 6-8 weeks after hospital discharge	**Follow-up** Standardized	- questions about inventory of symptoms, psychoeducation, and booklets	5 min
			- checking up on the experienced symptoms (if any) after mild traumatic brain injury	5-10 min
			- any new symptoms after mild traumatic brain injury that they did not experience before	5-10 min
			- indicate additional follow-up and provide contact information	5 min
	Telephone Available on demand by the participant until 6 months after the mild traumatic brain injury	Additional contact(s)	- any of the above-mentioned	5-15 min per contact

Y= years, Min = minutes

* The described time periods, durations, and frequencies are referred to as guidelines. The interventionist is allowed to modify these guidelines, for example, if participants experience many symptoms after the mild traumatic brain injury and more time for explanation is needed.

Table 2. Measurement instruments process evaluation.

Element	Operationalization	Participants' evaluation questionnaire	Interventionists' registration form	Interventionists' interview
Performance according to protocol (fidelity and dose delivered)	The extent to which intervention was implemented as planned		X	X
	Number, frequency, and duration of the sessions		X	
	The extent to which all of the intended components of the "Brains Ahead!" were delivered to participants	X	X	
	The extent to which all materials (written and verbal) were delivered	X	X	
Attendance and adherence (reach and dose-delivered exposure)	The proportion of target audience that participated in the intervention		X	
	Attendance rate		X	
	Overall engagement	X	X	
Opinion on the intervention (Dose received – satisfaction)	Overall opinion about the intervention	X		X
	Opinion about the value of the intervention	X		X
	Opinion about the value of the main elements of the intervention	X		X
	Opinion about the interventionist			
	Suggestions for improvement	X		X
	Barriers to implementation			
		X		X
				X

X = element processed within the questionnaire, registration form and/ or interview
**Elements based on Saunders[15]*

Caregivers of all patients and patients aged 12 years and older received a questionnaire after the first follow-up telephone call (session 2) to evaluate the care they received so far. In case the participants used additional telephone sessions, they received an extra questionnaire after each call, to evaluate the additional telephone sessions. The questionnaires were sent to the participants home and assessed: (1) what information had been received and/or read, (2) the perceived usefulness of the intervention and whether expectations were met on a 5-point Likert scale (1 = not at all useful – 5 = very useful), (3) their opinion on several statements about the purpose and content of the intervention and their opinion about the interventionist (1 = totally disagree - 5 = totally agree), and (4) open questions in which participants could express their opinion on the intervention.

After each session, the interventionists filled out a registration form, which recorded attendance rate, adherence, and deviations from protocol (e.g. whether any items were not discussed and reasons for not discussing these items). Information about the sessions (e.g., date, duration, content and whether more extensive information on certain topics is given) and the use of additional optional follow-up sessions (e.g. date, duration, content), were registered by the interventionist as well.

Finally, the researcher interviewed both interventionists after the final participant enrolled in the randomized controlled trial completed the intervention. The interview contained questions on their opinion about the content of and experience with providing the intervention.

All quantitative data gathered from anonymized evaluation questionnaires and registration forms were analysed with descriptive statistics using IBM SPSS statistics version 25. Answers to structured, categorical questions (e.g. multiple choice, yes/no, Likert-scales) were described in terms of percentages. Qualitative data as a result of open-ended questions included in the evaluation questionnaire were categorized based on their content and reported if at least half of the participants had given the same answer.

Results

In total, 60 participants were assigned to the “Brains Ahead!” intervention in either Erasmus University Hospital, Rotterdam (*N*=31) and Amphia Hospital, Breda (*N*=29). Results on attendance and adherence, to what degree the intervention was performed according to protocol, and the opinion on the intervention are presented in table 3.

Of the 60 participants, 58 participated in at least one of the sessions, and registration form data was collected for 57 participants. During the second session, registration form data was collected for all 55 participants. Only one participant used an additional follow-up session. Evaluation questionnaires were completed by 41 caregivers and by 21 of the 31 patients with mild traumatic brain injury aged 12 years and older. Active participation of the participants during the session was assessed by asking whether the participants asked questions during the meeting. Most participants actively asked questions about the information provided during session 1 but less during session 2.

Table 3. Results of the process evaluation

Attendance and adherence	**Participants N (%)**	
Participants assigned to intervention	60	
Attendance rates		
First session	58 (97%)	
Both sessions	55 (92%)	
No sessions	2 (3%)	
Additional follow-up	1 (2%)	
Collected registration form data		
First session	57 (98%)	
Second session	55 (100%)	
Completed evaluation questionnaires		
Caregivers	41 (71%)	
Patients aged 12 years and older	21 (68%)	
Active participation by participants		
First session	48 (83%)	
Second session	18 (31%)	
Performance according to protocol		
First session		
2-4 weeks after the injury	36 (62%)	
Mean duration (minutes)	47	
Inventory of complaints filled out	57 (98%)	
Standardized psychoeducation elements delivered to	53 (91%)	
Standardized take-home booklets handed out to	58 (100%)	
Individualized information and advice delivered to	48 (83%)	
Additional take-home hand-outs handed out to	40 (79%)	
Second session		
6-8 weeks after the injury	33 (60%)	
Mean duration (minutes)	15	
Standardized follow-up elements delivered to	27 (49%)	
Opinion on the intervention	**Patients (N=21)**	**Caregivers (N=41)**
Usefulness		
Very useful	-	13 (32%)
Useful	11 (52%)	23 (56%)
Somewhat useful	8 (14%)	4 (10%)
Not very useful	1 (5%)	1 (2%)
Not useful at al	1 (5%)	-
Expectation met		
Much more than expected	1 (5%)	1 (2%)
More than expected	4 (19%)	14 (34%)
As expected	12 (57%)	23 (56%)
Less than expected	3 (14%)	3 (8%)
Much less than expected	1 (5%)	-
Creating understanding of the consequences of MTBI		
Sufficient	20 (95%)	32 (78%)
Neutral	1 (5%)	9 (22%)
Insufficient	-	-
Helpful in return to activities and participation	13 (62%)	35 (88%)

For most participants, the first session took place 2-4 weeks after the injury, and the mean duration of session 1 was 47 minutes, ranging from 33 to 70 minutes. This is 13 minutes less than the planned duration of one hour. The intended components of session 1 of the Brains Ahead! intervention were delivered to participants according to protocol in 79 to 100% of the cases, depending on the specific component (see table 3).

For session 2, the mean duration of session 2 was 15 minutes, ranging from 10 to 36 minutes. This is 15 minutes less than the planned duration 30 minutes. The intended components of session 2 were delivered to 27 of the participants. The other 28 participants presented no new symptoms and the previous complaints (if any) were resolved at this point, making the provision of additional information and further checking up on experienced symptoms superfluous. Only one of the participants requested an additional follow-up.

During the interviews, the interventionists confirmed that the intervention was implemented as planned in most cases. For one patient and caregiver, the Dutch language made it more difficult to fill out the inventory of complaints. The interventionist improvised and helped them filling out the inventory by explaining the symptoms verbally. For another patient and caregiver, the psychoeducation was not provided completely due to many worries and uncertainties about coping with the trauma and posttraumatic stress. The interventionist improvised by giving this patient and caregiver the chance to relieve some stress and trying to provide more reassurance. Both interventionists noticed that the psychoeducational part of session 1 may have been somewhat too long for the youngest patients (aged six and seven years old). For these patients (11 out of 58 cases), they tried to shorten the information and improvised to fit the information to the patient's age.

On a scale from 1-10, caregivers and patients rated the intervention with mean scores of 8.1 (SD .9; range 5.0-10.0), and 7.6 (SD 1.2; range 5.0-10.0) respectively, and the interventionists both rated the intervention with an 8.0.

The usefulness of the intervention according to the caregivers and patients and the extent to which they believed the intervention met their expectations is presented in Table 3. Both interventionists scored the intervention as very useful, and felt that the intervention met the expectations of the participants and was individualized to an appropriate extent. The intervention sufficiently helped most of the caregivers and patients to a better understanding of the consequences of mild traumatic brain injury and return to activities and participation (see table 3). Both interventionists also reported that they felt that the content of the intervention sufficiently helped participants in a better understanding of the consequences and to a safe and full return to activities and participation after mild traumatic brain injury.

Table 4 presents the elements of the intervention rated on their value by the participants. Both interventionists reported that none of the elements were thought to be superfluous. With regard to the additional follow-up consults, the interventionists reported that the option to use this seemed to have a reassuring effect, though was not used. A shorter version for children aged 6 and 7 years old was recommended.

Table 4. The proportion of participants indicating elements as valuable

Element of the intervention	Patients (N=21)	Caregivers (N=41)
Inventory of complaints	8 (38%)	21 (51%)
Psychoeducational part	14 (59%)	25 (60%)
Verbal additional information on specific symptoms	10 (43%)	24 (59%)
Take-home information booklet	6 (24%)	14 (34%)
Hand-out additional information of specific symptoms	6 (24%)	13 (32%)
Telephone follow-up	1 (5%)	12 (29%)

Concerning the satisfaction with the interventionist, 39 caregivers and 18 patients reported that their trust in and contact with the interventionist was satisfactory. The other caregivers reported neutral on their trust in and contact with the interventionist, as well as one of the patients. Two patients reported to be unsatisfied about the contact with the interventionist, although their trust in the interventionist was neutral.

Some other useful responses were gathered through open-ended questions, on which caregivers reported that the information in the intervention was; reassuring (*N*=20), helpful in creating a better understanding of symptoms and recognizing them (*N*=34), helpful in explaining to their child why it was best to take some time to rest (*N*=24), helpful in making a safe plan to return to activities and participation (*N*=24), and provided suitable information for schools and the environment as well, resulting in a better overall understanding (*N*=8). Furthermore, almost half of the caregivers (49%) reported that they were happy to receive information and answers to their questions, but they would have preferred to receive the information right away at discharge from the emergency department.

Patients with mild traumatic brain injury reported on the open-ended questions that; it was appreciated that someone took time to listen to and converse about what happened and what to expect (*N*=10), the information provided useful tips and reassurance (*N*=11), and helpful in understanding when to take some extra rest and how to return to activities and participation (*N*=10). Two patients with mild traumatic brain injury reported that it was a lot of information for those who did not suffer from any symptoms.

The interventionists reported that it was important to acknowledge that the personal background was different for every participant. This emphasizes the added value and importance of the individualized approach of the intervention, ensuring that it is about that specific child, each with different symptoms. Since not all children with mild traumatic brain injury may be reached at the early stage after injury, the interventionists emphasized that the content of the intervention would be valuable for rehabilitation care as well.

Discussion

This study showed that the intervention "Brains ahead!" was largely performed according to protocol. The intended participants were reached and overall participants and interventionists were satisfied with the degree to which the intervention had helped the participants to better understand symptoms and to help the patient return to activities and participation after sustaining the mild traumatic brain injury. In addition to previous recommendations for early interventions directed at paediatric mild traumatic brain injury,[3] our study adds to the literature that an intervention designed highly in agreement with these recommendations (such as the Brains Ahead! intervention) is sufficiently feasible and found to be very useful among both providers and receivers.

In line with earlier results about the importance of reassurance and education for parents about the signs and symptoms of mild traumatic brain injury,[3,6] our results confirm that the appreciation for information was very high among children with mild traumatic brain injury and their caregivers. We also found that although the first session was performed in most cases conform intervention protocol, the second session was not. According to the interventionist this was due to the fact that most participants lacked the need for more information at that point. This is in accordance with the results of an earlier study by Bell et al.[7] which showed that one telephone follow-up, during which individual concerns can be addressed (comparable to what is provided in our session 1), is effective to optimize reassurance for the child and their caregivers.

Duration of most sessions was shorter than expected and the interventionists shortened the psycho-education for the youngest patients even more to better fit the information to the patient's age. Regarding the content of the intervention, we found that the psychoeducational and individualized parts of the intervention were most valuable to participants. Furthermore, almost half of the participants indicated on open ended questions that the information was preferably received at an earlier stage after the injury, for example at discharge from the hospital. This might be possible for the standardized information part, but not so much for the individualized part since this is for example subjected to the complaints the child experiences during the first days after the injury.

An important strength of this process evaluation was the use of both qualitative and quantitative research methods. Furthermore, since the outcomes of the trial were not known yet when the data of the process evaluation was analysed, the outcomes of the latter were not biased.[8] An important limitation of process evaluations in general is that these are only possible by self-report evaluation questionnaires. As a result, there will always be a risk of socially desirable answers. In this study, an attempt was made to reduce this risk as much as possible by anonymizing the evaluation questionnaires. Another limitation of this study is that fidelity (i.e. whether the intervention was performed according to protocol) was not measured by observation/video recordings, but with a self-report registration form, which may cause social desirability bias.

Preliminary results of our randomized controlled trial already showed that the intervention is effective on preventing long-term fatigue, post-concussive symptoms, and posttraumatic stress symptoms, and preventing the experience of a lower quality of life.This process evaluation has now shown that the “Brains Ahead!” intervention is sufficiently feasible. However, a number of findings have emerged that can be taken into account when optimizing the intervention for implementation.

Firstly, there clearly was need for standardized and for individualized information. This supports the use of the Brains Ahead! intervention, in which both standardized information and an individualized approach are imbedded in session one. Although the intervention is largely standardized which helps replication, tailoring the intervention to the needs of the participants can not be standardized.

Secondly, participants indicated that they preferred to receive the information at an earlier stage after the injury, for example at discharge from the emergency room. Regarding the content of the information, this would seem possible for the standardized part. For the individualized information and advice part, the content is personalized based on the individuals’ daily life functioning and on the symptoms the child experiences during the first days after the injury. Based on the literature, a substantial number of patients do not experience symptoms after mild traumatic brain injury and are expected to recover completely without intervention. Therefore, the individualized part of the intervention should be offered a little later, for example, 1-2 weeks after the injury, to those in need of this information.

Third, regarding the location and person delivering the information, emergency rooms lack the capacity to conduct an extensive intervention such as the “Brains Ahead!” intervention. Therefore, we advise referral to a - for this purpose well equipped - primary care setting such as general practice, shortly after discharge from the emergency department. However, since this study has shown that the complaints, questions, and needs of the participants can be very diverse, a positive effect is expected to be reached when the interventionist can respond to this by improvising and adapting the content to fit these needs. Since professionals in primary care generally are not experienced and educated in child rehabilitation after traumatic brain injury, they should at least be appropriately trained. This could, for example be accomplished by national or regional training days for general practitioners or physician assistants. Additionally, the interventionists emphasized that the content of the intervention would be valuable for rehabilitation care as well, since not all children with mild traumatic brain injury may be reached at the early stage.

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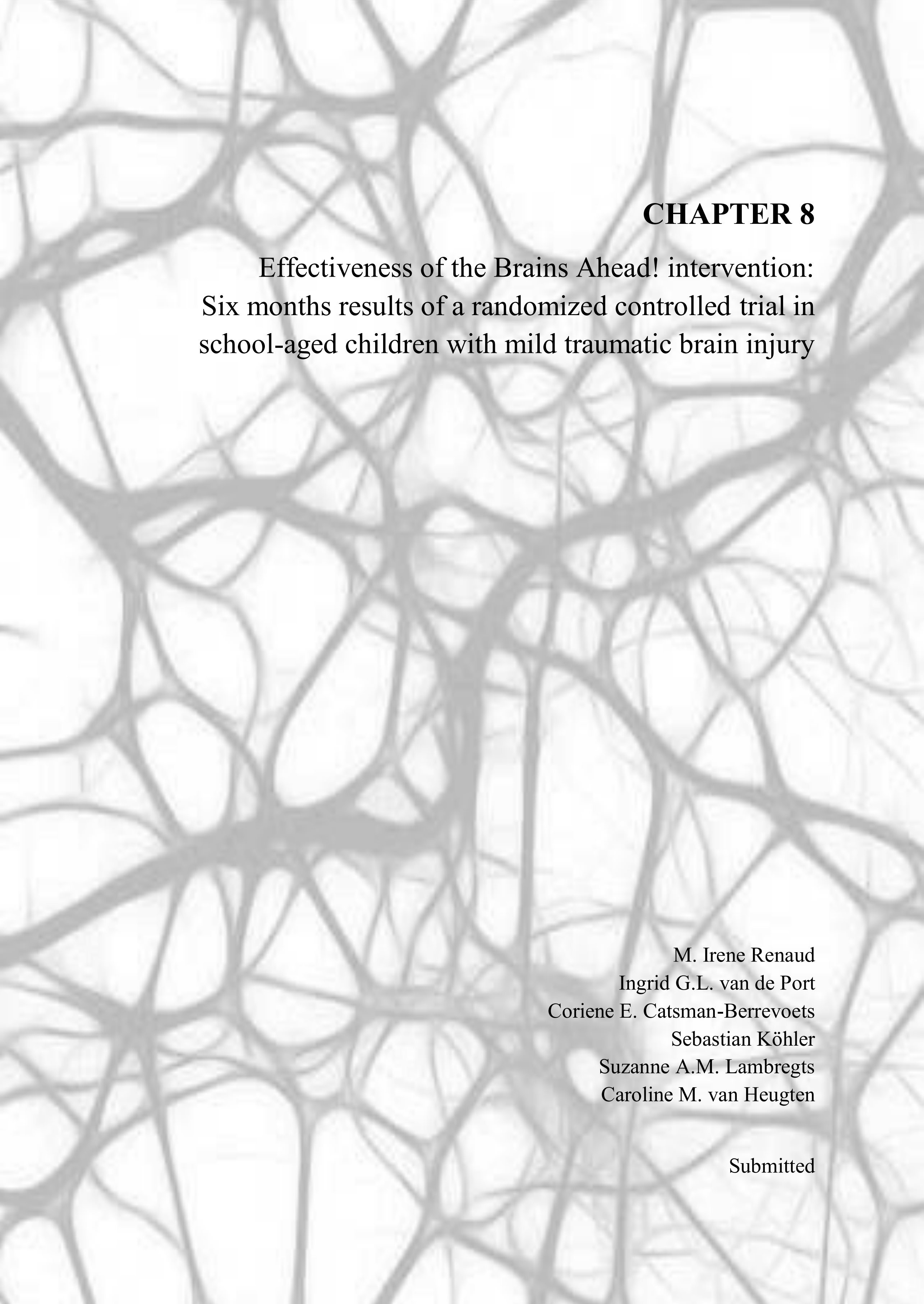

CHAPTER 8

Effectiveness of the Brains Ahead! intervention: Six months results of a randomized controlled trial in school-aged children with mild traumatic brain injury

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Abstract

Objective: To examine the effectiveness of Brains ahead! a psychoeducational intervention aimed to prevent long-term problems on activities and participation in children after mild Traumatic Brain Injury (MTBI).

Method: Participants were 124 children diagnosed with MTBI aged 6-18 years old and their caregivers. After randomization, participants in the intervention group received a face-to-face psychoeducational session with written take-home information and follow-up telephone call(s). Participants in the control group received usual care, consisting of a concise information brochure. Primary outcome was activities and participation (Child and Adolescent Scale of Participation (CASP)). Secondary outcomes were fatigue, postconcussive symptoms (PCS), posttraumatic stress symptoms (PTSS), and quality of life (QOL).

Results: Generalized Estimated Equation analyses showed that both groups improved over the first six months post-MTBI, but the intervention group scored not significantly better on the CASP. Mann Whitney U-tests showed that the intervention group reported significantly less fatigue, PCS, and PTSS, and better QOL compared to the control group at six months post-MTBI.

Conclusions: The Brains Ahead! intervention is beneficial over usual care to reduce fatigue, PCS, and PTSS and improve QOL. Lack of an effect on activities and participation may be due to the ceiling effect of the CASP.

Introduction

The worldwide incidence of traumatic brain injury (TBI) in children is high, with 280-1373 cases per 100,000 person-years in children age 0-18 years.[1-4] Follow-up care is usually only offered to children after moderate and severe TBI, but typically not after mild TBI (MTBI) because complete recovery is expected.[5-6] However, in 6-43% of the children, MTBI leads to long-term post-concussive symptoms (PCS),[7-9] which may cause limitations in activities and participation in different settings (i.e. at home, school and in the community).[10] For these children, adequate treatment at an early stage is essential, but research on this topic is scarce.[11]

Only two intervention studies have been conducted to improve the level of activities and participation after childhood MTBI.[12-13] Both studies used a discharge take-home information booklet describing symptoms and coping strategies for children and their parents.[12-13] The first study combined this booklet with a discharge interview, and a follow-up telephone call 24h after discharge.[12] Results suggest that activity limitations may be due to over reporting by anxious parents and therefore reassurance and education for parents about the symptoms of MTBI, which may aid children in returning to daily activities, is emphasized.[12] The other study implemented reassurance and education in the information booklet and found less PCS at three months post-MTBI in the intervention group.[13] Both studies found no intervention-effect on daily activities and participation compared to the control group.[12-13] In these studies, only the parent's perspective for outcome on activities and participation was examined.[12-13] Research, however, shows that outcome based on the perspective of the parent may differ from that of the child.[14] Studies on adult MTBI[15-16] show the beneficial effects of early, reassuring educational interventions and advice professionals to carefully monitor progress and offer early symptom-specific treatment when needed, and enable ready access to such a treatment during the first weeks of recovery.[17]

We developed 'the Brains Ahead! Intervention' which combines an inventory of symptoms, reassurance, standardized- and individualized psychoeducation and follow-up, aimed to prevent long-term problems on activities and participation.[11,18-19] The present study investigated the effectiveness of the MTBI Brains Ahead! intervention on activities and participation compared with usual care over the first six months post-MTBI, from the perspectives of both parents and children. We hypothesized that the intervention is more effective in preventing problems on activities and participation in the first six months post-MTBI compared to usual care. Furthermore, we expected the intervention to be superior over usual care for recovery on fatigue, PCS, posttraumatic stress symptoms (PTSS), and quality of life (QOL).

Methods

Design

This multicenter randomized controlled trial was nested in the larger Brains Ahead! multicenter prospective cohort study on activities and participation of children after MTBI. The study was approved by the medical ethics committee of Erasmus University Hospital in Rotterdam and by the local committees of the participating hospitals (MEC-2015-047, NL51968.078.14). All caregivers and children aged 12 years and older provided written informed consent. The study was registered in the Dutch Trial Register as NTR5153. Study details are described elsewhere.[18-19]

Participants

All children aged 6 to 18 years who presented with MTBI at the Emergency Departments of two Dutch hospitals (Erasmus University Hospital, Rotterdam; Amphia Hospital, Breda) between May 2015 and April 2018, and their caregiver(s) (i.e. parents or legal guardians), were eligible for participation.[18-19] Mild TBI was defined according to the criteria of the American Congress of Rehabilitation Medicine and the World Health Organization Collaborating Centre for Neurotrauma Task Force on Mild Traumatic Brain Injury.[20] Exclusion criteria were 1) a previous objectified head trauma, 2) progressive neurological problems or disease, 3) attending a daycare center or school for cognitively impaired children, and 4) insufficient knowledge of the Dutch language (child or caregivers).

