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Participation of children and youth with acquired brain injury

Kloet, A.J. de

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PARTICIPATION OF CHILDREN AND YOUTH WITH ACQUIRED BRAIN INJURY

Arend de Kloet

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PARTICIPATION OF CHILDREN AND YOUTH WITH ACQUIRED BRAIN INJURY

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	Prof. Dr. W.C. Peul

CONTENTS

LIST OF ABBREVIATIONS (used more than once)

ABI	Acquired Brain Injury
ADEM	Acute Disseminated Encephalo Myelitis
ADL	Activities of Daily Living
CASP	Child and Adolescent Scale of Participation
CAFI	Child and Adolescent Factors Inventory
CASE	Child and Adolescent Scale of Environment
CFFS	Child and Family Functioning Survey
CNS	Central Nervous System
CT	Computed Tomography
CVA	Cerebro Vascular Accident
DBC-codes	Diagnose-Behandel-combinatie codes (Dutch)
DLV	Dutch Language Version
EMC/ Erasmus MC	Erasmus Medical Centre
GCS	Glasgow Coma Scale
HI-BS	Head injury minus brain symptoms
HI+BS	Head injury with brain symptoms:
	HI+BS mild — Head injury with mild brain symptoms
	HI+BS moderate — Head injury with moderate brain symptoms
	HI+BS severe — Head injury with severe brain symptoms
ICD-codes	International Statistical Classification of Diseases codes
ICF	International Classification of Functioning, Disability and Health
ICF-CY	International Classification of Functioning, Disability and Health for Children and Youth
IQR	Inter Quartile Range
METC	Medical Ethical Committee
MRI	Magnetic Resonance Imaging
mRS	Modified Rankin Scale
MS	Multiple Sclerosis
N	Number
NTBI	Non-Traumatic Brain Injury
PedsQL™4.0	Paediatric Quality of Life Inventory
PedsQL™FIM	Paediatric Quality of Life Inventory Family Impact