Procedure

Eligible children with MTBI and their caregivers were registered at the participating hospitals and communicated to the researcher. Within the first week after MTBI, the researcher contacted caregivers by phone to ask if they were willing to participate in the study. Interested caregivers and children received written study information. The baseline measurement (T0) was scheduled 2 weeks post-MTBI, after written informed consent was obtained from caregivers and children above 12 years. After baseline measurements, participants were randomized into the intervention group or the control group (allocation ratio 1:1). Subsequently, the intervention group received the Brains Ahead! Intervention and the control group received usual care. Further measurements in both groups took place at three (T1) and at six months (T2) post-MTBI. All measurements took place at the participants' home.

Randomization and blinding

All measurements were performed by a researcher who was blinded to the group assignment (single-blinding). The success of blinding was checked by questioning the researcher about group allocation for all participants. Randomization was performed by an independent person, using computerized block randomization (block size = 8). The randomization scheme included stratification on age (6-12 or 12-18 years), gender (male or female), and hospital (Erasmus University Hospital, Rotterdam or Amphia Hospital, Breda). Caregivers were assigned to the same group as their child.

Interventions

The usual care consisted of a concise information brochure offered at discharge from the Emergency Room, containing recommendations to return to the general practitioner or hospital in case of increased symptoms during the first days after the injury.[18-19]

The Brains Ahead! intervention consisted of two sessions, and was administered by a health professional, experienced and educated in child rehabilitation after MTBI. The first session was offered within 2-4 weeks and the second session 6-8 weeks post-MTBI. The first session consisted of an inventory of symptoms and psychoeducation, both provided face-to-face at the hospital. The inventory of symptoms contains a list of known symptoms after MTBI. The child and caregivers indicated per symptom if the child experienced the symptom in order to enable focused psychoeducation. The psychoeducation contained standardized information on the causes, incidence, possible consequences of MTBI, and information and advice about returning to activities and participation, sensory sensitivity and load-bearing capacity after MTBI. Furthermore, it contained individualized information on the indicated symptoms by the child and advice directed to the child’s specific situation regarding activities and participation. The psychoeducation was provided both verbally and in a booklet for the child and a booklet for the caregiver.

The second session consisted of a follow-up contact by telephone during which the interventionist answered questions about the provided psychoeducation, if any, and inquiries about specific symptoms experienced after the MTBI. In case new PCS had emerged (for example concentration problems or fatigue emerging when returning to school after the summer holidays), participants received a short explanation about these symptoms by telephone and were sent extra standardized information about these symptoms. Extra telephone consultations were offered, but were used only once. A more detailed description of the rationale and description of the intervention can be found elsewhere.[19]

Measurements

All instruments have sound psychometric properties, and are recommended as instruments for evaluating outcomes in children after brain injury.[21-24,27-31]

Baseline characteristics

The electronic patient hospital file was used to collect the child's and caregivers' clinical and demographic characteristics at baseline, such as injury-related factors (i.e. Glasgow Coma Scale score (GCS), loss of consciousness (LOC), posttraumatic amnesia (PTA), cause of Injury), personal factors (i.e. age at injury, gender), and environmental (i.e. socioeconomic state (SES)) factors. SES was determined by using an occupational list, on which each occupation could be linked to a level (Centraal Bureau voor de Statistiek, 2010). Baseline information on the child's pre-injury functioning was collected by using the Child Behavior Checklist (CBCL)[21] and the Family Assessment Device - General Functioning (FAD-GF)[22].

Primary outcome

Activities and participation was assessed with the Child and Adolescent Scale of Participation – Dutch language version (CASP-DLV).[23-24] The 20 items of the CASP-DLV are categorized into the following settings: at home, in the community, at school, and in the environment, and can be scored on a four-point scale (1) age appropriate, (2) slightly impaired, (3) heavily impaired, (4) not capable. Summary scores are created by summing the item responses, dividing this number by the maximum possible score and multiplying this number by 100 to conform to a 100-point scale. A higher score represents better outcome. In case of missing and not applicable scores, the sum of the item responses is divided by the by the maximum possible score on the answered items. Since the CASP is well known for its ceiling effect,[25-26] we dichotomized the scores as follows: (0) deviant functioning/ any score <100, and (1) full functioning/ a score of 100, in comparison to their healthy/non-injured age-related peers. The CASP-DLV as filled out by the caregiver for children aged 6-18 years old was the primary outcome measure. Furthermore, children aged 10-18 years old filled out the CASP self-report.

Secondary outcome

Fatigue, CPS, PTSS and QOL were measured with several questionnaires that were filled out by the child and by the caregiver. Fatigue was measured with the Paediatric Quality of Life Inventory – Multidimensional Fatigue Scale (PedsQL-Fatigue). The PedsQL-Fatigue is an 18-item questionnaire that measures fatigue on a five point scale (0) never, (1) rarely, (2) sometimes, (3) often, (4) almost always.[27] The items are hereafter reverse-scored to a 0-100 scale, with a higher score indicating fewer symptoms of fatigue.

PCS was measured with the Health and Behaviour Inventory (HBI). The HBI is a 50-item questionnaire that measures the experience of PCS on a four point scale (1) never, (2) seldom, (3) sometimes, (4) often.[28] Total scores, ranging between 50 – 200, are calculated by adding the item-scores, with a lower total score representing fewer PCS.

PTSS was measured with the Impact of Event Scale (IES). The IES is a 34-item questionnaire measuring possible post-traumatic stress responses on a five point scale (1) never, (2) rarely, (3) sometimes, (4) often, (5) always.[29] The total score range is 34 – 170, with a lower score representing less symptoms.

QOL was measured with the Paediatric Quality of Life inventory – Quality of Life Scale (PedsQL-QoL). The PedsQL-QoL is a 23-item questionnaire that measures problems related to quality of life on a five point scale (0) never, (1) rarely, (2) sometimes, (3) often, (4) almost always.[30] The items are hereafter reverse-scored to a 0-100 scale, with a higher score indicating better quality of life.

Sample size

Sample size calculations were based on previous studies on pediatric TBI patients' participation that relied on the parent-reports of the CASP-DLV. For the CASP-DLV, a standardized difference of 0.5 was expected.[24] Based on an alpha of .05 and a power of .8, a minimum of 63 children per group was required (total 126). A drop-out rate of 10% was expected, therefore the desired number of participants was set at 140.

Statistical analyses

Differences between groups at baseline were checked with independent t-tests, Mann Whitney U-tests, and Chi-square tests where appropriate. Skewness between -1 and +1 was accepted to meet the assumption for normality.

The effectiveness of the intervention on the dichotomous CASP-DLV parent-report) was assessed using Generalized Estimating Equations (GEE), an extension of general linear models for repeated measures analysis. To model associations with the binary dependent variable, GEE analyses included a logit-link for the binomial family and an exchangeable working correlation matrix (also known as population-averaged or marginal logistic regression analysis). The analyses provide odds ratios (OR) and their 95% confidence interval (CI). The CASP DLV was included as dependent variable. Time of measurement, group assignment and the interaction between time of measurement and group (to model change-over-time) were included as independent variables.

Analyses were primarily performed for the dichotomized CASP-DLV parent report total scores and scores for different settings. In addition, we performed GEE analyses for the CASP self-report dichotomized total scores and dichotomized scores for different settings for children aged 10-18 years old. The intention-to-treat principle was used. Data were analyzed with IBM SPSS Statistics 25. The level of significance was set at $p<.05$ in two-sided tests. The effectiveness of the intervention on the secondary outcome measures at six months post-MTBI was assessed using Mann Whitney U-tests, since assumptions for normality were not met.

Results

Participant characteristics

The flow of participants is presented in Figure 1. Between May 2015 and April 2018, 124 participants were included in the study of which 123 completed the trial. After randomization, one participant dropped out of the intervention group because the parents believed it was better for their child not to be reminded about the MTBI.

Baseline characteristics are presented in Table 1. Tests showed no significant differences on demographic characteristics, premorbid functioning, and MTBI symptom characteristics between groups at two weeks post-MTBI. Furthermore, tests showed no significant baseline differences on the primary and secondary outcome measures (Tables 2 and 3), except for PCS as reported by the caregivers, with lower levels of PCS in the intervention group at baseline ($p= .048$).

Effects of the intervention

The total CASP-DLV score improved significantly over time between two weeks and six months post-MTBI, and so did the CASP-DLV scores in all different settings (home, community, school, and environment) (Table 2). This applies for both parent-reports as well as for the child self-report.

The intervention and control group were not significantly different on the CASP-DLV parent-report for children 6-18 years old, during the first six months post-MTBI (Table 4a). For children aged 10-18 years old from both the parents' and the child's perspective (Table 4b) a significant difference was found only in the community setting based on the caregivers' perspective. Since there were no children who reported full functioning on the total level of activities and participation at baseline (see Table 2), a GEE for this measure could not be performed. Therefore, we performed a logistic regression analysis, with the CASP-DLV as dependent variable and group allocation as independent binary variables.

Figure 1. Flow of participants

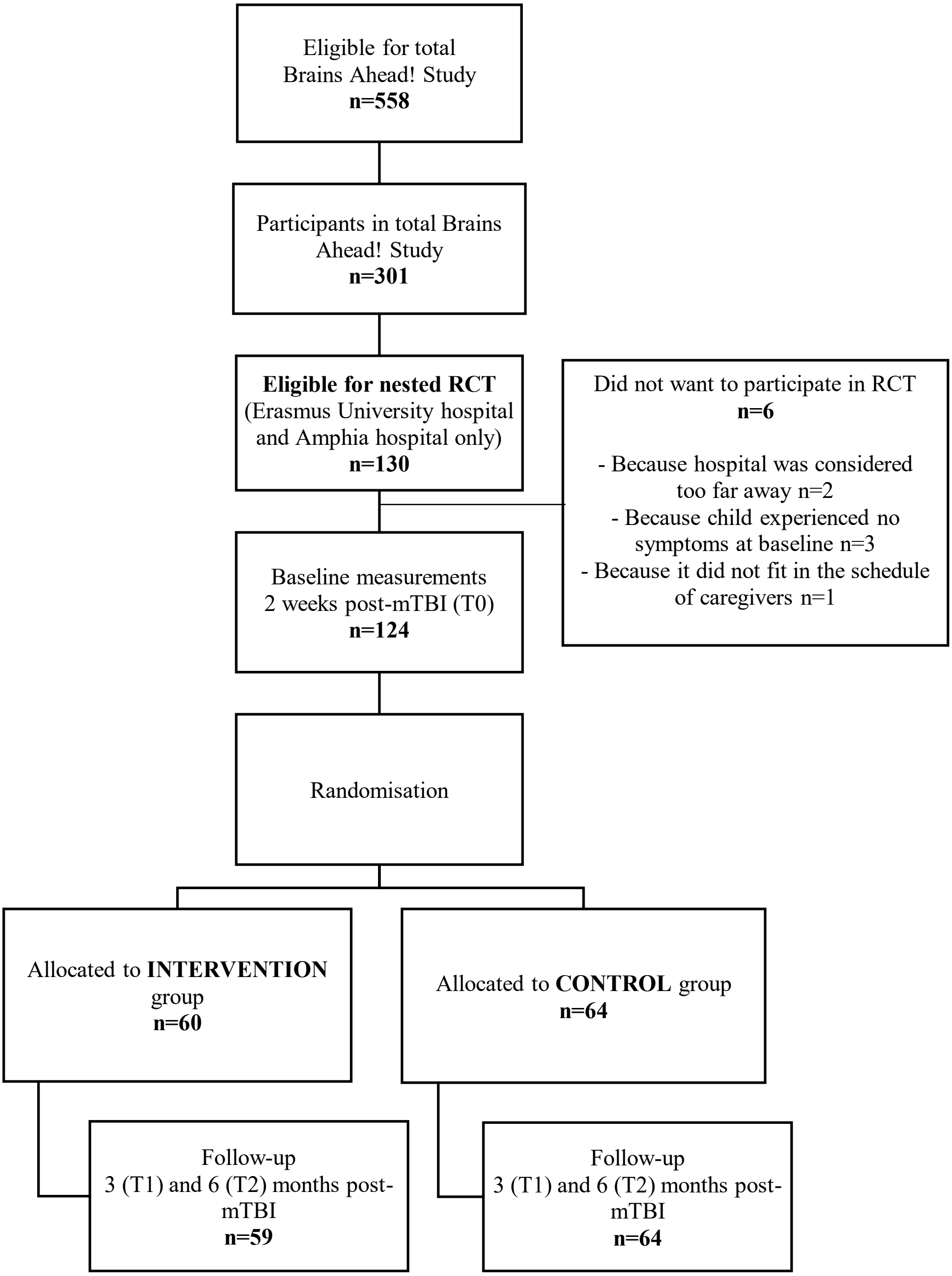

Table 1. Baseline characteristics at T0

	Characteristics	Control group (N=64)	Intervention group (N=60)
		N (%)	*N (%)*
Personal	Child gender: male	39 (60.9)	32 (53.3)
	Child age at injury in years (M, *SD*)	11.7, *3.5*	11.5, *3.3*
	(Min – Max, Range)	(6 – 17)	(6 – 17)
Injury-related	GCS:		
	13	5 (7.8)	5 (8.3)
	14	16 (25.0)	11 (18.3)
	15	43 (67.2)	44 (73.3)
	LOC duration:		
	None	31 (48.4)	27 (45.0)
	<2 minutes	19 (29.7)	21 (35.0)
	2-5 minutes	11 (17.2)	8 (13.3)
	>5 minutes	3 (4.7)	4 (6.7)
	PTA duration:		
	None	13 (20.3)	14 (23.3)
	<1 hour	33 (51.6)	35 (58.3)
	1-2 hours	5 (7.8)	2 (3.3)
	2-6 hours	10 (15.6)	6 (10.0)
	6-12 hours	2 (3.1)	2 (3.3)
	12-18 hours	0 (.)	0 (.)
	18-24 hours	1 (1.6)	1 (1.7)
	Cause of injury:		
	Traffic accident	20 (31.3)	23 (38.3)
	Sports accident	21 (32.8)	14 (23.3)
	Outdoor play accident	15 (23.4)	14 (23.3)
	Accident at school/work	3 (4.7)	5 (8.3)
	Accident at home	2 (3.1)	3 (5.0)
	Physical abuse	2 (3.1)	0 (0.0)
	Other	1 (1.6)	1 (1.7)
Environmental	SES:		
	Low	16 (25.0)	17 (28.3)
	Average	14 (21.9)	15 (25.0)
	High	34 (53.1)	28 (46.7)
Pre-injury functioning	Pre-injury Behavioral functioning (CBCL)		
	Normal score	55 (85.6)	53 (90.1)
	Mild impaired	5 (8.0)	5 (8.5)
	Severe impaired	4 (6.4)	2 (3.4)
	Pre-injury Family functioning (FAD-GF)		
	Healthy score	50 (78.1)	51 (85.0)
	Unhealthy score	14 (21.9)	9 (15.0)

GCS = Glasgow Coma Scale score, LOC = Loss of Consciousness, PTA= Posttraumatic amnesia, SES = Caregiver's Socioeconomic State, CBCL = Child Behavior Checklist T-scores, FAD-GF = Family Assessment Device – General Functioning

Table 2. Dichotomized descriptive outcome for primary outcome measure (CASP) over time*

		T0		T1		T2	
	CASP Setting	**Control group** *N (%)*	**Intervention group** *N (%)*	**Control group** *N (%)*	**Intervention group** *N (%)*	**Control group** *N (%)*	**Intervention group** *N (%)*
Caregiver report 6-18	Total	9 (14.1)	17 (28.3)	34 (53.1)	33 (55.0)	39 (60.9)	36 (60.0)
	At home	26 (40.6)	27 (45.0)	46 (71.9)	47 (78.3)	55 (85.9)	49 (81.7)
	In the community	25 (39.1)	20 (33.3)	43 (67.2)	42 (70.0)	51 (79.7)	44 (73.3)
	At school	24 (37.5)	26 (43.3)	50 (78.1)	45 (75.0)	55 (85.9)	53 (88.3)
	In the environment	21 (32.8)	26 (43.3)	44 (68.8)	38 (63.3)	45 (70.3)	45 (75.0)
Caregiver report 10-18	Total	7 (16.7)	7 (17.1)	20 (47.6)	23 (56.1)	24 (57.1)	26 (63.4)
	At home	16 (38.1)	14 (34.1)	29 (69.0)	32 (78.0)	35 (83.3)	36 (87.8)
	In the community	19 (45.2)	8 (19.5)	27 (64.3)	28 (68.3)	30 (71.4)	31 (75.6)
	At school	16 (38.1)	13 (31.7)	33 (78.6)	30 (73.2)	35 (83.3)	37 (90.2)
	In the environment	14 (33.3)	13 (31.7)	27 (64.3)	26 (63.4)	29 (69.0)	31 (75.6)
Self-report 10-18	Total	0 (.00)	3 (7.3)	11 (26.2)	20 (48.8)	10 (23.8)	20 (48.8)
	At home	4 (9.5)	6 (14.6)	21 (50.0)	27 (65.9)	22 (52.4)	30 (73.2)
	In the community	4 (9.5)	5 (12.2)	22 (52.4)	26 (63.4)	24 (57.1)	30 (73.2)
	At school	10 (23.8)	8 (19.5)	27 (64.3)	30 (73.2)	30 (71.4)	33 (80.5)
	In the environment	5 (11.9)	4 (9.8)	17 (40.5)	24 (58.5)	14 (33.3)	23 (56.1)

* Numbers represent the amount of children with dichotomized full functioning scores on the CASP at T0, T1 and T2
T0=two weeks post-MTBI, T1=3 months post-MTBI, T2=6 months post-MTBI

The regression analysis showed a significant result at three months (T1) post-MTBI (β=-.99, *p*= .036) and at six months (T2) post-MTBI (β=-1.11, *p*= .020), indicating a higher self-reported total level of activities and participation in the intervention group compared to the control group.

We found significant improvements at T2 (six months) post-MTBI on the PedsQL-Fatigue, the IES, the PedsQ-QoL, and the HBI, except for the HBI scores based on the parent reports (Table 5).

Table 3. Baseline descriptive outcome for secondary outcome measures (T0)

	N	Control M (SD)	Intervention M (SD)
PedsQL - Fatigue - Parents	124	62.39 (2.45)	65.32 (2.33)
PedsQL - Fatigue - Children	124	62.74 (2.01)	63.18 (2.14)
PCS HBI - Parents	124	98.31 (2.89)*	90.70 (2.86)*
PCS HBI - Children	106	99.67 (2.60)	99.40 (2.94)
PedsQL - QoL - Parents	124	69.94 (2.43)	72.33 (2.46)
PedsQL - QoL - Children	124	71.77 (2.02)	75.21 (1.79)
PTSS IES - Parents	124	62.30 (2.18)	60.42 (1.97)
PTSS IES - Children	106	65.02 (2.26)	61.06 (1.78)

M = Mean, PedsQL- Fatigue = Paediatric Quality of Life inventory – fatigue scale, PCS = Postconcussive symptoms, HBI = Health and Behavior Inventory, PedsQL- QoL = Paediatric Quality of Life inventory – Quality of Life scale**,** PTSS = Posttraumatic Stress Symptoms, IES = Impact of Event Scale
* Significant difference at baseline between groups

Table 4a. Intervention effect on the CASP-DLV (primary outcome measure) - Randomization * Time

		Wald χ^2 interaction	*df*	*p*	OR	95% CI for OR
Total	T0-T1-T2	3.739	2	.154		
	T0-T1	3.657	1	.077	2.692	.976 – 7.428
	T0-T2	2.454	1	.117	2.240	.817 – 6.146
Home	T0-T1-T2	2.497	2	.287		
	T0-T1	1.194	1	.275	1.827	.620 – 5.385
	T0-T2	.105	1	.746	.845	.305 – 2.340
Community	T0-T1-T2	1.500	2	.472		
	T0-T1	.122	1	.727	1.210	.415 – 3.525
	T0-T2	.619	1	.431	.684	.266 – 1.760
School	T0-T1-T2	.755	2	.685		
	T0-T1	.093	1	.761	1.198	.374 – 3.841
	T0-T2	.746	1	.388	1.517	.589 – 3.908
Environment	T0-T1-T2	2.119	2	.347		
	T0-T1	.355	1	.551	1.349	.504 – 3.606
	T0-T2	2.053	1	.152	1.994	.776 – 5.128

NB: GEE outcome CASP-DLV parent-reports 6-18 years old
T0=two weeks post-MTBI, T1=3 months post-MTBI, T2=6 months post-MTBI

Success of blinding

The researcher answered the correct group allocation in 73 (59%) of the cases.

Table 4b. Intervention effect for primary outcome measure - parent- and child reports 10-18 years old

			Wald χ^2 interaction	*df*	*p*	OR	95% CI for OR
CASP-DLV Child Reports 10-18 years old *N*=83	**Total**	T0-T1-T2					
		T0-T1					
		T0-T2					
	Home	T0-T1-T2	.158	2	.924		
		T0-T1	.137	1	.711	.741	.152 – 3.622
		T0-T2	.049	1	.826	.844	.188 – 3.798
	Community	T0-T1-T2	.190	2	.909		
		T0-T1	.167	1	.682	.728	.159 – 3.332
		T0-T2	.061	1	.805	.837	.205 – 3.425
	School	T0-T1-T2	1.163	2	.559		
		T0-T1	.832	1	.362	.545	.148 – 2.007
		T0-T2	1.048	1	.306	.512	.142 – 1.844
	Environment	T0-T1-T2	1.708	2	.426		
		T0-T1	1.625	1	.202	.345	.067 – 1.771
		T0-T2	1.384	1	.239	.385	. 079 – 1.887
CASP-DLV Parent Reports 10-18 years old *N*=83	**Total**	T0-T1-T2	.251	2	.882		
		T0-T1	.040	1	.841	.878	.248 – 3.108
		T0-T2	.217	1	.641	.732	.198 – 2.716
	Home	T0-T1-T2	1.008	2	.604		
		T0-T1	.223	1	.636	.722	.187 – 2.784
		T0-T2	.994	1	.319	.529	.151 – 1.850
	Community	T0-T1-T2	6.081	2	.048		
		T0-T1	3.932	1	.047	.269	.073 - .985
		T0-T2	5.437	1	.020	.245	. 075 - .799
	School	T0-T1-T2	1.150	2	.563		
		T0-T1	.822	1	.365	.524	.130 – 2.119
		T0-T2	.001	1	.982	1.014	.291 – 3.486
	Environment	T0-T1-T2	.253	2	.881		
		T0-T1	.200	1	.655	.760	.228 – 2.534
		T0-T2	.004	1	.950	.964	.306 – 3.037

Randomization * Time

T0=two weeks post-MTBI, T1=3 months post-MTBI, T2=6 months post-MTBI

Table 5. Intervention effect on secondary outcome measures (T2)

	T2		T2		
	Control M (SD)	**Intervention M (SD)**	***N***	***U***	***p***
PedsQL - Fatigue - Parents	73.81 (2.12)	80.11 (2.10)	123	1468.000	.033
PedsQL - Fatigue - Children	69.86 (2.30)	77.26 (2.28)	123	1438.500	.023
PCS HBI - Parents	83.69 (3.07)	79.51 (3.15)	123	1659.500	.247
PCS HBI - Children	92.05 (3.39)	82.04 (3.26)	105	1043.5	.037
PedsQL - QoL - Parents	76.51 (2.82)	86.42 (1.71)	123	1472.500	.035
PedsQL - QoL - Children	80.81 (1.95)	88.47 (1.36)	123	1299.500	.003
PTSS IES - Parents	49.77 (1.85)	44.22 (1.56)	123	1293.500	.003
PTSS IES - Children	61.70 (3.00)	50.19 (1.91)	105	945.500	.007

PedsQL- Fatigue = Paediatric Quality of Life inventory – fatigue scale, PCS = Postconcussive symptoms, HBI = Health and Behavior Inventory, PedsQL- QoL = Paediatric Quality of Life inventory – Quality of Life scale, PTSS = Posttraumatic Stress Symptoms, IES = Impact of Event Scale

Discussion

Children with MTBI and their caregivers reported increasing levels of activities and participation of the child during the first six months post-MTBI, irrespective of group allocation. We found that the procedure of the Brains Ahead! intervention did not significantly add to the total level, and the level of activities and participation in different settings over time post-MTBI, but caregivers in the intervention group rated children aged 10-18 years to be more active and to participate more in the community compared to the control group. Although not significant, more children in the intervention group self-reported full functioning on the level of activities and participation in all different settings compared to the control group at three and six months post-MTBI. This difference in settings resulted in a significant higher total level of activities and participation in the intervention group compared to the control group.

In addition, children with MTBI and caregivers who received the Brains Ahead! intervention, reported significant less functional- (fatigue and PCS) and posttraumatic stress symptoms and an improved QOL at six months post-MTBI compared to those who received usual care. Caregivers in the intervention group reported less PCS at baseline compared to the control group, which could explain why – in contrast to the other outcome measures - a non-significant improvement on PCS by caregivers was found. These findings indicate that the Brains Ahead! intervention has the potential to decrease functional and posttraumatic stress symptoms and increase quality of life after MTBI in children.

The results of our study correspond to earlier intervention studies in children after MTBI, showing an intervention effect on PCS and stress symptoms,[13] but not on the daily level of activities.[12-13] To the best of our knowledge, this is the first study to add positive results on quality of life after MTBI in children who received an early psychoeducational intervention. Furthermore, our study adds to the literature that perspectives of children and caregivers concerning activities and participation differ. In addition, decisions of caregivers on letting their child return to daily activities or not, for example based on anxiety of the caregiver, affects the level of activities and participation as reported by the child as well. Therefore, we emphasize the importance of assessing both perspectives in future studies and in clinical settings.

What distinguishes the Brains Ahead! intervention from existing interventions is the individualized approach, giving specific attention to those symptoms the individual child experiences, and to the personal situation of each child and family in making a plan to return to activities and participation. Although it is known that not all children suffer from all possible symptoms after MTBI, this is the first intervention to first screen for symptoms per child and then integrate this screening into the provision of information. This ensures that, although partly standardized information is given, the intervention is now more child-specific, and an information overload is prevented.

This study has several strengths. First, in previous studies, mixed TBI-samples with small groups of children with MTBI were included, providing little insight into activities and participation for this specific group. We included children with MTBI only, and assessed children of all school ages (6-18) who suffered from MTBI and their caregivers. Second, the study design, implementing a nested RCT in a multicenter longitudinal prospective cohort, enabled us to investigate the effectiveness of the intervention on a relatively short-term basis. We believed this was an efficient way of investigating this group of participants from an ethical perspective as well. And third, the outcome instruments used in this study are recommended for evaluating outcomes in children after brain injury,[31] and based largely on the International Classification of Functioning, Disability and Health for Children and Youth (ICF-CY).

This study also has some limitations. First, children and adolescents with MTBI were recruited from emergency departments of hospitals, and may therefore not be representative of the larger population such as those children who do not receive acute medical care. Second, with regard to data collection, retrospective ratings of pre-injury functioning of the child and the family was gathered. This may be a concern for bias, although ratings were collected within two weeks post-MTBI, which seems surmountable.

The lack of effectiveness of the intervention on activities and participation. may be explained by the idea that, although children may suffer from symptoms such as fatigue, PCS PTSS and a lower perceived QOL, they may still participate fully on all activities despite their symptoms. Children may keep doing so for quite some time, before on the long term their untreated symptoms become a heavier burden and the energy to keep participating in all activities might start to decline. Therefore, future studies should aim at a longer follow-up time post-MTBI.

Another reason for the lack of effectiveness of the intervention on activities and participation may be the ceiling effect on the CASP. The CASP seems a reliable instrument to assess activities and participation in children with more severe head injuries, but may not be the best measure for children with MTBI. To the best of our knowledge, though, a better instrument to assess activities and participation in children after MTBI at this point does not yet exists. We emphasize the importance of developing an instrument that is more sensitive in distinguishing levels of activities and participation among children with mild brain injuries.

The lack of effectiveness on activities and participation of our intervention may also be explained by the fact that most children recover completely after MTBI without intervention. In our study, the intervention was provided to all children with MTBI, while it might be better to provide it only to those who are at risk for long-term problems on activities and participation. For this, prognostic factors for long-term outcomes in activities and participation should be identified.

Currently, feasibility of the Brains Ahead! intervention process is being evaluated and prognostic factors for outcome on activities and participation are examined. Findings of these studies may further support implementation of the intervention in clinical practice, especially to those who are at risk for long-term problems. Furthermore, long-term follow-up data in this cohort study-sample will be collected at 1.5 and 5 years post-MTBI and maybe useful for future trial designs.

Conclusion

Superiority for the intervention over usual care was found for fatigue, PCS, PTSS and QOL. Effect on activities and participation should be studied using other more sensitive outcome measures and extend at a more long term follow up. Despite the lack of effect found on activities and participation, we recommend implementation of the intervention because of the positive effect on functional outcome and quality of life.

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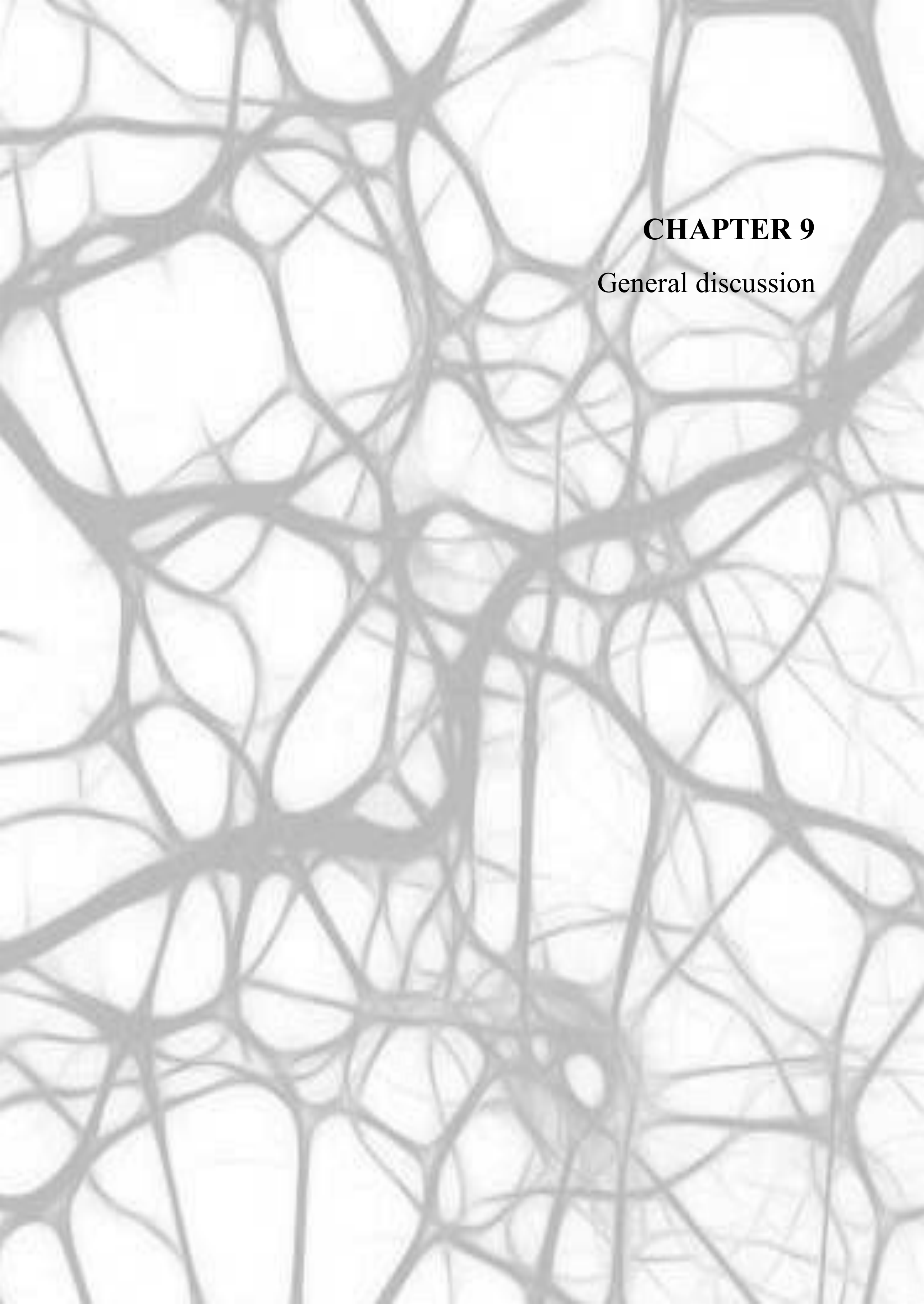


CHAPTER 9

General discussion

The present thesis describes the Brains Ahead! study, which consists of two main studies into activities and participation. The International Classification of Functioning, Children and Youth version (ICF-CY) provides a holistic framework for the consequences of childhood traumatic brain injury on participation, and defines participation as involvement in life situations.[1] The main objectives of the first study in this thesis, the multicenter longitudinal prospective cohort study, was to examine the course of activities and participation after mild traumatic brain injury (MTBI) in children and adolescents and examine predictors for outcome. The main objective of the second study was to develop and examine the feasibility and effectiveness of the Brains Ahead! intervention for children and adolescents with MTBI and their caregivers in a randomized controlled trial study, which was nested in the prospective cohort study. This chapter starts with an overview of the main findings. Subsequently, methodological strengths and limitations of our studies are discussed. In addition, clinical implications and recommendations for future research are presented.

Main findings

Most children recover and psychosocial factors are superior in predicting outcome

In the studies described in chapters 3 and 4 the focus was on the natural course of activities and participation during the first six months after MTBI in children and adolescents, for how many children long-term problems on activities and participations are reported, and how they are best predicted.

Chapter 3 described the course of activities and participation during the first six months in different settings (e.g. at home, at school, in the community and in the environment), and for several activity domains (e.g. recreational, active physical, social, skill-based and self-improvement activities) and from different perspectives (e.g. self-report and caregiver report). In general, the results showed that the level of activities and participation was lowest at two weeks post-injury, increased up to three months post-injury, and stabilized up to six months post-injury in most settings and activity domains. Caregivers evaluated their child's level of activities and participation in different settings more positive compared to the evaluation of the children themselves. Depending on the perspective and setting chosen, 34% to 64% of the children with MTBI still participate less in comparison to their peers at six months post-injury.

Chapter 4 focused on the predictive value of factors within the health condition, function, activities, environment, and personal categories for outcome on activities and participation six months after MTBI in children and adolescents. The results showed that predictors for children who are at risk for long-term consequences on activities and participation differ per setting (e.g. at home, in the community, at school, and in the environment) and per chosen perspective (e.g. either child or caregiver). When selecting those children wo are at risk for decreased activities and participation after pediatric MTBI, not injury-related factors but more behavioral problems and worse family functioning pre-injury, more symptoms post-injury and less resumption of activities should be considered. Since our final models only explained only a small proportion of the variance in outcome on activities and participation after MTBI, other factors, such as coping styles, emotion-regulation, personality traits, social support, and other comorbid problems, may add to the prediction.

The Brains Ahead! intervention is effective and feasible

Chapter 5 described the results of a scoping review on what is known about early interventions for children after MTBI and what is recommended for future development of such interventions. Most interventions for children with MTBI are designed to reduce symptoms, and are not specifically designed to improve the level of activities and participation. Evidence from the scarce literature on interventions for children after MTBI, combined with results from mixed TBI sample studies, and literature on interventions aimed at improving activities and participation after MTBI in adults, suggest that information and education should always be offered, ideally followed by a consultation in which personalized reassurance is given. The family should be involved and problem-solving interventions seem effective. In addition, clinical recommendations suggest a step-by-step return to both cognitive and physical activities.

Although a substantial number of children experiences limitations on the level of activities and participation six months after MTBI, there are no studies on interventions that are set up in order to prevent these limitations. Therefore, we developed the Brains Ahead! psychoeducational intervention, which is described in chapter 6. This is the first intervention that prospectively intends to prevent long-term problems related to activities and participation in children and adolescents aged 6 to 18 years old following MTBI. The Brains Ahead! psychoeducational intervention combines an inventory of symptoms, psychoeducation, and follow-up, and involves the child's family in the process.

In chapters 7 and 8 the results of the feasibility and effectiveness of the Brains Ahead! intervention were presented. Chapter 7 showed that the intervention is sufficiently feasible, participants indicated that the intervention was useful in helping them to better understand the injury and its consequences, and also had helped them to return to activities and participation. Further findings showed that the timing of the intervention could be improved, and preferably should be offered to patients and caregivers as soon as possible after the MTBI. Also, it was found that one informational and reassuring follow-up contact probably is enough to help better understanding of symptoms and return to activities and participation after MTBI. The results of our randomized controlled trial (chapter 8) showed that the Brains Ahead! intervention was found to be superior over usual care at reducing fatigue, post-concussive symptoms (PCS), posttraumatic stress symptoms (PTSS), and at improving Quality of life (QOL) after paediatric MTBI, but no significant effect on activities and participation was found.

When connecting the findings of chapters 7 and 8, it seems that although participants indicate that they are very satisfied with the Brains Ahead! intervention and it was helpful in making a safe plan to return to activities and participation, this does not per se result in full return to activities and participation on a measurement scale.

Natural recovery and predictors for outcome after pediatric MTBI

Activities and participation are very important for the development of a child, since it helps children to acquire different skills and competencies, grow physically and cognitively, develop their own identity and set different life goals.[2] Chapter 3 of the present thesis adds to the literature that, consistent with pediatric literature on PCS, most children naturally return to maximum level of activities and participation within three months after MTBI. In a substantial number of children, however, the level of activities and participation at six months post-injury is still evaluated as less in comparison to peers.

Chapter 4 of the present thesis added furthermore, that children after MTBI should be screened for maladaptive pre-injury factors (behavioral functioning of the child, and family functioning), more (PCS and PTSS) symptoms in the first two weeks post-injury and less resumption of activities in the early post-injury period, in order to find out who is at risk for such an adverse outcome. Predictors, however, differed between the perspectives of the caregiver and the children.

Since our predictive model (chapter 4, figure 1) only explains a small proportion of the variance in natural outcome on activities and participation after MTBI, other factors may add to the prediction. Psychological resilience, for example, was found to play an important role in the recovery from concussion in adolescents.[3] Anxiety and the experience of depressive symptoms are thought to be important mediators for this relationship, and therefore, should also be considered.[3]

It is important to recognize that outcomes may be worse due to the way of messaging the injury. Health care providers can guide the relationship between anxiety and resilience, and thereby possibly induce a better recovery from MTBI, based on their professional status and their ability to reassure patients.[4]

Reassurance is thought to be one of the key features of intimate interaction, often found in relatives and friends, which is part of the concept structure of social support.[5] Therefore, in addition to health care professionals, reassurance may also be found in social support from caregivers and peers. Social support from family and friends was also found to be of direct influence to participation in general, and after brain injury,[6-7] as was involvement of family and relatives in treatment programmes.[8] Notably, it is suggested that social support is one of the leading environmental factors determining participation, along with negative attitudes of community members.[9] Positive reinforcement, which can be provided by family and friends in general or as a characteristic of treatment, may therefore explain positive effects on individual goal achievement.[8] Furthermore, the child's perceived self-efficacy may function as internal reinforcement, since it may play a fundamental role in one's ability to reduce discrepancy between achievements and expectations.[10] It was found that children after MTBI often appear to lack confidence in their ability to perform during physical activities as compared to before their injury.[11] Furthermore, motivation may also be affected after MTBI and could also influence participation.[4,11]

The core elements of resilience include a higher level of self-control and motivation towards accomplishments, higher levels of positive emotions, and engagement with social activity, and a higher level of emotional stability.[12] These elements are found to be more prominent in some personality traits (e.g. conscientiousness and extraversion) than in others (e.g. neuroticism).[12] In adult stroke patients, pro-active coping, self-efficacy and extraversion were found to be adaptive psychological factors for participation outcome, while passive coping and neuroticism were found to be maladaptive psychological factors.[13-18] Neurotic personality traits and maladaptive coping were also found to directly predict outcome after MTBI in the adult population.[19-20] However, reversible, symptoms after adult MTBI such as stress and inflammatory responses, may also alter coping skills and personality.[21] Like adults, children and adolescents can also be described in terms of personality traits, but full understanding of youth personality traits at this point requires additional research at the intersection of personality, developmental, and clinical psychology.[22]

In the long term, resilience and the extent to which an individual is easily reassured may therefore be dependent on factors such as personality, coping styles and the child's emotion-regulation, but also stress and anxiety. Furthermore, self-esteem is considered to be one of the most important pillars of healthy personality development, and has a positive relationship with resilience as well.[12] Finally, other comorbid problems (such as chronic pain), substance abuse, and protracted litigation may influence outcome after MTBI as well.[23]

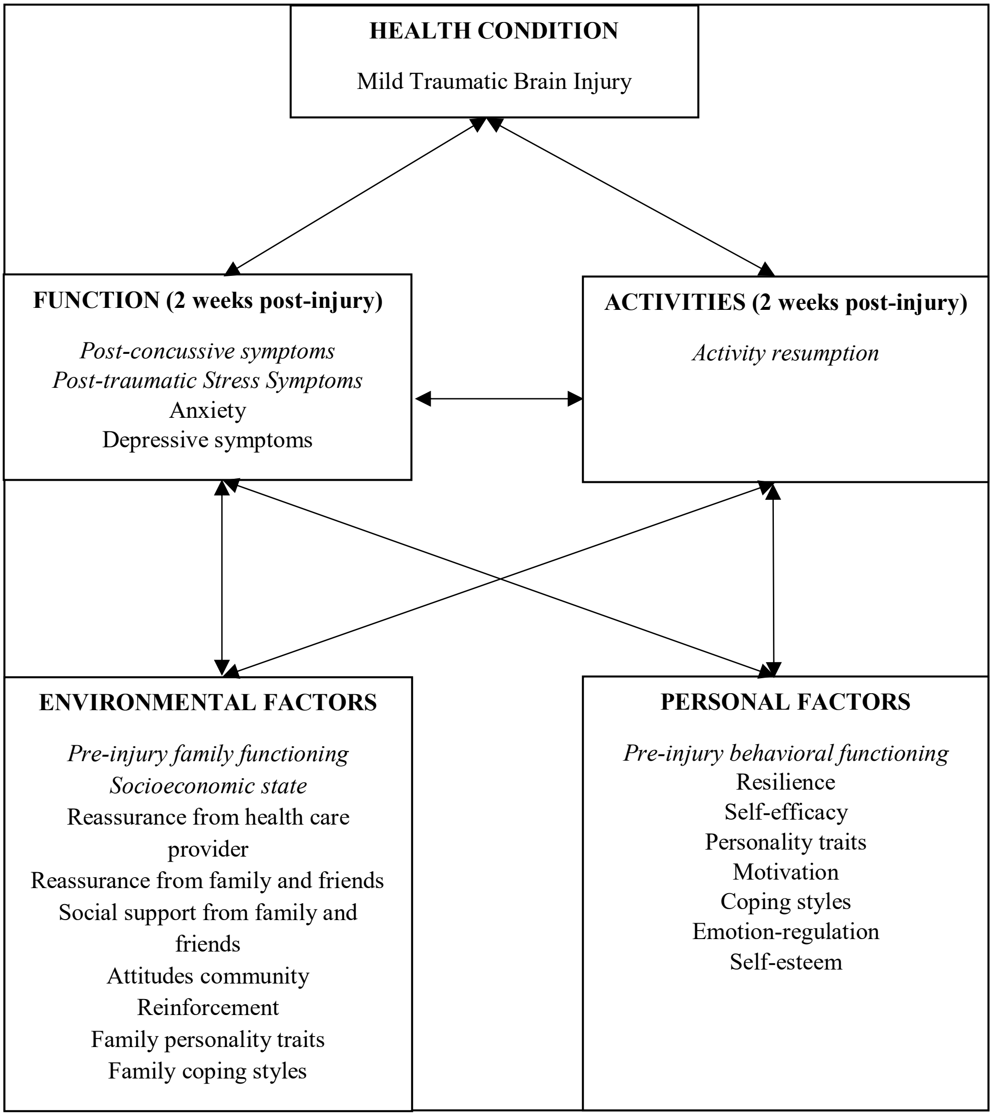
As can be derived from above, especially personal-and environmental factors are found to predict participation outcome after acquired brain injury in general. This is consistent with the statement that the definition of participation as involvement in a life situation needs to be extended with subjective psychological aspects. The abovementioned possible predictors for participation outcomes are found in studies including adults with MTBI and/or children with mixed TBI severity and/ or other varieties of acquired brain injury, and are, at this point, not yet investigated in one comprehensive predictive model for paediatric MTBI. Nevertheless, it is expected that the majority of additional factors predicting outcome on activities and participation after MTBI are also to be found in personal and environmental categories. Therefore, a proposal of our improved predictive model with relevant predictors based on the categories from the ICF-CY model is presented in Figure 1 of this chapter.

The Brains Ahead! intervention for children with MTBI and their caregivers

During brainstorm-meetings with the Brains Ahead! project group in de period before drafting the study-design, child-neurologists and child-rehabilitation professionals specialized in working with children after traumatic brain injury, indicated that there was a need for educational information and reassurance at an early stage after pediatric MTBI. The project group furthermore discussed that provision of education and reassurance may help reduce the number of children appealing to professional care for mainly resilience, and those in need for long-term treatment. Following our suggested predictors for outcome, those children who are at risk for long-term problems after MTBI, may benefit from a psychoeducational intervention.

Prior to the development of our Brains Ahead! intervention, we knew that information and education should always be offered, ideally followed by a consultation in which personalized reassurance is given. Furthermore, the family should be involved and clinical recommendations suggest a step-by-step return to both cognitive and physical activities (chapter 5). We implemented these important early intervention features in the Brains Ahead! intervention for children after MTBI and their caregivers and investigated its feasibility and effectiveness (chapters 6, 7, and 8).

Figure 1. Proposed model of relevant predictors based on the categories from the ICF-CY model



Italic: Predictive factors included in the Brains Ahead! study
Other: Proposal of possible other predictive factors

At recruitment, children and caregivers indicated that the received information from usual care at discharge was lacking, and that they had many unanswered questions on the recovery process, occurring symptoms and how to decide on return to activities and participation, but did not know who to turn to. This confirmed the need for information at an early stage after the injury.

Our feasibility study showed that the Brains Ahead! intervention was evaluated as highly useful by the children and their caregivers, and it was found that their expectations of the intervention were mostly met (chapter 7). Furthermore, the intervention was not more effective on preventing long-term problems on activities and participation in comparison to usual pediatric care after MTBI, but it was superior in preventing long-term function symptoms (fatigue, PCS, and PTSS) and was more beneficial for a better perceived quality of life (chapter 8).

From chapters 7 and 8 it can be derived that although participants indicate that the Brains Ahead! intervention is useful and met their expectations, this does not per se result in a significant improvement on a measurement scale. Similar findings were found in a study that investigated the effect of a cognitive rehabilitation program in a group of patients with acquired brain injury.[24] They also suggest that focusing on what patients want to achieve themselves, in other words patient-based measurement, is probably more important than intervention-based measures, focusing on the intervention goal(s) without taking personal goals into account.[24]

In our study, the CASP is more an intervention-based measure, because it measures the level of activities and participation in different settings compared to age-related peers, but does not measure the degree to which the participants feels satisfied with the activities and participation level. Examination of participation, while considering the subjective dimension of participation, such as satisfaction or feeling proud about participating, may provide a more complete overview.[6,25]

In the current ICF-CY model, the definition of participation is limited to involvement in a life situation.[1] In a review of language, definitions, and constructs used in participation intervention research with children, it was found that the terms participation and engagement are both tend to be used interchangeably, but that participation restriction can also be seen as low engagement involvement.[26] In accordance with previous studies[6,27] we emphasize that optimal participation is a personal, subjective experience, through which children are able to derive meaning from their engagement in life, and we support the idea of extension of the ICF-CY definition by subjective psychological aspects of participation.[6,28-30]

The findings of our study are in line with those of an intervention primarily aimed at preventing societal participation problems, and secondarily aimed at preventing function problems and the caregivers well-being in patients after cardiac arrest.[31] In this study, also no significant effect on the primary participation outcome was found, but survivors scored better on secondary outcome measures.[31] This also adds to the idea that participation in its current definition, is perhaps not what we should be examining and interventions should target, but more attention to the subjective psychological aspects of participation is warranted.

Although the intended effect on the level of activities and participation was not achieved, which could be explained by the various reasons mentioned in this thesis, we believe that the Brains Ahead! intervention could successfully be implemented in order to help reduce the number of children appealing to professional care shortly after discharge, and those in need for long-term treatment. The process of the Brains Ahead! intervention in its current form, may, however, need some adjustments (such as timing and distribution of the intervention-components) in order to better match with clinical practice possibilities and the whishes from the children and their caregivers.

Towards a stepped care approach

As can be derived from the above, most children recover completely without support, some children do benefit, and others do not benefit (enough) from a psychoeducational intervention. It seems that there is no 'one size fits all' when it comes to care for children after MTBI. Prognostic factors can be used to set up a stratified approach, which can lead to improved care efficiency and higher health gains.[32] Based on our study findings and with respect to the knowledge from clinical practice, the recovery of children after MTBI can largely be divided into three categories, for which a stepped care approach also seems appropriate:

(1) The largest group of children, who are not at risk for an adverse outcome based on the screening of predictive factors, and who are believed to naturally recover completely from MTBI, do not need an intervention. Conform clinical guidelines,[33-34] these children and their caregivers should receive written information at hospital discharge, including the advice to return to their general practitioner in case questions on the recovery process arise.

(2) The children who are at risk for an adverse outcome based on the screening of predictive factors, should receive an intervention including personalized education, with additional follow-up. This study developed the Brains Ahead! intervention, which, after some practical adjustments, may be a good care-suggestion for these children who are at risk for adverse outcome after MTBI.

(3) Not all children who are at risk for long-term problems may sufficiently benefit from an intervention such as Brains Ahead! We did not investigate this, but based on the proposed importance of psychosocial factors such as personality and

coping for outcome after brain injury, we suggest that this would apply for children who are vulnerable for trauma, have a low self-image and self-esteem and who tend to worry a lot. These children may benefit from an additional treatment, such as cognitive behavioural therapy,[35] and/ or treatment focusing on processing of the trauma (such as EMDR[36-38]), and/ or systemic psychotherapy.[39]

Methodological strengths and considerations

Strengths

The two Brains Ahead! studies have several strengths. First, the study design, implementing a nested RCT in a multicenter longitudinal prospective cohort, enabled us to investigate the effectiveness of the intervention on a relatively short-term basis. We believed this was an efficient way of investigating this group of participants from an ethical perspective as well, and, therefore, a strength of the study (chapter 2).

A further strength of our study was that it largely based the use of study-instruments on recommendations for evaluating outcomes in children after brain injury by the inter-agency Pediatric TBI Outcomes Workgroup,[40] and on the International Classification of Functioning, Disability and Health for Children and Youth (ICF-CY) (chapter 2). In addition, predictors for activities and participation were also examined within the categories of human functioning following the ICF-CY framework, and were in the current study, as added value to the existing literature, investigated in one comprehensive model (chapter 4).

Regarding the studied sample, previous mixed TBI-sample studies, in which small groups of children with MTBI were included, provided little insight into activities and participation for this specific group.[25,41-47] The added value of the our study in comparison to these previous studies was that we included a large population of children with MTBI only, and assessed children of all school ages (6-18) who suffered from MTBI as well as their caregivers (chapters 3 and 4).

Regarding the strengths of our intervention study, we were the first to develop and examine the feasibility and effectiveness of an early psychoeducational intervention for children and adolescents with MTBI and their caregivers aimed at preventing long-term problems (chapters 7 and 8). Our intervention study has multiple other strengths. Most of them can be captured under the research methods and reporting we used in the Brains Ahead! study, which are highly in agreement with the Medical Research Council (MRC) framework for development, evaluation and implementation of complex interventions.[48]

For developing a complex intervention, they suggest that the first step is to identify existing evidence, what matches with our carried out scoping review into the role of early intervention in improving the level of activities and participation in youths after mild traumatic brain injury (chapter 5). The second suggested step is to identify and develop theory, with the rationale for the complex intervention and a theoretical understanding of the likely process of change by drawing on existing evidence. This matches with our paper on the rationale and description of the treatment protocol of the Brains Ahead! intervention for children and adolescents with mild traumatic brain injury and their caregivers (chapter 6).

For the evaluation of a complex intervention, the MRC first suggest assessing effectiveness with a randomized controlled study, that matches with our carried out randomized controlled trial study on the effectiveness of the Brains Ahead! intervention in school-aged children six months after mild traumatic brain injury (chapter 8).

The next suggested step is to decide which outcomes are most important, which are secondary, and how they will deal with multiple outcomes in the analysis. They furthermore suggest that it is important to consider which sources of variation in outcomes matter and to plan appropriate subgroup analyses. This matches with our chapter 2, in which we already determine our primary outcome measure (the Child and Adolescent Scale of Participation; CASP), and secondary outcome measures, which we largely based on recommendations for evaluating outcomes in children after brain injury by the inter-agency Pediatric Outcome workgroup, and the ICF-CY. In the introduction and methods sections of our chapter 8, we, furthermore, explain the importance of analysing for subgroups of caregivers and patients aged 10-18 years old separately in order to make a reliable comparison based on differences in perspectives.

The final step in the proposed framework is to perform a process evaluation, in order to provide valuable insight into why an intervention fails or has unexpected consequences, or why a successful intervention works and how it can be optimised. They suggest a process evaluation nested inside a trial, which can be used to assess fidelity and equality of implementation, clarify causal mechanisms, and identify contextual factors associated with variation in outcome. This matches with our process evaluation of the Brains Ahead! intervention for children and adolescents with mild traumatic brain injury (chapter 7).

Another important strength of our process evaluation was the use of both qualitative and quantitative research methods. In addition, the outcomes of the trial did not bias the outcome process evaluation, since outcome of the latter was analysed first.[49] Altogether it seems that our study fits the total package of the MRC framework for appropriate methods and reporting of complex interventions.[48]

Considerations

Although the studies in this thesis had several strengths, there were also some important limitations. First, our study design had the advantage of time enabling the conduction of the RCT-study parallel to the cohort-study. However, in case the cohort-study on predictors for problems on activities and participation had been conducted prior the RCT, this would have enabled targeting the intervention to those children who were at risk for long-term problems, which may had enlarged the effectiveness of it.

Second, children and adolescents with MTBI were recruited from hospital's emergency departments, and may therefore not be representative of the larger population as this excludes those who do not receive acute medical care. Next, a relatively large number of children who were eligible for participation in the study could not be reached, which influences the external validity. From the number of eligible participants who were reached however, almost 80% chose to participate.

Population research is needed to find out how the children who were missing in this study, function on the level of activities and participation. Better registration of patients' personal information into the hospitals electronic patient files may further help prevent inclusion-bias. We believe bias based on the (non-) existence of complaints after MTBI is minimalized by the fact that participants were included very shortly after the injury.

Concerning socioeconomic state (SES), however, mainly families with high SES were included, which seems apparent for participating in patient studies. Since SES was not found to be an important predictor for outcome on activities and participation in most settings within our study, we doubt that this would have influenced our study results. Enthusiasm for participation in patient studies by lower SES families may be enlarged by nourishing the need for these kinds of studies in, for example, schools and/ or general practitioner settings, or by offering a substantial reward for participation.

Another limitation of this study was that the intended effect on the level of activities and participation was not achieved, which could be explained by the various reasons mentioned in this thesis. One of the reasons may be that, although at the point of developing the study-protocol it seemed the best option, and a better instrument at this point still does not exist, at the time of analyzing our data and interpreting the results, our primary outcome measure for activities and participation (CASP), seemed to lack the sensitivity to differentiate for mild traumatic brain injury. We tried our best to cope with the ceiling effect of this measure, by dichotomizing the outcome into either full functioning on the level of activities and participation, or deviant functioning – defined as every score below full functioning.

Another reason may be that the CASP does not include subjective psychological aspects of participation, but it is limited to involvement in life situations in different settings, therefore providing us with a less complete view of participation.[1-2,6,28-30]

Another consideration may be that we were now targeting participation as an outcome and therefore a dependent variable, while perhaps we should focus on participation as a process, or an independent variable, which can be seen as a predictor or an entry point for changes at the activity and body function/structure level.[50] Interventions at the level of the body and/ or society may be necessary to promote participation in individuals, but neither alone is likely to be sufficient.[50] In addition, the family of participation-related constructs (fPRC) framework addresses issues at the level of de individual in context, and expands the activity and participation domain of the ICF-CY by further detailing related constructs within an overarching environmental framework.[26]

Considering our process evaluation, an important limitation of process evaluations in general, is that such evaluations are only possible by self-report questionnaires. As a result, there will always be a risk of socially desirable answers. In this study, an attempt was made to reduce this risk as much as possible by anonymizing self-reports. Another limitation of this study process evaluation is that fidelity (i.e. whether the intervention was performed according to protocol) was not measured by observation/video recordings, but with a self-report registration form as well.

Implications for clinical practice

The process of the Brains Ahead! intervention may need some adjustments (such as timing and distribution of the intervention-components) in order to better match with clinical practice possibilities and the whishes from the children and their caregivers. Based on the findings from our process evaluation, the intervention in its current form does not allow implementation in the hospital's emergency departments. Referral of patients at risk to primary care for the intervention at discharge from the emergency department, however, may be a suitable option. Since it was found that complaints, questions, and needs of the participants can be very diverse, providers of the intervention should, preferably, be experienced and educated in child rehabilitation after TBI, or should at least be appropriately trained.

Furthermore, we found that one informational and reassuring follow-up contact probably is enough to help better understanding of symptoms and return to activities and participation after MTBI, since further follow-up possibilities were very rarely used. During the recruitment period, it appeared that most children and caregivers were relieved when the child was discharged and hurried home, with the questions on the recovery process, occurring symptoms, and the need for individualized advice on returning to activities and participation emerging in the following days. Possibly, standardized information could be offered directly by primary care after referral from the emergency department, and more individualized information focused on the child's symptoms and advice on activities and participation fitting their personal situation, being offered either at a scheduled appointment one or two weeks after the injury, or scheduled at the patients request.

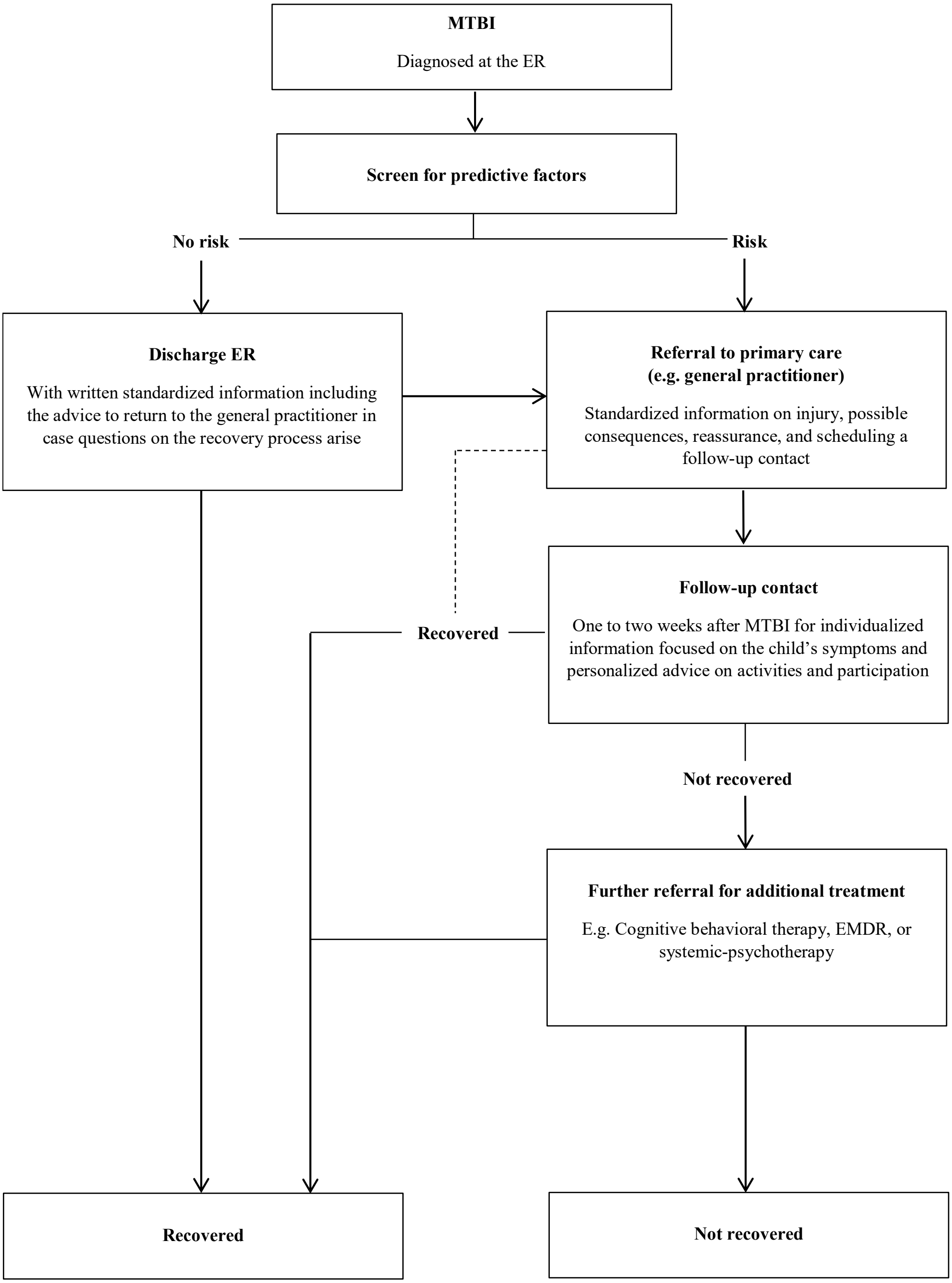
These minor adjustments in the intervention process can easily be made, and perfectly fits the proposed stepped-care approach, see Figure 2 of this chapter. Such a stratified management approach to target the provision of primary care may, in addition to improved care efficiency and higher health gains, provide substantial economic benefits compared with the current usual care.[32]

Directions for future research

Our study only included children who were admitted to the emergency room with MTBI. In order to learn more about the larger population of children with MTBI, including those who do not receive acute medical care, population research is needed. In the Dutch city of Rotterdam, a large population cohort-study following children from birth up to adulthood, was conducted (Generation R) and is currently extended with a new cohort-study (Generation R Next).[51-52] Adding questionnaires and instruments that are specific to MTBI related problems to their study-protocol, may help us differentiate between those receiving acute medical care after MTBI, and those who do not.

The intended effect of the intervention on the level of activities and participation was not achieved, which could be explained by the various reasons mentioned earlier in this thesis. As mentioned, the primary outcome measure (CASP) seemed to lack the sensitivity to differentiate for mild traumatic brain injury. Currently, the CASP is restricted to answering that the child either functions comparable to age-related peers or less. Therefore, information on children that for example functioned better in comparison to age-related peers prior to the injury, reduced to comparable to peers after the injury is lost. Possibly, adding to the multiple choice options that the child functions better or much better in comparison to age-related peers in the Child and Adolescent Scale of Participation (CASP), may help overcome this problem.

Figure 2. Proposed stepped-care approach for children with mild traumatic brain injury



Either way, we emphasize the importance of developing an instrument that is not only more sensitive in distinguishing levels of activities and participation among children with MTBI, but also captures the subjective psychological aspects of participation, such as satisfaction and the qualitative nature of engagement and meaning for children after MTBI.[6,25]

Another possibility is that future interventions should focus more on the underlying constructs of participation, such as reassurance and reduction of anxiety.[3,5,7-8,50] Although reassurance is recommended after MTBI (chapter 5), different types of reassurance (e.g. affective and/ or cognitive) in primary care may affect outcome differently.[53-54] Recently, a measure of consultation-based reassurance in primary care for people with low back pain was developed, and found to be reliable and valid for this purpose.[55] Literature shows that reassurance is a complex process, involving an interaction of patient experience, thoughts and beliefs, and emotions in a social context, as well as an outcome measured in health behavior.[54] Therefore, we suggest that the understanding of what reassurance is and how it is best provided within the context of children with MTBI should be investigated. In order to do this, a valid and reliable measure of the process of reassurance after MTBI in children should be developed.

Since the child's level of participation after MTBI is differently experienced by caregivers and children, and predictors also differed between the perspectives, for future studies it is important to carefully choose a perspective. One can think of the idea that for younger children caregivers may have a more complete view of theirs child's functioning, and therefore caregivers might be the primary perspective, while older children spend more time after school with friends and out of their parents' sight, and it might be better to primarily investigate their perspective instead. Regarding social support and reassurance from family, parents with an active coping style, may contribute to the motivation of the child to return to activities and participation, while on the other hand, worrying parents may contribute to maintaining of symptoms instead.[56] The interaction of caregivers with the child after MTBI is a key-element of effective interventions, and should be concerned when or if choosing perspective for outcome.[57-58]

We propose a stepped-care approach for children after MTBI with the first step being differentiation based on suggested risk factors for long-term problems, and the second step being differentiation between those who benefit sufficiently from an intervention such as the Brains Ahead! intervention, and those who need additional treatment. Implementing this stepped-care approach in clinical practice and evaluating its effects would take us another step further into connecting research findings with clinical demands regarding pediatric MTBI. In case the results of such an approach turn out to be promising, investigation of the cost-effectiveness of this approach could support broader implementation.[32]

As the Brains Ahead! intervention in its current form does not permit implementation at the emergency department, we suggest referral to primary care at discharge. Another option may be found in the field of e-health. Possibly, written and online (video) education may be evenly sufficient in reduction and prevention of long-term problems. Currently, such a study is being conducted amongst adolescents and adults with MTBI in The Netherlands; the MOVIE-trial [Trial NL5355 (NTR5465]. In case of effectiveness of this trial, the content of the Brains Ahead! intervention may be used for online implementation focused on children with MTBI. Although the results of our study provide useful information for selecting those children who are at risk for long-term problems, our final models only declared a small proportion of the variance in outcome on activities and participation after MTBI. To complete the predictive model (figure 1 of this chapter), future studies may for example also think of resilience, motivation for returning to activities and participation, coping styles of children and caregivers, the child's self-efficacy and emotion-regulation, the child's and caregivers personality traits, the level of social support from caregivers and peers, and other comorbid problems, such as chronic pain, substance abuse, life stress and protracted litigation.[3-5,7-23]

Although injury related factors do not play an important role in the prediction of outcome after MTBI, possibly, other biological factors that relate to anxiety might. For example alterations in the HPA-axis and autonomic nervous system, which were found to play an important role in the development of paediatric anxiety disorders,[59] may also be considered, since higher levels of PTSS symptoms were found to predict an adverse outcome in our present study. However, reversible, symptoms after MTBI such as stress and inflammatory responses, may also alter coping skills and personality.[21] When attempting to complete the predictive model for outcome on activities and participation after paediatric MTBI, future studies should mainly focus on personal-and environmental psychosocial factors. These findings are in agreement with findings in adult in MTBI, in which predictors were also found in psychosocial categories, and not injury-related.[19,21]

Studies into outcome on activities and participation after MTBI in adults have not yet investigated the predictive value of resumption of activities during the first weeks after the injury on activities and participation outcome. In children, less resumption of activities during the first weeks MTBI was found to be a predictor for decreased functioning on activities and participation at long-term (chapter 4). Therefore, we encourage future studies into outcome on activities and participation to investigate the predictive value of activity resumption short-term after injury in the adult MTBI population as well.

Conclusion

Most children recover naturally from MTBI completely and do not need interventions. Children with adverse pre-injury behavioral symptoms, adverse pre-injury family functioning, higher levels of symptoms and less resumption of activities during the first weeks after the injury are at risk for long-term problems. Those children may benefit from psychoeducational interventions, such as the Brains Ahead! intervention. Children aged 10-18 years old seem to benefit more from such interventions than their caregivers.

The Brains Ahead! intervention is feasible and effective for preventing long-term symptoms and problems on quality of life. It needs adjustments on timing and distribution of the intervention-components, in order to better match with clinical practice possibilities and the whishes from the children and their caregivers. Some children are more vulnerable to trauma, and tend to worry a lot in general, causing the experience of symptoms which are not injury-related. These children may need additional treatment, focusing on more personal and family-systematic factors, such as coping styles of children and caregivers, the child's self-efficacy and emotion-regulation, the child's and caregivers personality traits.

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Summary

Each year, 19,000 children aged 6 to 18 years old suffer from traumatic brain injury in the Netherlands, of which approximately 80% is classified as mild traumatic brain injury (MTBI). In general, children are expected to recover completely after MTBI, without treatment. However, in 6-43% of the children, MTBI leads to long-term post-concussive symptoms, such as headache, decreased concentration, fatigue, and anxiety or emotional problems, which may cause limitations in activities and participation at home, school and in sports. Activities and participation are very important for the development of a child, since it helps children to acquire different skills and competencies, grow physically and cognitively, develop their own identity and set different life goals. Little is known about the natural course of activities and participation after MTBI, and how children who are at risk for problems are best predicted. Early recognition of these children is crucial and enables the application of early and focused interventions.

The studies presented in this thesis aimed to examine the level of activities and participation of children and adolescents up to six months after a MTBI and to identify possible predictors for outcome. Furthermore, we aimed to investigate the feasibility and effectiveness of an early psychoeducational intervention, which was developed to prevent long-term symptoms and to establish a more successful return to activities and participation after MTBI in children and adolescents, in comparison to usual care.

Chapter 2 presents the study protocol of the Brains Ahead! study. This multicenter prospective longitudinal cohort study with a nested randomized controlled trial investigated the natural course of activities and participation after MTBI in school-aged children and predictors for outcome. Participants in the randomized controlled trial were randomly assigned to either the psychoeducational intervention group or the usual care control group.

Furthermore, we evaluated the feasibility and effectiveness of a combined standardized and personalized face-to-face psychoeducational intervention with written take-home information booklets. The Brains ahead! Intervention was compared to usual care, consisting of a concise information brochure. Primary outcome measure was activities and participation, measured with the Child and Adolescent Scale of Participation (CASP). Children and their caregivers were evaluated two weeks, three months and six months after the MTBI.

In **chapters 3 and 4**, the results from the multicentre prospective cohort study are presented. For this study, 698 children with MTBI were considered for participation, of whom 140 were excluded based on the exclusion criteria. Furthermore, a total of 257 persons did not participate, from which the vast majority (168) could not be reached. Finally, 60 participants received the Brains Ahead! Intervention, and were excluded from the analyses. Complete datasets within the multicentre prospective cohort study were available for 231 children.

Chapter 3 describes the natural course of activities and participation of 231 children in the first six months after MTBI. Primary outcome measure of the natural course of activities and participation was the CASP, measuring activities and participation in home, school, community, and environmental settings. Furthermore, the natural course of activities and participation was measured with the Children's Assessment of Participation and Enjoyment (CAPE), which showed the level of resumption of activities after the injury.

The results showed that the level of activities and participation increased significantly between two weeks and three months and stabilized up to six months after MTBI. This accounted for both measures, CASP and CAPE. In the group of children aged 10 to 18 years old, the caregivers' perspective differed from that of the children, with the caregivers evaluating their child's level of activities six months after the injury more positive (66% fully recovered) compared to the child's own evaluation (36% fully recovered).

Overall, the findings indicated that most children return to maximum level of activities and participation over time after MTBI, without the need of treatment. In some children, however, the level of activities and participation at six months post-injury was evaluated as less in comparison to peers.

We investigated the predictors for a risk of decreased problems with activities and participation after MTBI, and the results are described in **chapter 4.** Predictors were categorized according to the International Classification of Functioning, Disability and Health for Children and Youth (ICF-CY), and included; injury-related factors (e.g. Glasgow Coma Scale score, presence of posttraumatic amnesia, loss of consciousness, and the cause of the injury), symptoms (fatigue, post-concussive symptoms, and posttraumatic stress symptoms), resumption of activities in the first two weeks after MTBI, personal factors (pre-injury behavioral functioning of the child, age at the time of injury, and gender), and environmental factors (pre-injury family functioning and socioeconomic status (SES)).

Univariate and multivariate logistic regression analyses were used to determine the predictive value of these factors. The results showed that predictors for children who are at risk of long-term consequences on activities and participation differ per setting and per chosen perspective (child or caregiver). Adverse pre-injury behavioral functioning of the child, adverse pre-injury family functioning, lower parental SES, more stress symptoms post-injury, more post-concussive symptoms, and less resumption of activities in the first two weeks post-injury, predict decreased activities and participation after pediatric MTBI.

It seemed that not injury-related factors but psychosocial factors should be considered when children are screened for an unfavorable outcome. Since our model declared only a small part of the total variance on activities and participation, other factors may add to the prediction, such as coping styles, emotion-regulation, personality traits, social support, and other comorbid problems of both children and caregivers, and should be investigated in future studies.

Chapter 5 presents the results of our scoping review into what is known about early interventions for children after MTBI and what the recommendations for development of such interventions are. The results of this study show that the literature on this topic is scarce, and more high quality studies are needed. From the few studies that investigated this topic, we learned that information and education about the injury and its consequences are recommended, ideally followed by a consultation in which individualized advice and reassurance is provided. The family should be involved, and clinical recommendations suggest a step-by-step return to activities and participation. Based on these findings, we developed the Brains Ahead! intervention.

In **chapter 6** the rationale and description of the Brains Ahead! intervention treatment protocol are described. The Brains Ahead! intervention was developed to prevent long-term symptoms, and to establish a more successful return to activities and participation after MTBI in children. The intervention consists of two sessions.

The first session is a face-to-face psychoeducational session at two to four weeks after the injury, during which standardized information on causes, incidence, and consequences of the injury, and on returning to activities and participation, sensory sensitivity, and load-bearing capacity is provided. This information is complemented with individualized information on the specific symptoms the child experiences (if any), and individualized advice on returning to activities and participation based on the individual's personal situation and goals.

The second sessions consists of a scheduled telephone contact at six to eight weeks after the injury. During this session, the professional providing the intervention follows-up on if the information provided during session one was fully understood, on the specific symptoms the child experienced (if any), on the occurrence of new symptoms, and on the personalized advice on returning to activities and participation. If suitable, adding or removing steps was discussed. Hereafter, participations were offered the option to contact the interventionist for additional telephone sessions, for example in case new symptoms occurred or further questions on the return to activities and participation raised.

In **chapters 7 and 8**, the results on the feasibility and effectiveness of the Brains Ahead! intervention are presented. Of the children enrolled in the multicentre prospective cohort study, 130 children were eligible for the randomized controlled trial study. Six of them did not participate, leaving 124 children enrolled in the randomized controlled trial study. After randomization, 60 children were allocated to the intervention group, and 64 to the control group.

Chapter 7 describes the findings of the process evaluation study, which investigated the degree to which the Brains Ahead! intervention was implemented as intended. Among the children with MTBI and caregivers who were allocated to the intervention group, we investigated involvement in and satisfaction with the intervention.

The results of this study show that children with MTBI and their caregivers were in general very satisfied with the "Brains Ahead!" intervention. They were most satisfied with reassurance and creating a better understanding of symptoms and recognizing them. Of the two sessions that were offered, the first session seems to be the most important.

Moreover, the intervention seems feasible and with a few minor adjustments it would be recommended for implementation in clinical settings if proven effective. The minor adjustments enhance that is important to think carefully about who should receive, and who should deliver the intervention, and when and where the intervention should take place.

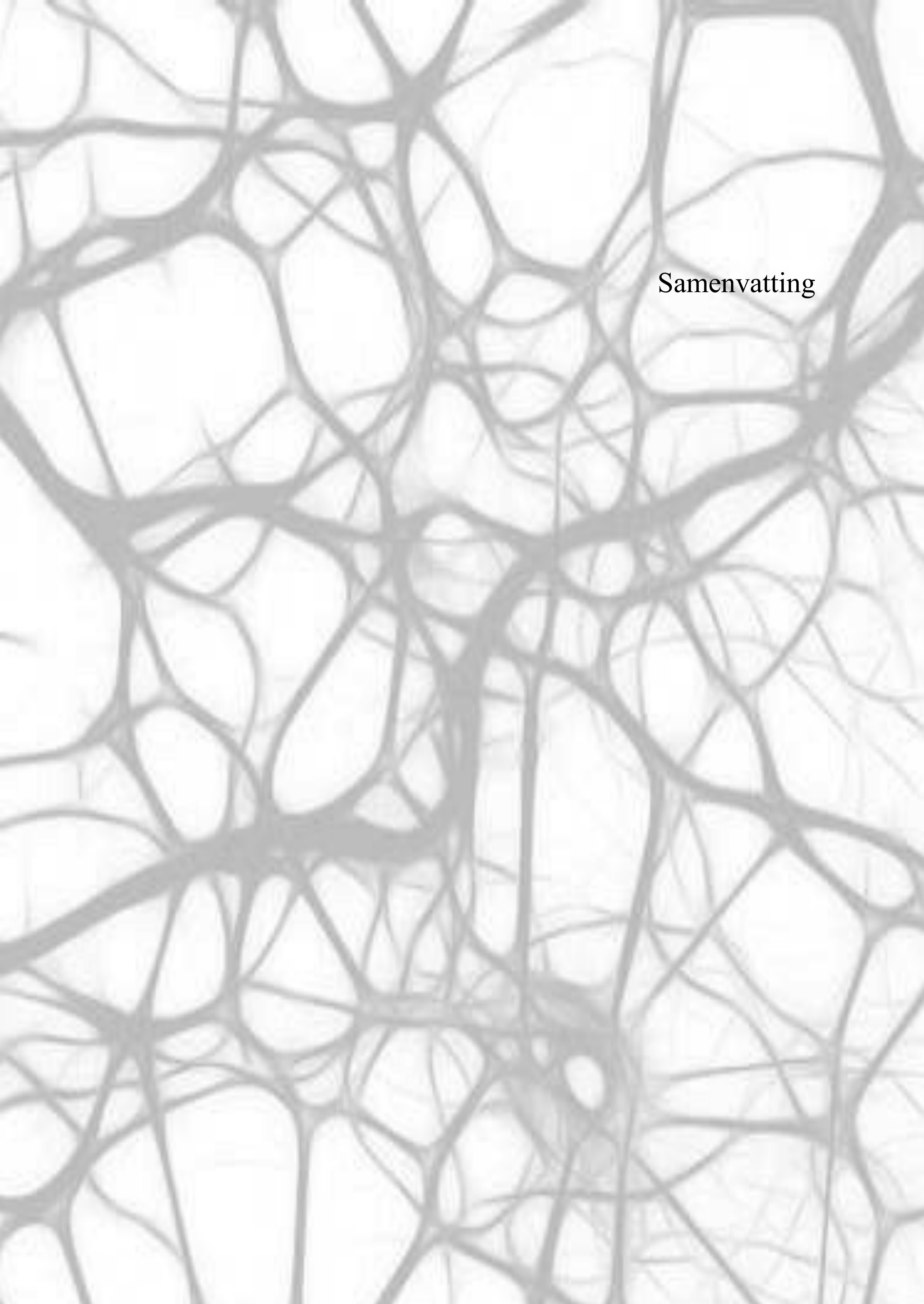
In **chapter 8**, the results of the randomized controlled trial into the effectiveness of the Brains Ahead! intervention compared to care as usual are described. The primary goal of the intervention was to prevent long-term problems on activities and participation, measured with the CASP. Secondary, the intervention aimed to prevent long-term fatigue, post-concussive symptoms, posttraumatic stress symptoms, and a decreased quality of life.

Our results showed that the Brains Ahead! intervention is beneficial over usual care to reduce fatigue, post-concussive symptoms, and posttraumatic stress symptoms, and improve quality of life. Both groups improved over the first six months after MTBI, but the intervention group did not reach significantly better results on activities and participation. Lack of an effect on activities and participation may be due to the ceiling effect of the outcome measure, the CASP.

Altogether, we would recommend the Brains Ahead! intervention for use in clinical practice, with some minor adjustments on timing and distribution of the content.

Finally, **chapter 9** summarizes the main findings of the studies in this thesis. Furthermore, methodological strengths and limitations of our study are discussed. The chapter finishes with clinical implications, for which we propose a stepped-care approach for children after MTBI, and recommendations for future research.

Samenvatting



In Nederland lopen jaarlijks ongeveer 19.000 kinderen tussen de 6 en 18 jaar traumatisch hersenletsel op door een val of een ongeval. Het merendeel van deze hersenletsels wordt geclassificeerd als licht traumatisch hersenletsel (LTH). Overal het algemeen is de verwachting dat kinderen van nature volledig herstellen van LTH, zonder dat hier behandeling voor nodig is. Echter, bij 6 tot 43% van de kinderen zorgt LTH voor langdurige postconcussieve klachten, zoals hoofdpijn, verminderde concentratie, vermoeidheid, en angst of emotionele problemen. Deze klachten kunnen zorgen voor moeilijkheden bij activiteiten en participatie thuis, op school of bij het sporten.

Activiteiten en participatie zijn zeer belangrijk voor de ontwikkeling van kinderen, want het helpt hem om zich diverse vaardigheden en competenties eigen te maken, fysiek en cognitief te groeien, een eigen identiteit te ontwikkelen en eigen levensdoelen te stellen. Er is maar weinig bekend over het natuurlijk herstel op het gebied van activiteiten en participatie na LTH en op basis waarvan voorspeld kan worden welke kinderen risico lopen op langdurige problemen. Tijdige herkenning van deze kinderen is cruciaal en zorgt ervoor dat vroegtijdige en gerichte interventies aangeboden kunnen worden.

De Brains Ahead! studies in dit proefschrift hadden als doel om het niveau van activiteiten en participatie bij kinderen en adolescenten tot zes maanden na het LTH te onderzoeken en voorspellende factoren voor problemen op de langere termijn te identificeren. Daarnaast was het doel om de praktische haalbaarheid en het effect van een psychoeducatieve interventie te onderzoeken, gericht op het voorkomen van langdurige symptomen en om een succesvol herstel op het gebied van activiteiten en participatie te bewerkstelligen bij deze groep kinderen en jongeren. Deze psychoeducatieve interventie werd vergeleken met de standaardzorg.

In **hoofdstuk 2** wordt het onderzoeksprotocol van de Brains Ahead! studie beschreven. In deze multicenter prospectieve longitudinale cohortstudie met een geneste gerandomiseerde gecontroleerde trial is het natuurlijk beloop van activiteiten en participatie na LTH bij schoolgaande kinderen onderzocht. Daarnaast is onderzoek gedaan naar factoren die het risico op problemen op het gebied van activiteiten en participatie voorspellen. Deelnemers aan de gerandomiseerde gecontroleerde trial werden willekeurig aan de psychoeducatieve interventiegroep of aan de standaardzorg controlegroep toegewezen.

Verder is de praktische haalbaarheid en het effect van de interventie onderzocht, bestaande uit een combinatie van gestandaardiseerde en gepersonaliseerde face-to-face psychoeducatie, aangevuld met informatieboekjes die de deelnemers mee naar huis namen. De standaardzorg bestaat uit een beknopte informatiefolder. De primaire en belangrijkste uitkomstmaat was activiteiten en participatie, gemeten met de Child and Adolescent Scale of Participation (CASP). Metingen bij de kinderen en hun ouders/verzorgers vonden plaats op twee weken, drie maanden en zes maanden na het LTH.

In de **hoofdstukken 3 en 4**, staan de resultaten van de multicenter prospectieve cohortstudie beschreven. Er waren 698 kinderen met LTH in overweging genomen voor deelname aan de studie, van wie 140 geëxcludeerd werden op basis van de exclusiecriteria. Verder hebben in totaal nog 257 kinderen niet aan de studie meegedaan, van wie het merendeel (168 kinderen) niet bereikt werden. Tenslotte werden 60 deelnemers uit de analyses voor deze studie verwijderd, omdat zij de Brains Ahead! interventie ontvingen. Er waren complete datasets van 231 kinderen beschikbaar voor de multicenter prospectieve cohortstudie.

Hoofdstuk 3 beschrijft een studie naar het natuurlijk beloop van activiteiten en participatie van 231 kinderen gedurende de eerste zes maanden na LTH. De primaire uitkomstmaat van het natuurlijk beloop van activiteiten en participatie was de CASP, waarmee activiteiten en participatie thuis, op school, in de buurt en in de wijdere omgeving kan worden gemeten. Daarnaast was het natuurlijk beloop van activiteiten en participatie gemeten met de Children's Assessment of Participation and Enjoyment (CAPE), waarmee inzicht werd verkregen in de mate waarin activiteiten werden hervat na LTH.

Uit de resultaten komt naar voren dat het niveau van activiteiten en participatie significant toeneemt tussen twee weken en drie maanden, en stabiliseert tot aan zes maanden na het LTH. Dit gold voor beide meetinstrumenten, CASP en CAPE. Het perspectief van de kinderen in de leeftijd van 10 tot 18 jaar verschilde van dat van hun ouders/verzorgers. De ouders/verzorgers evalueerden het niveau van activiteiten en participatie van hun kind op zes maanden na het letsel positiever (66% volledig hersteld) dan de kinderen zelf (36% volledig hersteld).

Over het algemeen lieten de resultaten zien dat de meeste kinderen volledig herstellen op het gebied van activiteiten en participatie over de tijd na LTH, zonder dat hier behandeling voor nodig is. Bij sommige kinderen was het niveau van activiteiten en participatie op zes maanden na LTH echter lager, wanneer vergeleken met leeftijdsgenoten.

We onderzochten voorspellers voor risico op problemen op het gebied van activiteiten en participatie na LTH. De resultaten staan beschreven in **hoofdstuk 4**. Voorspellers waren onderverdeeld in categorieën, gebaseerd op de International Classification of Functioning, Disability and Health for Children and Youth (ICF-CY), namelijk; letsel-gerelateerde factoren (Glasgow Coma Scale score, aanwezigheid van posttraumatische amnesie, bewustzijnsverlies, en de oorzaak van het letsel), symptomen (vermoeidheid, postconcussieve symptomen en posttraumatische stress symptomen), de mate waarin activiteiten werden hervat in de eerste twee weken na LTH, persoonlijke factoren (pre-morbide gedragsfunctioneren van het kind, leeftijd ten tijde van het letsel, en geslacht), en omgevingsfactoren (pre-morbide familiefunctioneren en sociaal-economische status (SES)).

Univariate en multivariate logistische regressieanalyses werden gebruikt om de voorspellende waarde van deze factoren te bepalen. Uit de resultaten kwam naar voren dat voorspellers voor kinderen die risico lopen op problemen op het gebied van activiteiten en participatie na LTH, verschillen per setting (thuis, op school, in de buurt of in de wijdere omgeving) en op basis van het gekozen perspectief (kind of ouders/verzorgers). Slechter pre-morbide gedragsfunctioneren van het kind, minder gezond pre-morbide familie-functioneren, lagere SES, meer stress symptomen na het letsel, meer postconcussieve symptomen en lagere mate van hervatting van activiteiten in de eerste twee weken na LTH, voorspelden problemen op het gebied van activiteiten en participatie op 6 maanden.

Blijkbaar zijn niet de letselgerelateerde factoren, maar juist de psychosociale factoren belangrijk wanneer wordt gekeken welke kinderen risico lopen op problemen na LTH. Ons model kon slechts een klein deel van de totale variantie in activiteiten en participatie verklaren. Andere factoren kunnen bijdragen aan de voorspelling, waarbij kan worden gedacht aan coping stijlen, emotie-regulatie, persoonlijkheidstrekken, sociale steun, en andere co-morbide problemen van kinderen en/of hun ouders/verzorgers.

In **hoofdstuk 5** staan de resultaten van onze beschrijvende review over wat er bekend is over de inhoud en het effect van vroegtijdige interventies voor kinderen na LTH en wat de aanbevelingen voor de ontwikkeling van zulke interventies zijn. Uit de resultaten van deze studie komt naar voren dat de literatuur op dit gebied erg schaars is en meer studies van hoogwaardige kwaliteit nodig zijn. Vanuit de paar studies die hier wel onderzoek naar hebben verricht, komt naar voren dat informatie en educatie over het letsel en de consequenties ervan tot de aanbevelingen behoort, idealiter aangevuld met een gesprek waarin gepersonaliseerde adviezen en geruststelling worden geboden. Het gezin dient erbij betrokken te worden, en een stapsgewijze hervatting van activiteiten en participatie wordt klinisch gezien geadviseerd. Op basis van deze bevindingen hebben wij de Brains Ahead! interventie ontwikkeld.

Hoofdstuk 6 beschrijft de achtergrond en inhoud van het Brains Ahead! interventie behandelprotocol. De Brains Ahead! interventie was ontwikkeld met als doel om langdurige symptomen na LTH bij kinderen te voorkomen, en een succesvol herstel op het gebied van activiteiten en participatie te bewerkstelligen. De interventie bestaat uit twee sessies.

De eerste sessie is een face-to-face gesprek wat twee tot vier weken na het letsel plaatsvindt en waarin gestandaardiseerde psychoeducatie wordt gegeven over oorzaken, incidentie, en consequenties van LTH, en over het hervatten van activiteiten en participatie, prikkelgevoeligheid, en belasting en belastbaarheid. Deze informatie wordt aangevuld met gepersonaliseerde informatie over de specifieke symptomen die het kind ervaart (indien deze er zijn), en gepersonaliseerde adviezen rondom de hervatting van activiteiten en participatie, rekening houdend met de persoonlijke situatie en doelen van het individuele kind.

De tweede sessie bestaat uit een gepland telefonisch gesprek, zes tot acht weken na het letsel. Bij dit gesprek vraagt de professional die de interventie uitvoert na of alle informatie die in de eerste sessie is verschaft duidelijk was. Verder wordt nagegaan hoe het gaat met de eventuele specifieke symptomen die het kind ervaart, of er zich nieuwe symptomen hebben gemanifesteerd, en tevens wordt het advies omtrent de hervatting van activiteiten en participatie opgevolgd. Indien hiertoe aanleiding was, werd gezamenlijk overlegd of er aan het hervatten van activiteiten stappen moesten worden toegevoegd of juist konden worden overgeslagen. Na de tweede sessie werd aan deelnemers de optie geboden om op eigen initiatief contact met de professional die de interventie gaf op te nemen voor aanvullende telefonische gesprekken, bijvoorbeeld wanneer er zich nieuwe symptomen zouden voordoen, of in het geval er aanvullende vragen omtrent het hervatten van activiteiten en participatie opkwamen.

In de **hoofdstukken 7 en 8** staan de resultaten over de praktische haalbaarheid en het effect van de Brains Ahead! interventie beschreven. Van de kinderen die deelnamen aan de multicenter prospectieve cohortstudie, kwamen er 130 in aanmerking voor deelname aan de gerandomiseerde gecontroleerde trial studie. Zes van deze kinderen kozen om niet mee te doen aan de studie, waardoor er 124 kinderen voor de gerandomiseerde gecontroleerde trial studie werden geïncludeerd. Na randomisatie werden er 60 kinderen aan de interventiegroep toegewezen, en 64 aan de controlegroep.

In **hoofdstuk 7** staan de bevindingen van de procesevaluatie studie beschreven, waarmee is onderzocht in hoeverre de Brains Ahead! interventie was geïmplementeerd zoals bedoeld. Bij de kinderen met LTH die toegewezen waren aan de interventiegroep en hun ouders/verzorgers, hebben we de mate van betrokkenheid en tevredenheid betreffende de interventie onderzocht.

De resultaten van dit onderzoek laten zien dat kinderen met LTH en hun ouders/verzorgers over het algemeen zeer tevreden over de Brains Ahead!

interventie waren. Zij waren het meest tevreden met de ontvangen geruststelling en de mate waarin de interventie ervoor zorgde dat zij symptomen na LTH beter konden herkennen en begrijpen. Van de twee geboden sessies werd de eerste als het meest belangrijk beoordeeld.

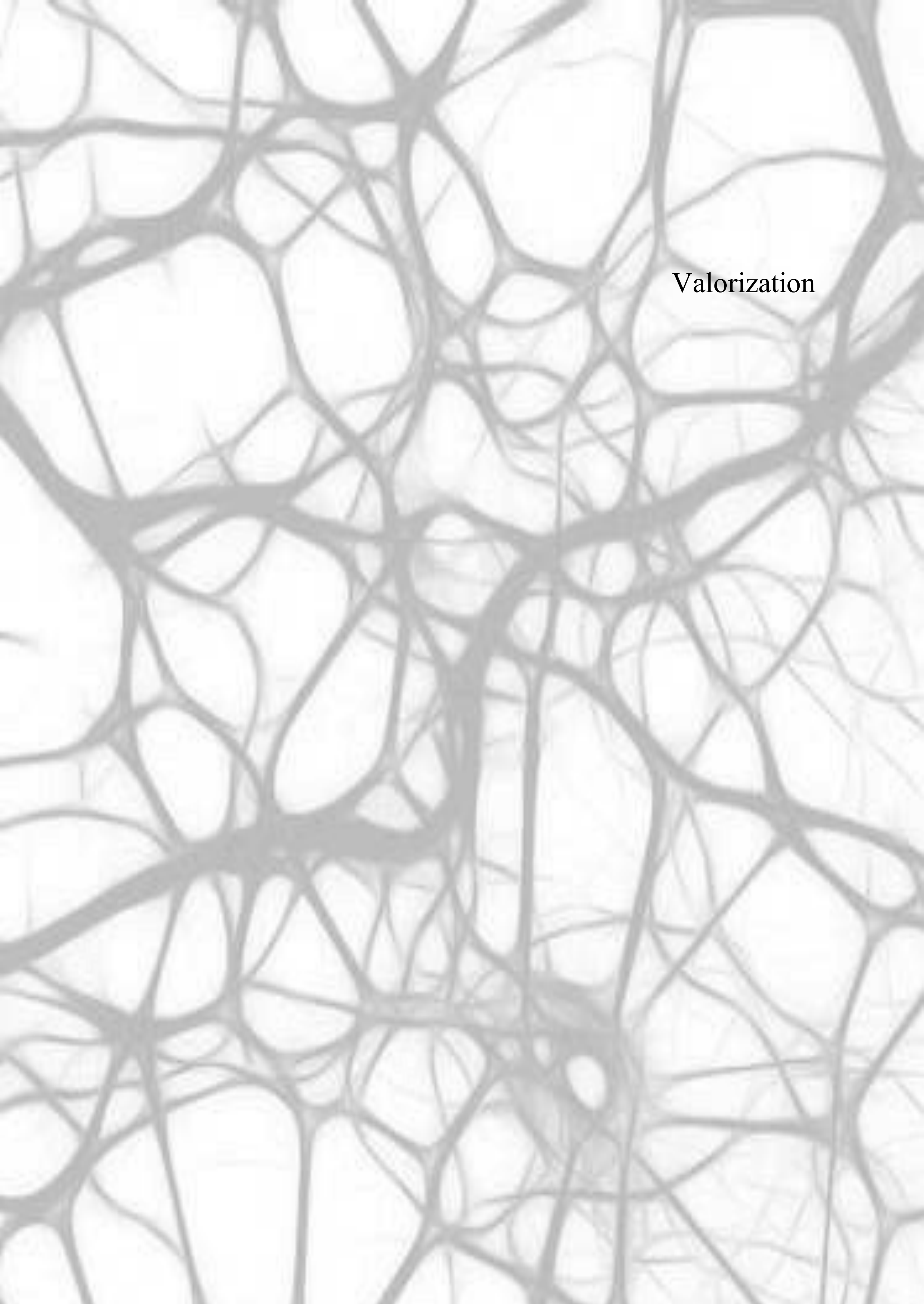
Al met al lijkt de uitvoering van de Brains Ahead! interventie haalbaar, en zouden wij deze met enkele kleine aanpassingen aanbevelen voor implementatie in de klinische praktijk, mits effectiviteit bewezen kan worden. De enkele aanpassingen dienen te worden gezien in het kader van wie de interventie specifiek zou moeten ontvangen, door wie deze uitgevoerd zou moeten worden in de praktijk, en wat de meest geschikte plaats voor uitvoer van de interventie is.

In **hoofdstuk 8**, staan de resultaten van de gerandomiseerde gecontroleerde trial beschreven, waarbij het effect van de Brains Ahead! interventie in vergelijking met de standaardzorg is onderzocht. Het primaire doel van de interventie was het voorkomen van langdurige problemen op het gebied van activiteiten en participatie, gemeten met de CASP. Secundair had de interventie als doel om langdurige vermoeidheid, postconcussieve symptomen, posttraumatische stress symptomen, en een verminderde kwaliteit van leven te voorkomen.

De resultaten van dit onderzoek laten zien dat de Brains Ahead! interventie een gunstiger effect heeft ten opzichte van de standaardzorg, waar het gaat om het reduceren van vermoeidheid, postconcussieve symptomen, posttraumatische stress symptomen, en het verbeteren van de kwaliteit van leven bij kinderen na LTH. Zowel de interventie- als de controlegroep verbeterden op het gebied van activiteiten en participatie gedurende de eerste zes maanden na het LTH, maar de interventiegroep behaalde niet significant betere resultaten op dit gebied. Dat er geen effect op het gebied van activiteiten en participatie wordt gezien zou mogelijk verklaard kunnen worden door het plafondeffect van het meetinstrument, de CASP.

Al met al bevelen wij de Brains Ahead! interventie aan voor gebruik in de klinische praktijk, na enkele aanpassingen wat betreft timing en verdeling van de inhoud.

In **hoofdstuk 9** zijn de belangrijkste bevindingen van de studies in dit proefschrift samengevat. Verder worden in dit hoofdstuk de sterke punten en limitaties op methodologisch vlak bediscussieerd. Tenslotte wordt in dit hoofdstuk stilgestaan bij klinische implicaties, waarbij wij een stepped-care-approach voorstellen voor kinderen na LTH, en presenteren wij onze aanbevelingen voor toekomstig onderzoek.



Valorization

Relevance

A traumatic brain injury (TBI) is a form of acquired brain injury, and refers to sudden damage to the brain resulting from external mechanical force, for example when the head hits an object due to accidents at home, school or in traffic, or when an object pierces the skull and enters brain tissue.[1-2] Each year, a number of approximately 13,000 children and adolescents aged between 0-24 years old suffer a traumatic brain injury (TBI) in The Netherlands, the majority (80%) of which are mild (MTBI).[3-4]

In our research we used the definition of MTBI according to the criteria established by the American Congress of Rehabilitation Medicine (ACRM) and the WHO Collaborating Centre for Neurotrauma Task Force on Mild Traumatic Brain Injury[5]: 'a Glasgow Coma Scale (GSC) score of 13-15 and at least one of the following: (1) loss of consciousness of no more than 30 minutes, (2), Post Traumatic Amnesia (PTA) no longer than 24 hours, (3) any alteration in mental state at the time of the injury, (4) focal neurological deficit(s) that may or may not be transient'.

Most children with MTBI are expected to recover completely and do not receive any follow-up care after discharge from the emergency department.[6] However, when children return home after MTBI, between 6-43% of them suffer from a variety of symptoms.[7-11] These symptoms are often defined as post-concussive symptoms (PCS) and may be found in the physical (e.g. headache), cognitive (e.g. trouble concentrating), emotional (e.g. stress), and behavioural (e.g. irritability) domains, and can last up to six months post-injury or longer.[7-11] As a consequence of these symptoms, children after MTBI may experience trouble or limitations in the area of activities and participation such as in school, social relations and play[12-14,] (chapter 3).

Activities and participation are very important for the development of a child, because it helps children to develop different skills and competencies, develop physically and cognitively, develop their own identity and set different life goals.[15] Therefore, healthcare providers for children with MTBI should focus on early prevention of limitations in this area.

Since most children are expected to fully recover from MTBI, we have to look for ways to organize healthcare services especially for children with MTBI who may not recover completely by nature. Therefore, the first step we took was to predict which children may benefit from follow-up care after discharge from the emergency department (chapter 4). Preventive treatment care is preferred because the symptoms that children may experience after MTBI are often not recognized and therefore not treated adequately. The second step we took was the development and evaluation of an early psychoeducational preventive intervention (the Brains Ahead! intervention) for children with MTBI and their caregivers.[16]

The results of the studies into the feasibility and effect of this intervention were positive (chapters 7 and 8). Therefore, we believe that the Brains Ahead! intervention is valuable for society and recommend it for use in clinical practice. In order to fit the intervention to the Dutch healthcare organization, we suggest a stepped-care approach for children after MTBI (chapter 9).

Target groups

The findings of our research are of relevance for children with MTBI, their parents or caregivers, healthcare professionals, and health policy-makers.

Children with MTBI will profit from our research as it emphasizes that not all children recover completely from MTBI by nature. The need for information at discharge from the emergency room/hospital in general has become clearer, especially for those children who are at risk for long-term problems based on the predictors for outcome after MTBI. The first steps into the construction of a prediction model have been taken, and the importance of personal and psychosocial factors is emphasized (chapter 4). For children who are at risk for long-term problems after MTBI, we developed an early psychoeducational intervention,[16] with promising feasibility and effect results (chapters 7 and 8). The intervention is partly standardized and partly individualized, and as a consequence, the healthcare process can be better tailored to the individual needs of children who are at risk for long term problems after MTBI.

Parents or caregivers of children with MTBI are expected to profit from our research as it points out that indeed, many children seem to recover completely by nature, which may be reassuring. The research also highlights the importance of taking the perspective of the caregiver along in the recovery process, since it may differ from that of the child itself. Furthermore, it emphasized the need to involve the family in the follow-up care process, and provide them with reassurance, information on symptoms that can be expected after the injury, and individualized advice on how to let their child return to activities and participation, which elements are all embedded in the Brains Ahead! intervention.[16] Parents or caregivers may feel strengthened by the obtained knowledge on MTBI in children and more ensured about what is wise when stimulating their child to return to activities and participation.

Healthcare professionals working in the field of children with MTBI (e.g. neurologists, general practitioners, psychologists, occupational therapists, and rehabilitation specialists) will profit from our findings as well. Our study provides knowledge on predictors of outcome which helps them to decide which children need to be followed up in order to prevent long term problems from occurring. Secondly, our study provides a psychoeducational intervention, with standardized elements that can easily be implemented in healthcare.[16] Although the intervention's primary purpose is prevention of long-term problems after childhood MTBI, the standardized information may also be used to provide patients and their caregivers with psychoeducation in child rehabilitation care.

Finally, our results are of importance for health policy-makers. In the past few years, much has been studied about the recovery of children from MTBI. Our study emphasizes that, since most, but not all children recover naturally from MTBI, follow-up care for these children should be organized. Taking the organizational matters of several clinical settings (e.g. emergency departments, general practitioners) into account, we provide the health policy-makers with a stepped-care approach for children after MTBI that fits the Dutch healthcare organization, may improve care efficiency and help to achieve higher health-related gains (chapter 9).

Activities and products

Our results help to detect those children who are at risk of long-term problems after MTBI based on predictive factors. The importance of personal and psychosocial factors for the prediction of outcome after childhood MTBI is emphasized, and should be further investigated to complete the prediction model.

For the children who are at risk of long-term problems, we developed the Brains Ahead! intervention. The intervention consists of a standardized and individualized psychoeducational session with written take-home information, and follow-up telephone call(s). Reassurance, information about causes, possible consequences, and advice about returning to activities and participation are main elements of the intervention. The elements are described in more detail in the treatment protocol of the Brains Ahead! intervention for children and adolescents with mild traumatic brain injury and their caregivers in chapter 6.[16]

The results of our research show that children who are at risk for long-term problems after MTBI may benefit from the Brains Ahead! intervention. The findings also show that the Brains Ahead! intervention in its current form needs some adjustments in order to better match with clinical practice possibilities and the whishes from the children and their caregivers.

Altogether, these findings both challenged and supported us to create the proposal of a stepped-care approach for children after MTBI (chapter 9). During the study, we learned that most children and caregivers were relieved when the child was discharged from the emergency department and hurried home, with the questions on the recovery process, occurring symptoms, and the need for individualized advice on returning to activities and participation emerging in the following days. Since time and manpower is lacking at the emergency department, standardized information could be offered directly by primary care after referral from the emergency department. More individualized information focused on the child's symptoms and advice on activities and participation fitting their personal situation, could be offered either at a scheduled appointment one or two weeks after the injury, or scheduled at the patient's request. Such a stratified management approach to target the provision of primary care may, in addition to improved care efficiency and higher health gains, provide substantial economic benefits compared with the current usual care.[17]

Innovation

In our research we highlighted that a substantial number of children suffer from problems after MTBI, and experience restrictions in activities and participation. Up until now, the usual care for all children leaving the emergency department after MTBI consists of a concise information brochure, with recommendations to return to the general practitioner or hospital in case of frequent vomiting, increasing drowsiness, and/ or an increase in other complaints during the following days.[18]

Since most children recover completely from MTBI by nature, not all children need further follow-up care. Our research was innovative in providing knowledge on predictive factors for long-term problems on activities and participation after childhood MTBI, and was the first to examine multiple predictors from a biopsychosocial perspective following the relevant ICF-CY categories[19] in one comprehensive model, from both the perspective of the caregiver and the child (chapter 4). With this knowledge, a better early identification of children who are at risk of long-term limitations and might benefit from early interventions is possible.

The results of our scoping review into what is known about early interventions for children after MTBI, taught us that information and education about the injury and its consequences are recommended, ideally followed by a consultation in which individualized advice and reassurance is provided. The family should be involved, and clinical recommendations suggest a step-by-step return to activities and participation (chapter 5). Based on these findings, we developed the Brains Ahead! intervention for children with MTBI.[16]

The Brains Ahead! intervention was innovative in prospectively intending to prevent long-term problems related to activities and participation in children and adolescents aged 6 to 18 years old following MTBI. The intervention combines an inventory of symptoms, psychoeducation, and follow-up, and involves the child's family in the process.

Our intervention study was carried out highly in agreement with the Medical Research Council (MRC) framework for development, evaluation and implementation of complex interventions.[20] This framework suggests that for developing and evaluating complex interventions, the following steps should be passed; (1) to identify existing evidence, (2) to identify and develop theory, with the rationale for the complex intervention and a theoretical understanding of the likely process of change by drawing on existing evidence, (3) to assess effectiveness with a randomized controlled study, (4) to decide which outcomes are most important, which are secondary, and how they will deal with multiple outcomes in the analysis, (5) to consider which sources of variation in outcomes matter and to plan appropriate subgroup analyses, and (6) to perform a process evaluation, in order to provide valuable insight into why an intervention fails or has unexpected consequences, or why a successful intervention works and how it can be optimised. They suggest a process evaluation nested inside a trial, which can be used to assess fidelity and equality of implementation, clarify causal mechanisms, and identify contextual factors associated with variation in outcome.

Although it might seem evident that development and evaluation of complex interventions should be constructed following such fundamental frameworks, the actual number of studies adopting all framework steps is limited. The study-and treatment protocol of Brains ahead! were published and may be used as a model for new researches wanting to follow this framework.

Finally, our research offers a stepped-care approach plan to innovate and optimize the healthcare for children with MTBI (chapter 9).

Schedule and implementation

The Brains Ahead! intervention is feasible and effective for preventing long-term symptoms and problems on quality of life. Implementation of the intervention in clinical settings is therefore recommended. The process of the Brains Ahead! intervention, however, needs some adjustments on timing and distribution of the intervention-components in order to better match with clinical practice possibilities and the whishes from the children and their caregivers, and to fit the proposed stepped-care approach for children with MTBI. The minor adjustments in the Brains Ahead! intervention process that are needed for this purpose, are described in further detail in chapter 9 of this manuscript.

The proposed stratified management approach to target the provision of primary care may, in addition to improved care efficiency and higher health gains, provide substantial economic benefits compared with the current usual care. Funding is necessary to finance the adjustment-process of the intervention, and implementation in clinical settings as intended. Furthermore, health policy-makers should be involved in the process of integrating the stepped-care approach for children after MTBI in the Dutch healthcare organization. One can, for example, think of the funding and organization of the training that general practitioners or physician assistants may need in order to carry out the Brains Ahead! intervention, and the proper distribution of the written standardized information. Possibly, opportunities may also be found in providing parts of the information by e-health. However, funding would be needed to convert the written information to e-health accessible information as well, and precautions for use by the general population without the guidance of trained professionals should be concerned.

Distribution of the knowledge that was collected with our research was performed in several ways. In order to share knowledge with other researchers, study-and treatment protocols were published in international journals. Furthermore, newsletters were published on a regular basis to inform healthcare professionals, participants and other interested parties about the study-progress and outcomes. The newsletters could be downloaded at the Brains Ahead! website: www.brainsahead.nl.

Furthermore, the design and outcomes of the two Brains Ahead! studies were presented at several national and international conferences. Examples of the national conferences are The Brain Awareness Week (2015 and 2018), Hersenletselcongres (2016, 2017, and 2018), and Samen Nog Beter congress (2017). Examples of the international conferences are the International Conference on Pediatric Acquired Brain Injury (IPBIS Rome 2017, and Belfast 2018), International Brain Injury Association (IBIA 2016), and the Conference in Neuropsychological Rehabilitation of the Special Interest Group of the WFNR (Granada 2019). Also, presentations about the designs and outcomes of the Brains Ahead! studies were given to the participating hospitals in the studies, and several other interested parties such as rehabilitation centers, psychiatry/psychology departments of hospitals, and national workgroups for children with acquired brain injury. Finally, an invited symposium “What’s new, what’s next?’ Kinderen met traumatisch hersenletsel” was organized, during which the final results of the Brains Ahead! studies were shared.

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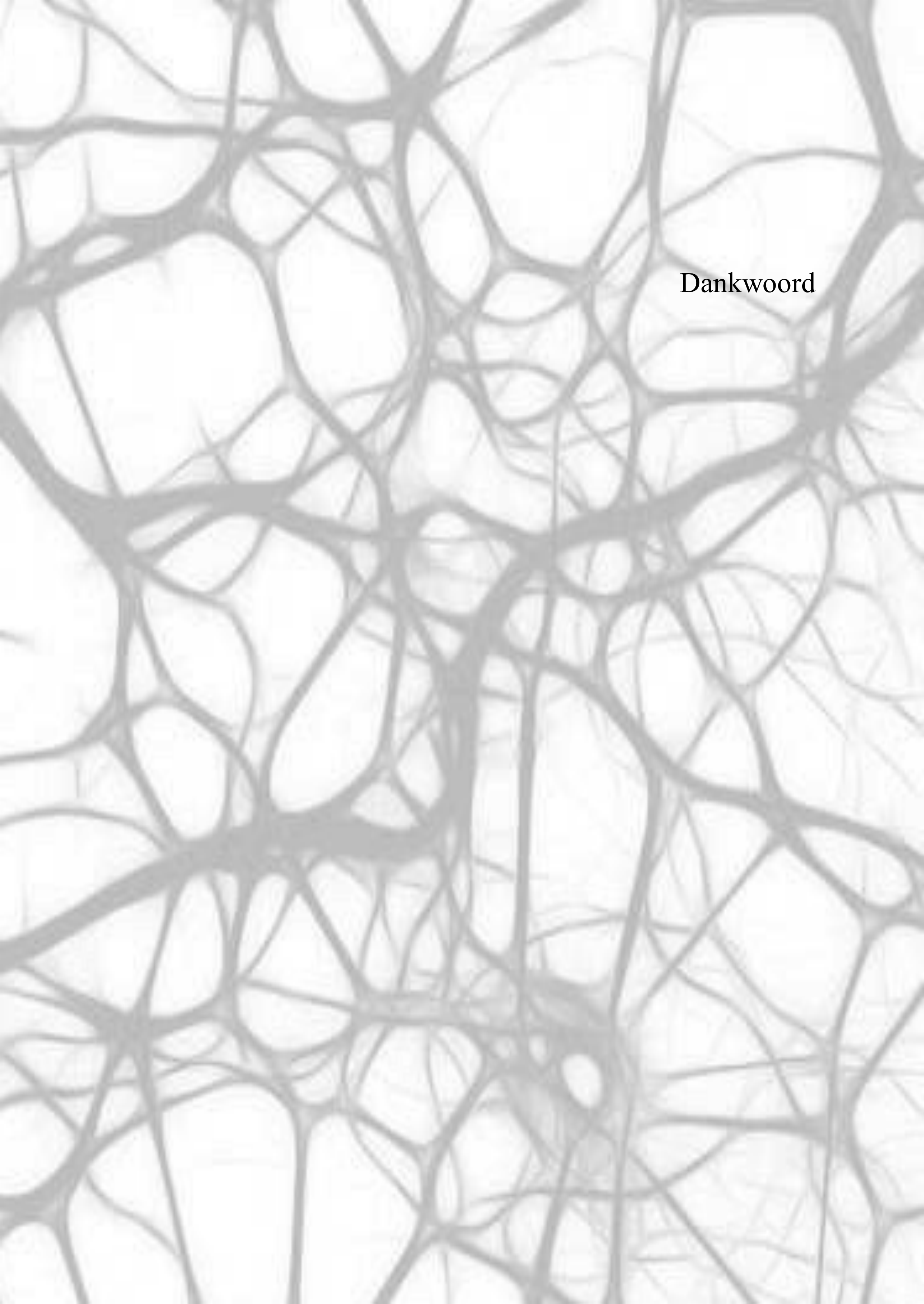
Dankwoord



“Waarom moeilijk doen, als het samen kan?”

Als de dag van gisteren herinner ik mij nog het schrijven van mijn sollicitatiebrief voor dit promotie-traject, en na precies 5 jaar ligt het er dan – mijn proefschrift. Wat weet ik nog goed dat ik zo twijfelde of ik dit wel moest doen, omdat statistiek niet bepaald mijn sterkste punt was. En wat heb ik er geen dag spijt van gehad dat ik ervoor ben gegaan. Niet alleen vanwege het prachtige onderwerp, maar vooral ook vanwege de fijne samenwerking met alle betrokkenen bij de uitvoering van het onderzoek en de totstandkoming van dit proefschrift. Graag bedank ik de vele mensen die op welke wijze dan ook bij hieraan hebben bijgedragen.

Allereerst alle kinderen, jongeren en hun ouders die aan dit onderzoek hebben deelgenomen. Wat ben ik jullie dankbaar voor de tijd en energie die jullie hebben geïnvesteerd door aan het onderzoek mee te doen. Keer op keer werd ik hartelijk ontvangen voor de metingen bij jullie thuis en deelden jullie met mij wat de hersenschudding voor jullie betekende. Dit hield mij gedurende de jaren steeds weer gemotiveerd, en hierdoor vergaarde ik veel inzichten voor het onderzoek. Ook kwam ik er mede hierdoor achter dat mijn hart toch wel daar ligt waar de wetenschap en de klinische praktijk samenkomen.

Graag bedank ik mijn promotieteam voor alle kundige en vriendelijke begeleiding in de afgelopen jaren. Caroline, wat een fijne promotor ben je voor mij geweest. Door jou heb ik voor het eerst geleerd hoe ik korter en bondiger kan schrijven. Je hielp mij beter tot de kern te komen en jouw enthousiasme voor het vak werkt wat mij betreft aanstekelijk. Dankbaar ben ik je ook voor jouw oog voor de ontwikkeling van mij als persoon, je duidelijkheid, geduld en openheid hierin. Een kwaliteit jou als promotor ontzettend siert. Ingrid, wat heb ik van jou als mijn co-promotor veel geleerd over het belang van duidelijke doelen stellen en passende methoden te kiezen. Wat ben ik je dankbaar voor de vele malen dat ik soms zelfs diep in de nacht tijdens je vakanties alsnog reacties van je mocht ontvangen op mijn grote twijfels rondom statistische kwesties, maar ook op allerhande onderzoeksvragen. Ik had het gevoel altijd bij je terecht te kunnen als ik het even niet meer zag. Coriene, wat heb ik aan jou een fijne co-promotor gehad als het ging om knopen doorhakken, out of de box denken en vooral natuurlijk ook jouw praktijkervaring als kinderneuroloog. Ook al waren mijn deadlines vaak strak en scherp, altijd maakte jij tijd om stukken van feedback te voorzien. Wat heb ik mij ook steeds gesterkt gevoeld door jouw positieve woorden rondom mijn inzet voor de inclusie van deelnemers en de geschreven papers. Suzanne, ook jou wil ik graag bedanken voor jouw bijdrage aan mijn promotie-traject.

Ook al kwam mijn proefschrift voor jou net iets te snel waardoor duidelijk werd dat je geen officiële co-promotor zou kunnen zijn, toch bleef je nauw betrokken. Je hebt mij aan veel mensen binnen het vakgebied voorgesteld en daarmee voor mij en het onderzoek vele deuren geopend. Dank voor het meeschrijven aan de papers en voor jouw input vanuit de kinderrevalidatie.

Ook wil ik graag de leden van de beoordelingscommissie, prof. dr. Rudolf Ponds, prof dr. Jeanine Verbunt, prof. dr. Joukje van der Naalt en dr. Ingrid Rentinck, danken voor het lezen en beoordelen van mijn proefschrift.

Het Brains Ahead! project werd financieel mogelijk gemaakt door het Johanna Kinderfonds in samenwerking met Handicap.nl (voorheen Revalidatiefonds), waarvoor ik deze fondsen veel dank verschuldigd ben. Ook dank ik Maastricht University en Revant Revalidatiecentrum Breda voor het mogelijk maken van de verschijning van dit proefschrift.

Bij de opstart van het onderzoek is de Brains Ahead! onderzoeksgroep gevormd, met daarin vele mensen, werkzaam bij de deelnemende ziekenhuizen of meedenkende revalidatiecentra die ik dank verschuldigd ben voor hun bijdrage aan het onderzoek en dit proefschrift. Allereerst dank aan de deelnemende ziekenhuizen en de hoofdonderzoekers per centrum: Erasmus MC – Sophia Kinderziekenhuis, Coriene, mijn co-promotor; Amphia ziekenhuis, Johanneke de Rijk- van Andel; Rijnstate ziekenhuis, Katinke van Dijk, voor wie speciale dank voor je persoonlijke betrokkenheid bij zowel het onderzoek als bij mij als persoon, en jouw grote inzet om deelname van het Rijnstate ziekenhuis werkelijkheid te maken; Ziekenhuis Gelderse Vallei, Tineke Oosterveld-Bonsma; HagaZiekenhuis, Els Peeters; Haaglanden Medisch Centrum, Korné Jellema, voor wie ook speciale dank voor het meedenken- en schrijven aan de paper over het beloop van activiteiten en participatie na licht traumatisch hersenletsel (hoofdstuk 3); Reinier de Graaf ziekenhuis, Daan Kamphuis; en Elisabeth TweeSteden ziekenhuis, Jikke-Mien Niermeijer. Ook het ondersteunende personeel en enkele andere geïnteresseerde personen van deze ziekenhuizen wil ik graag bedanken, in het bijzonder Marjolein, Margreet B, Margreet van A en Maayke (Erasmus MC-Sophia Kinderziekenhuis), Karin (Haaglanden Medisch Centrum), Wendy, Ria, Silvie, Frank en Nicole (Amphia ziekenhuis). Daarnaast dank aan de overige leden van de Brains Ahead! onderzoeksgroep: Henk Hendricks, Douwe Rijpsma en Dolf Boerman (Rijnstate ziekenhuis), Bea Kievit (Ziekenhuis Gelderse Vallei), Robert Pangalila (Rijndam Revalidatie), Sandra te Winkel (de Hoogstraat Revalidatie) en Frederike van Markus (Basalt Revalidatie).

Bij deze groep, maar ook op andere plekken in dit dankwoord en proefschrift horen thuis Arend de Kloet (Basalt Revalidatie) en Nicole Bovens (Revant Revalidatie). Arend, dank voor je inspiratie vanuit jouw eigen promotieonderzoek en het meedenken-en schrijven over het opzetten van mijn promotieonderzoek (hoofdstuk 2). Met het oog op de toekomst ligt jouw hart bij het samenbrengen van alle wetenschappelijke onderzoeken en de klinische vragen uit de praktijk op het gebied van kinderen en jongeren met hersenletsel. Dank dat ik daarin heb mee mogen denken o.a. ook als gedeeld secretaris bij de HeJ werkgroep Onderzoek en Ontwikkeling. Nicole, dank voor jouw enthousiasme over het onderzoek, jouw gigantische inzet voor het mede-ontwikkelen van de Brains Ahead! interventie en het uitvoeren hiervan in de ziekenhuizen met de vele deelnemers. Ook dank voor jouw persoonlijke betrokkenheid en de wijze waarop ik samen met jou heel prettig diverse presentaties over het onderzoek heb mogen geven. Fijn dat je jouw ervaringen steeds hebt willen delen en mee hebt willen schrijven aan onze paper over het interventieprotocol (hoofdstuk 6).

Vanuit de standplaats van mijn onderzoek Revant Revalidatiecentrum te Breda heb ik ook vele mensen leren kennen en te bedanken voor de getoonde interesse en ondersteuning in de afgelopen jaren. In het bijzonder Aukje, Jacqueline, Mayken, Wilma, Bart en iedereen van de managementsgang veel dank. En natuurlijk Ilona, mijn fijne kamergenootje en inmiddels mede-promovendus. Wat hebben we de afgelopen jaren hoge pieken en diepe dalen zowel op onderzoeksgebied als persoonlijk vlak met elkaar mogen delen. Wat ben ik je dankbaar voor je betrokkenheid en dat mijn plaatsje op de nogal wisselende dagen en tijden dat ik aanwezig was steeds beschikbaar kon zijn. Jouw flexibiliteit om de kamer met mijn vele stagiaires te delen, jouw onuitputbare vriendelijkheid en je oprechte interesse zullen mij altijd bijblijven.

Vanuit Maastricht University ben ik dank verschuldigd aan Annemie, Seb en Jolanda. Annemie, dank voor de altijd snelle acties en reacties voor wat betreft benodigde stukken voor het onderzoek en proefschrift, en voor je attente berichten op persoonlijk vlak. Seb, dank voor je inzicht in de statistische methoden, hulp bij de interpretatie van de resultaten en je prettige medewerking aan onze paper over het effect van de interventie (hoofdstuk 8). Jolanda, dank dat je met een verfrissende en nauwkeurige blik hebt willen meewerken aan de paper over de procesevaluatie (hoofdstuk 7). Ik heb er heel veel aan gehad om iemand met ervaring op dit gebied hiervoor in mijn team te hebben.

Verder ben ik van Maastricht University de leden van het Expertisecentrum Hersenletsel Limburg dankbaar voor hun interesse in mijn onderzoek en de ondersteuning van een aantal van mijn presentaties. En niet te vergeten, ontzettend bedankt voor de fantastische dagen bij het congres in Granada tijdens de hectische afrondingstijd van dit proefschrift. Ook al was ik er bij eerdere uitjes steeds niet bij geweest, jullie hebben mij absoluut het gevoel gegeven dat ik welkom was, het voelde in Granada als een warm bad.

Aan alle leden van de HeJ werkgroepen Onderzoek en Ontwikkeling, en Revalidatie; heel veel dank voor de steeds weer opnieuw getoonde interesse in het onderzoek, de ondersteuning tijdens de vele presentaties erover door het hele land, en de door jullie verkregen nieuwe inzichten. Met ontzettend veel plezier ben ik lid van de werkgroepen geweest in de afgelopen jaren, wat een prachtige verzameling van enthousiaste en kundige mensen in het vakgebied heb ik daar leren kennen. Ik wens de werkgroepen een goed onderhoud en een fijne samenwerking, ook onderling, toe in de komende jaren. In het bijzonder dank aan Anne en Jeroen, jullie hebben de IPBIS congressen voor mij naast heel interessant ook ontzettend gezellig gemaakt. Anne, dankjewel voor je aanstekelijke optimisme en dat je ons duet in de karaokebar naar een hoger niveau wist te tillen. Jeroen, heel prettig vond ik het om naast het werkvlak ook met jou soms te kunnen sparren over de verdeling van werk en een thuisfront met een jong gezinnetje. Dank ook dat je mij steeds bij presentaties, vaak samen met Femke, hebt willen ondersteunen, ook al hadden jullie mijn verhaal al meerdere keren gehoord.

Gedurende het onderzoek zijn vele stagiaires betrokken geweest bij de dataverzameling, het invoeren en het controleren van de data. Frederique, Lauren, Kaylynn en Taylie, ontzettend bedankt voor jullie inzet, zonder jullie was het nooit gelukt. In het bijzonder bedank ik stagiaires Lisanne, Joyce, Lilliane, Melissa en Carina. Lisanne, wat een fijne eerste stagiaire had ik aan jou en wat heerlijk dat je wilde blijven om de interventie uit te voeren en om samen met mij aan een paper over een meetinstrument voor postconcussieve klachten te werken (to be continued). Joyce, ik weet bijna niet waar ik moet beginnen zoveel heb je voor mij betekend gedurende mijn promotie-traject. Als beginnend stagiaire werd je behoorlijk voor de leeuwen gegooid, maar je bleef staan, hielp mij bij werkelijk alle stukjes die bij het onderzoek te bedenken zijn, en hebt al mijn werkzaamheden opvangen tijdens mijn reis naar Nieuw-Zeeland. Je voorzag waar we tegenaan zouden lopen en dacht altijd mee om passende oplossingen te vinden. Super flexibel, onwijs betrokken ook op persoonlijk vlak, en zeer betrouwbaar, heel erg blij was ik dat ook jij bij het onderzoek betrokken wilde blijven als mijn onderzoeksassistent. Wij blijven elkaar zeker nog zien. Lilliane, foutjes die al driemaal over het hoofd waren gezien haalde jij er altijd nog uit. Naast al je andere extra hulp, vooral ook veel dank voor jouw heel secure controlewerk. Melissa, toen het niet langer in de tijd van Joyce paste om onderzoeksassistent te zijn kon ik mij geen betere vervangster wensen dan jij. Wat heb je het fantastisch opgepakt tijdens mijn zwangerschaps-en bevallingsverlof. Heel veel dank voor al jouw harde werken, flexibiliteit en betrokkenheid. Carina, wat kwam jij als mijn laatste stagiaire op het perfecte moment. Plannen en organiseren kun je als de beste en je hebt me dan ook erg geholpen met de afsluitende stukken voor het metingendeel van onderzoek, heel veel dank daarvoor. Leuk dat ik ook samen met jou in het volgende stuk van het onderzoek kon duiken, waarbij ik heel fijn met je heb samengewerkt aan het schrijven van de paper over de procesevaluatie (hoofdstuk 7).

Aan Boy Akkerman, Nina van Styrum en Marius Peters, bedankt voor de vormgeving van de illustraties voor de interventie, de cover van dit boekje en het Brains Ahead! logo, en de website voor het onderzoek. Ik had het zelf niet beter kunnen verzinnen en zeker niet kunnen maken.

Tijdens de laatste loodjes rondom de afronding van mijn proefschrift heb ik ook veel steun ondervonden aan de collega's van mijn nieuwe baan bij de Polikliniek Kinder- en Jeugdpsychiatrie/ Psychologie van het Erasmus MC-Sophia Kinderziekenhuis. Met name iedereen uit het team Ontwikkelingsstoornissen en in het bijzonder mijn lieve, zeer attente kamergenootje Yasmine, en ook Annemarie, Jill en André. Dank voor jullie meeleven en meedenken in deze laatste periode en de welkome kopjes koffie en gebakjes.

Ook aan al mijn vriendinnen heel veel dank voor jullie steun in de afgelopen jaren. Aan mijn gezellige mede-bootcamp-mama's Suzanne, Sonja, Nynke en Sarah, jullie maakten dat de sportieve afleiding die ik zocht naast het onderzoek en met een dikke buik ook nog eens hartstikke leuk werd. Bedankt dat jullie mij het gevoel gaven dat het niet niks was waar ik mee bezig was, dat heeft me er menigmaal doorheen geholpen.

Onderzoeksbuddies vanaf het prille begin; Nikita en Nita, hoe bijzonder toch dat jullie altijd mijn deadlines onthielden en vroegen hoe het met mijn papers ging en of ik al reacties had ontvangen. Heel erg bedankt voor jullie steun en medeleven en dat ik soms gewoon even lekker tegen jullie aan mocht klagen als het tegenzat.

Aan Liza, Esmee, Kèren, Angela, Merel, Lisette en Juul, bedankt voor jullie ondersteuning, de keren dat ik laat uit een meting zo bij jullie kon aanschuiven voor een maaltijd, de oppasbeurten toen ik laat moest doorwerken, de avondjes uit ter afleiding en het begrip dat ik tijdens de afrondingsmaanden van het proefschrift meer vriendschap moest nemen dan dat ik kon geven. Jullie hebben mij nooit het gevoel gegeven dat ik mij hierover schuldig hoefde te voelen en daarvoor ben ik jullie enorm dankbaar.

Karin en Janneke, vriendinnen voor al bijna zo lang ik mij kan heugen en ook al spraken wij elkaar in de afgelopen jaren zeker niet dagelijks, toch waren jullie altijd up-to-date wat betreft mijn bezigheden en oprecht geïnteresseerd. Heel fijn dat jullie ook bij dit belangrijke stuk van mijn leven betrokken wilden zijn.

Mijn lieve SJD-vriendinnen Hettie, Zairaeh en Wieneke, onwijs bedankt dat jullie me aan het lachen maakten als ik soms even niet meer zag zitten, dat ik bij jullie uit het niets mocht huilen met als gevolg dat ik het licht weer zag, dat ik bij jullie uitzinnig mocht zijn als het meezat en jullie er altijd voor in waren om de kleinste overwinningen met mij te vieren, voor de gesprekken over wat er echt toe doet in het leven, dat ik bij jullie mijzelf kan zijn zonder dat het me energie hoeft te kosten. Speciale dank aan Hettie, dat je altijd net even lekker verder prikt tot de bedoelde snaar is geraakt. Ook al ben ik je op het moment dat het gebeurt zelf niet altijd even dankbaar, je laat me erdoor groeien op de lange duur en dat is me heel dierbaar. Wat fijn dat jij bij dit voor mij speciale moment mijn paranimf wilde zijn.

Christine, jouw naam hoort eigenlijk op heel veel plekken in dit proefschrift thuis; mijn enige collega van Maastricht University die ook onderzoek naar NAH bij kinderen doet, mede-EHL-genootje door dik en dun, mede-secretaris van de HeJ werkgroep Onderzoek en Ontwikkeling, IPBIS-en andere congressen-buddy, paranimf…en vooral een hele lieve vriendin. Vanaf het eerste moment voelde ik een fijne klik met jou en wat is onze vriendschap in de afgelopen jaren gegroeid. Bedankt voor de keren dat ik bij jou in Maastricht mocht logeren, dat ik lief en leed over werkelijk alle stukjes van het onderzoek met je mocht delen, en dat jij kon aanvullen waar ik het niet meer wist. Zeker in laatste maanden waarbij wij exact dezelfde deadline voor ons proefschrift hadden zochten we veel contact. We deelden de druk, en naast die drukte stond je ook voor me klaar toen er privé wat minder vrolijke dingen speelden. We blijven elkaars wetenschaps-klinische connectie in de toekomst, maar bovenal ook vriendinnen. De goede lunches houden we erin.

Tot slot bedank ik van mijn familieleden mijn lieve nichtjes Carla, Heleen en Marieke, en ook tante Anneke, bedankt voor jullie interesse, meeleven en dat jullie mij het gevoel gaven dat ik met iets bijzonders bezig was. Dank ook voor de heerlijk welkome afleiding die jullie mij in de vele escaperooms hebben bezorgd in de afgelopen jaren. Wat ben ik blij dat we deze bijzondere band delen.

Tante Herma en oom Herman, bedankt ook dat jullie steeds vroegen hoe het ervoor stond en mijn blijdschap deelden op het moment dat ik het proefschrift had ingeleverd. Jullie woorden voelden voor mij alsof het die van mijn vader hadden kunnen zijn, weinig van stuk maar met krachtig veel inhoud.

Nersing en Petra, wat heb ik jullie steun in de afgelopen jaren gewaardeerd en wat is het prettig dat ik al bijna twaalf jaar ook bij jullie mag zijn zoals ik ben. Het zat hem in de kleine dingetjes van jullie kant die mij zoveel steun brachten, ik bof met zulke schoonouders.

Dyaran en Martijne, hoe gaaf is het om jullie als zwager en schoonzusje te hebben. Jullie stonden in de afgelopen jaren echt altijd klaar als er hulp nodig was, op onderzoeksgebied, klusgebied en persoonlijk vlak. Bedankt voor alle gezellige spelletjesavonden en dat er nog maar vele mogen volgen. Nu op naar jullie eigen promoties.

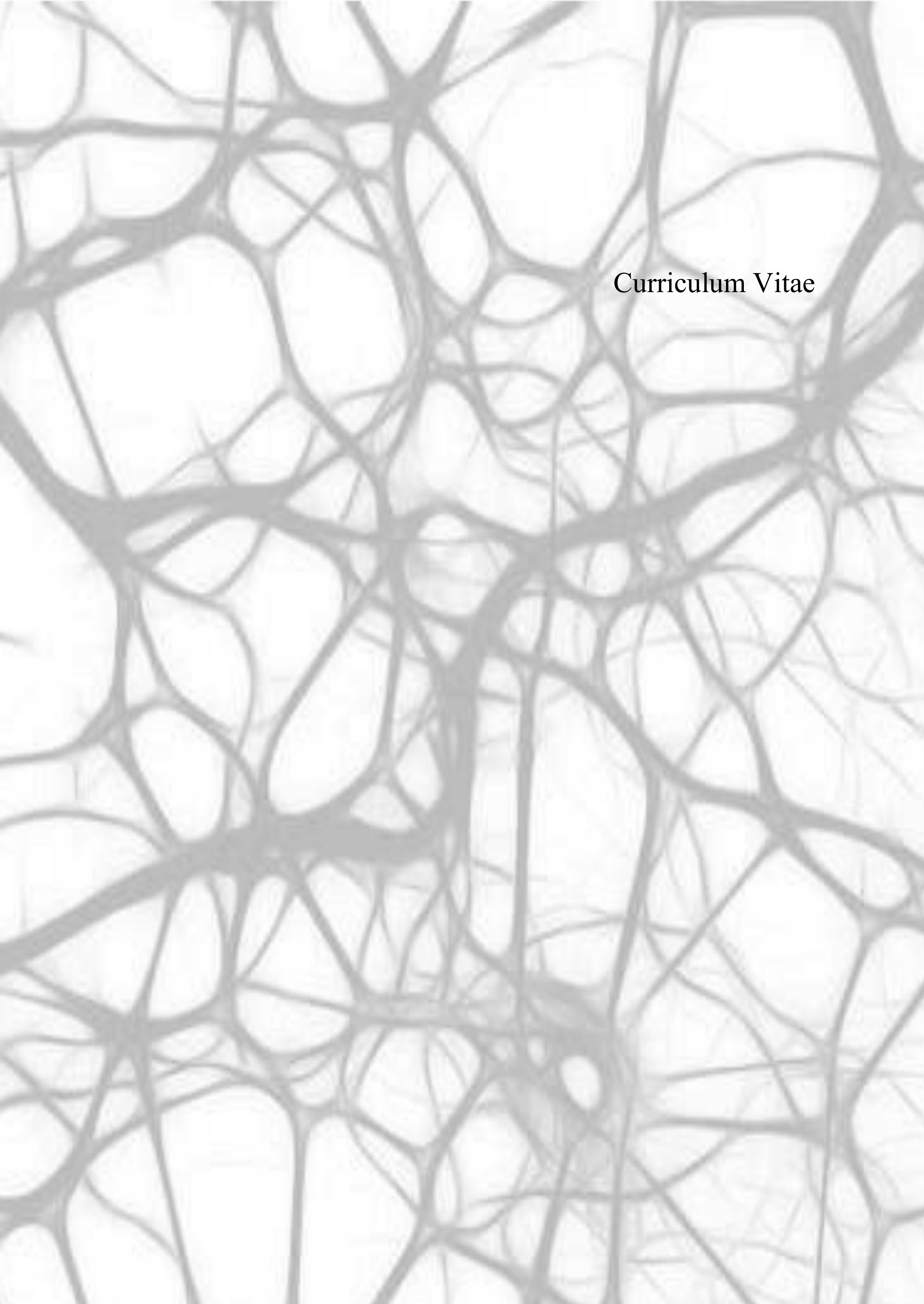
Melissa, mijn lieve zus. Ook al zijn we nog zo anders, toch hebben we ook best heel wat gemeen. Eén van die dingen is toch wel dat we elkaar altijd weten te vinden als het er echt toe doet. Niet altijd was het voor jou even duidelijk waar ik mee bezig was, maar je liet me weten dat je aan me dacht en gaf me complimentjes die me sterker maakten. Fijn het gevoel te hebben dat je trots op me bent.

Lieve mama, dankjewel dat ik bij je aan mocht schuiven na late metingen voor een hapje eten en voor het oppassen in de laatste stressvolle maanden van de afronding van dit proefschrift. Zeker in het begin was het soms wat wazig voor je wat mijn promotieonderzoek nu eigenlijk betekende, maar je gaf me vertrouwen in mijn eigen kunnen en bovendien dacht je er altijd aan om ook de trots die papa zou hebben gevoeld met mij te delen.

Lieve papa, elk stukje wat je kon heb je meegemaakt; wachten op mij tijdens mijn sollicitatie waar ik achteraf gezien ziek van de spanning voor was, je was erbij tijdens mijn eerste-en tweede jaargesprek in Maastricht, je snapte zo goed waar ik mee bezig was, stimuleerde mij altijd om het beste uit mezelf te halen, terwijl je me tegelijkertijd het gevoel gaf dat wat ik ook deed, het voor jou echt goed genoeg was. Helaas mocht het niet zo zijn dat je mijn verdediging nog mee kon maken, maar ik weet hoe trots je op me bent en dat je op me wacht om het ooit samen alsnog te kunnen vieren.

Allerliefste Sjanil, wat ben je mijn grote held geweest in de afgelopen jaren. Zo wist je mij, wanneer ik als een ware Gargamella mijn haat voor elektronische apparaten die nodig waren voor het onderzoek, zoals tokens, de laptop of een printer weer eens stond te uiten, altijd te kalmeren. Als ik tot midden in de nacht per se een analyse wilde afronden, omdat ik niet zou kunnen slapen als het niet was gelukt, dan wachtte je altijd op mij. In de laatste maanden voor afronding van het proefschrift heb je zoveel van de zorgen rondom de verbouwingen, de verhuizing en Sep op je genomen, en was je tegelijkertijd ook nog geheel onverdiend mijn boksbal. Veel bewondering en heel dankbaar ben ik voor dat je allemaal voor me hebt over gehad. Wat ben ik gelukkig dat ik samen met jou mijn leven en onze lieve Sep mag delen.

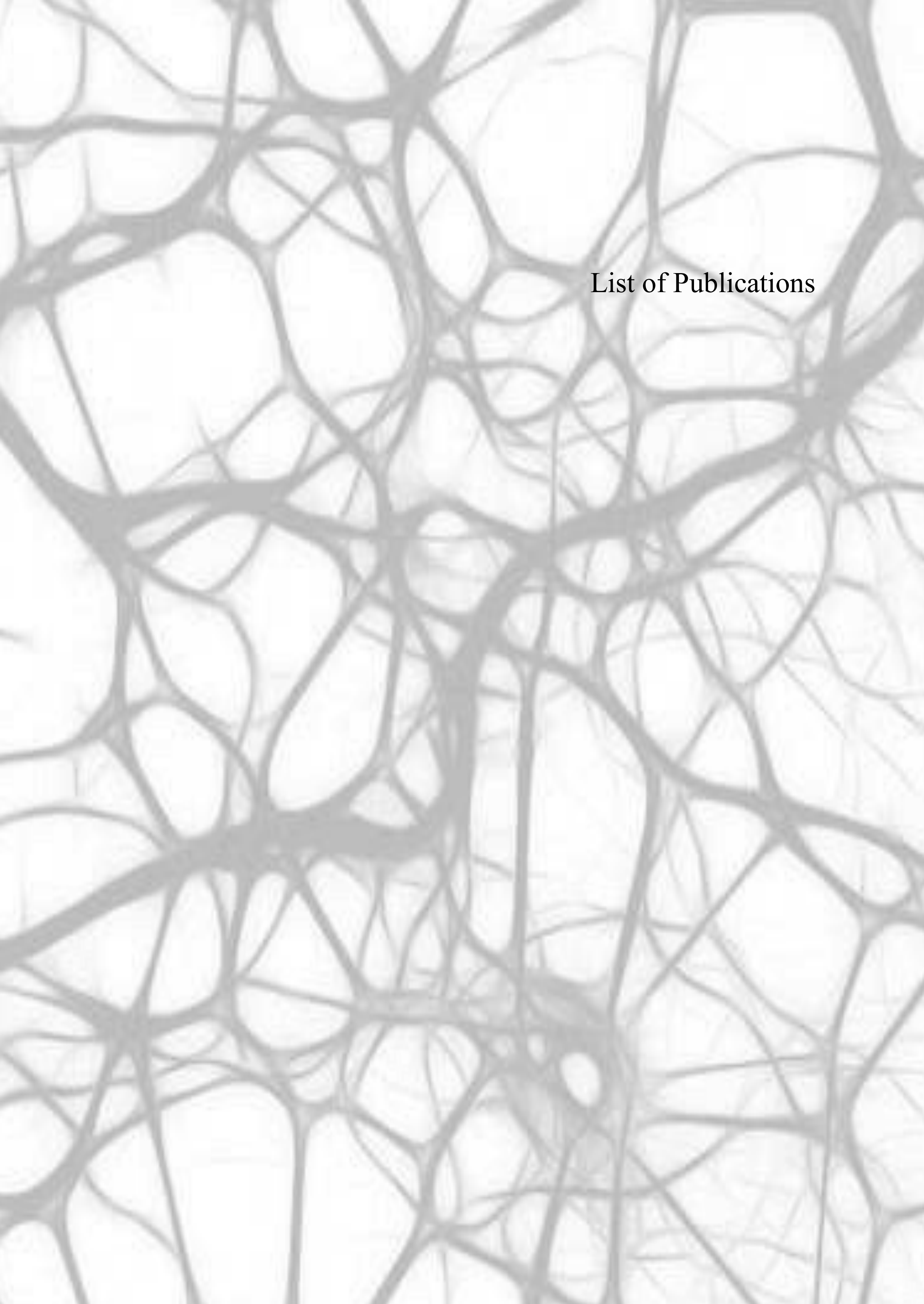
Lieve, lieve Sep, wat was het heerlijk om na een lange werkdag altijd jouw stralende lach en vrolijkheid om me heen te hebben. Dat gaf me keer op keer weer de energie om een nieuwe dag aan te kunnen. Wat ben ik blij dat je er bent!



Curriculum Vitae

Irene Renaud werd op 7 juni 1986 geboren te Delft. In 2003 behaalde zij haar HAVO diploma aan De Lage Waard te Papendrecht. Hierna is Irene begonnen aan de HBO opleiding Sociaal Juridische Dienstverlening te Rotterdam, waar zij in 2007 haar diploma voor behaalde. Hierna heeft zij twee jaren Rechten gestudeerd aan de Erasmus Universiteit, waarbij zij zich niet kon voorstellen dat zij dit vak gedurende haar verdere leven uit zou moeten voeren en daarom in 2009 de overstap naar Psychologie heeft gemaakt. In 2013 behaalde Irene haar Bachelor diploma psychologie bij de Universiteit Leiden. Om af te studeren koos Irene hierna de richting klinische neuropsychologie, waarvoor zij haar klinische-en haar onderzoeksstage allebei in het Erasmus MC – Sophia Kinderziekenhuis heeft gevolgd. In 2014 studeerde Irene af in de richting klinische neuropsychologie aan de Universiteit Leiden. Na haar afstuderen bleef Irene werkzaam binnen het Erasmus MC – Sophia Kinderziekenhuis op de afdeling Kinder-en Jeugdpsychiatrie en Psychologie als neuropsycholoog binnen het team ontwikkelingsstoornissen. In oktober 2014 begon zij als promovendus aan de Universiteit Maastricht van waaruit zij werd gedetacheerd in Revant Revalidatiecentrum te Breda. Sinds 2015 was zij gedeeld secretaris voor de landelijke werkgroep Hersenletsel en Jeugd (HeJ) – Onderzoek en Ontwikkeling. In 2015 behaalde Irene verder het certificaat Academic Writing for PhD-students en in 2016 slaagde zij voor de Basiscursus Klinisch Onderzoekers (BROK). Vanaf 2018 volgde Irene naast haar PhD-werkzaamheden de Basiscursus Cognitieve Gedragstherapie – richting Kind en Jeugd, waarvoor zij bij het Erasmus MC – Sophia Kinderziekenhuis afdeling Kinder-en Jeugdpsychiatrie en Psychologie binnen het team internaliserende stoornissen ruimte vond om in de praktijk te kunnen oefenen. In februari 2019 behaalde Irene haar diploma voor de Basiscursus Cognitieve Gedragstherapie – richting Kind en Jeugd. Sindsdien is zij werkzaam als neuropsycholoog bij het Erasmus MC – Sophia Kinderziekenhuis afdeling Kinder-en Jeugdpsychiatrie en Psychologie binnen het team ontwikkelingsstoornissen.

List of Publications



International publications

- Renaud, M.I., van de Port, I.G., Catsman-Berrevoets, C.E., Bovens, N., Lambregts, S.A., van Heugten, C,M. (2018). The Brains Ahead! intervention for children and adolescents with mild traumatic brain injury and their caregivers: rationale and description of the treatment protocol. Clin Rehabil., 32(11), 1440-1448.
- van Heugten, C., Renaud, I., Resch, C. (2017). The role of early intervention in improving the level of activities and participation in youths after mild traumatic brain injury: a scoping review. Concussion, 2(3), CNC38.
- Renaud, M.I., Lambregts, S.A.M., de Kloet, A.J., Catsman-Berrevoets, C.E., van de Port, I.G.L., van Heugten, C.M. (2016). Activities and participation of children and adolescents after mild traumatic brain injury and the effectiveness of an early intervention (Brains Ahead!): study protocol for a cohort study with a nested randomised controlled trial. BioMed Central, 17, 236-247.

Submitted articles

- Renaud, MI., van de Port, I.G., Catsman-Berrevoets C.E., Köhler, S., Lambregts, S.A., van Heugten, C,M. Effectiveness of the Brains Ahead! intervention: Six months results of a randomized controlled trial in school-aged children with mild traumatic brain injury. Journal of Head Trauma Rehabilitation.
- Renaud, MI., van de Port, I.G., Catsman-Berrevoets C.E., Jellema, K., Lambregts, S.A., van Heugten, C,M. Activities and participation in the first six months after mild traumatic brain injury in children and adolescents: the Brains Ahead study, a prospective longitudinal cohort study. Journal of Head Trauma Rehabilitation.
- Renaud, M.I., Klees, C., Haastregt J., Catsman-Berrevoets C.E., van de Port, I.G., Lambregts, S.A., van Heugten, C,M. Process evaluation of Brains Ahead!: an intervention for children and adolescents with mild traumatic brain injury.
- Renaud, M.I., Lambregts, S.A.M., van de Port, I.G.L., Catsman-Berrevoets, C.E., van Heugten, C.M. Predictors of activities and participation six months after mild traumatic brain injury in children and adolescents.

International conferences and presentations

International Conference on Paediatric Acquired Brain Injury (IPBIS):

- Renaud, M.I., van de Port, I.G., Catsman-Berrevoets, C.E., Bovens, N., Lambregts, S.A., van Heugten, C,M. The Natural Course of Activities and Participation in Children and Adolescents up to Six Months After Mild

Traumatic Brain Injury. Third International Conference on Paediatric Acquired Brain Injury. Belfast, September 2018. (oral)

- Renaud, M.I., van de Port, I.G., Catsman-Berrevoets, C.E., Bovens, N., Lambregts, S.A., van Heugten, C,M. The Brains Ahead! Intervention for Children and Adolescents with Mild Traumatic Brain Injury and their Caregivers: Rationale and description of the treatment protocol. Third International Conference on Paediatric Acquired Brain Injury. Belfast, September 2018. (oral)
- Renaud, M.I., Bosma, L., van de Port, I.G., Catsman-Berrevoets, C.E., Lambregts, S.A., van Heugten, C,M. Postconcussive symptoms and its predictors in children and adolescents up to six months after Mild Traumatic Brain Injury. Second International Conference on Paediatric Acquired Brain Injury. Rome, September 2017. (oral)
- Van Heugten C.M., Renaud, M.I., Resch, C. The Role of Early Intervention in Improving the Level of Activities and Participation in Youths after Mild Traumatic Brain Injury: A Scoping Review. Second International Conference on Paediatric Acquired Brain Injury. Rome, September 2017. (poster)

International Brain Injury Association - World Congress on Brain Injury (IBIA):

- Renaud, M.I., Lambregts, S.A.M., de Kloet, A.J., Catsman-Berrevoets, C.E., van de Port, I.G.L., van Heugten, C.M. Activities and participation in children and adolescents after mild traumatic brain injury and the effectiveness of an early intervention: design of the Brains Ahead! Study. International Brain Injury Association - Eleventh World Congress on Brain Injury. Den Haag, March 2016. (poster)

Conference in Neuropsychological Rehabilitation of the Special Interest Group of the WFNR

- Renaud, M.I., van de Port, I.G., Catsman-Berrevoets, C.E., Lambregts, S.A., van Heugten, C.M. Outcome and predictors of activities and participation six months after mild traumatic brain injury in children and adolescents: the Brains Ahead study, a prospective longitudinal cohort study. 16th Conference in Neuropsychological Rehabilitation of the SIG-NR-WFNR. Granada, June 2019. (oral)
- Renaud, M.I., van de Port, I.G., Catsman-Berrevoets, C.E., Köhler, S., Lambregts, S.A., van Heugten, C.M. Effectiveness of the Brains Ahead! intervention: A randomized controlled trial in school-aged children with mild traumatic brain injury and caregivers. 16th Conference in Neuropsychological Rehabilitation of the SIG-NR-WFNR. Granada, June 2019. (oral)

National conferences and presentations

Brain Awareness Week:

- Renaud, M.I., van de Port, I.G., Catsman-Berrevoets, C.E., Bovens, N., Lambregts, S.A., van Heugten, C,M. Het natuurlijk beloop van activiteiten en participatie bij kinderen en adolescenten tot 6 maanden na licht traumatisch hersenletsel. Brain Awareness Week. Den Haag, September 2018. (oral)
- Renaud, M.I., Lambregts, S.A.M., de Kloet, A.J., Catsman-Berrevoets, C.E., van de Port, I.G.L., van Heugten, C.M. Activiteiten en participatie bij kinderen en adolescenten na licht traumatisch hersenletsel en het effect van een vroege interventie: design van de Brains Ahead! studie. Symposium "Een stille epidemie? Traumatisch Hersenletsel bij kinderen" Brain Awareness Week. Den Haag, Maart 2015. (poster)

Hersenletselcongres:

- Renaud, M.I., van de Port, I.G., Catsman-Berrevoets, C.E., Bovens, N., Lambregts, S.A., van Heugten, C,M. Het natuurlijk beloop van activiteiten en participatie bij kinderen en adolescenten tot 6 maanden na licht traumatisch hersenletsel en voorspellende factoren. Hersenletselcongres. Ede, November 2018. (oral)
- Renaud, M.I., Bosma, L., van de Port, I.G., Catsman-Berrevoets, C.E., Lambregts, S.A., van Heugten, C,M. Postconcussieve klachten na licht traumatisch hersenletsel bij kinderen: voorspellende waarde van letselgerelateerde- , kind-specifieke-, en omgevings- factoren. Hersenletselcongres. Ede, november 2017. (oral)
- Renaud, M.I., Lambregts, S.A.M., de Kloet, A.J., Catsman-Berrevoets, C.E., van de Port, I.G.L., van Heugten, C.M. Activiteiten en participatie bij kinderen en adolescenten na licht traumatisch hersenletsel en het effect van een vroege interventie: design van de Brains Ahead! studie. Hersenletselcongres. Ede, November 2016. (oral)

Samen Nog Beter congres:

- Renaud, M.I., Lambregts, S.A.M., de Kloet, A.J., Catsman-Berrevoets, C.E., van de Port, I.G.L., van Heugten, C.M. Activiteiten en participatie bij kinderen en adolescenten na licht traumatisch hersenletsel en het effect van een vroege interventie: design van de Brains Ahead! studie. Samen Nog Beter Congres. Zeist, oktober 2017. (oral)

Invited Symposium: 'What's new, what's next?' Kinderen met traumatisch hersenletsel.

- Renaud, M.I., van de Port, I.G., Catsman-Berrevoets, C.E., Lambregts, S.A., van Heugten, C,M. Activiteiten en participatie bij kinderen en adolescenten na licht traumatisch hersenletsel en het effect van een vroege interventie: resultaten van de Brains Ahead! studie. Revant Revalidatiecentrum. Breda, juni 2019. (oral)

Other

Dutch presentations at the participating hospitals from Brains Ahead! (all oral):

"Renaud, M.I., Lambregts, S.A.M., de Kloet, A.J., Catsman-Berrevoets, C.E., van de Port, I.G.L., van Heugten, C.M. Activiteiten en participatie bij kinderen en adolescenten na licht traumatisch hersenletsel en het effect van een vroege interventie: design van de Brains Ahead! studie."

- De refereerbijeenkomst centrum RDGG in Delft op 17 november 2016;
- De refereerbespreking van de SEH in het Erasmus MC op 25 juni 2015;
- De Polivergadering kinderneurologie (chirurgie, neurologie en SEH) in het MC Haaglanden op 12 mei 2015;
- De refereerbijeenkomst van de afdeling orthopedie in het Amphia Ziekenhuis op 27 februari 2015;
- De refereerbijeenkomst van de afdeling kinderneurologie in het Erasmus MC – Sophia Kinderziekenhuis op 23 februari 2015;
- De refereerbijeenkomst van de kinderafdeling in het Amphia Ziekenhuis op 5 februari 2015;

Dutch presentations for other interested parties:

"Renaud, M.I., Lambregts, S.A.M., de Kloet, A.J., Catsman-Berrevoets, C.E., van de Port, I.G.L., van Heugten, C.M. Activiteiten en participatie bij kinderen en adolescenten na licht traumatisch hersenletsel en het effect van een vroege interventie: design van de Brains Ahead! studie."

- De researchvergadering kinder- en jeugdpsychiatrie/psychologie in het Erasmus MC – Sophia Kinderziekenhuis op 23 juni 2016. (oral)
- Artsenoverleg standplaats Revant Revalidatiecentrum Breda op 28 april 2016. (oral)
- Unitoverleg standplaats Revant Revalidatiecentrum Breda op 5 februari 2016. (oral)

- De polivergadering kinder- en jeugdpsychiatrie/psychologie in het Erasmus MC – Sophia Kinderziekenhuis op 13 mei 2015. (oral)
- Research Day van de vakgroep NP&PP op de UM op 30 maart 2015. (oral)
- Research Day FPN van de UM op 29 januari 2015. (poster)
- Bij onderzoeksoverleg standplaats Revant Revalidatiecentrum Breda op 16 december 2014 (oral).;

Dutch presentations at national working groups for children with acquired brain injuries (all oral):

“Renaud, M.I., Lambregts, S.A.M., de Kloet, A.J., Catsman-Berrevoets, C.E., van de Port, I.G.L., van Heugten, C.M. Activiteiten en participatie bij kinderen en adolescenten na licht traumatisch hersenletsel en het effect van een vroege interventie: design van de Brains Ahead! studie.”

- Bijeenkomst van de Landelijke werkgroep NAH op 11 november 2015.
- Bijeenkomst van de NAH onderzoeksgroep op 19 januari 2015.

Guest lectures:

- Renaud, M.I., Lambregts, S.A.M., de Kloet, A.J., Catsman-Berrevoets, C.E., van de Port, I.G.L., van Heugten, C.M. Beloop van activiteiten en participatie na licht traumatisch hersenletsel bij kinderen en voorspellers. Gastcollege AIOS Neurologie. Erasmus MC – Sophia Kinderziekenhuis, November 2018.
- Renaud, M.I., Lambregts, S.A.M., de Kloet, A.J., Catsman-Berrevoets, C.E., van de Port, I.G.L., van Heugten, C.M. Activities and participation of children and adolescents after mild traumatic brain injury and the effectiveness of an early intervention (Brains Ahead!): study protocol for a cohort study with a nested randomized controlled trial. Gastcollege Psychologie studenten – Keuzevak: Neuropsychology- child; Maastricht University, September 2016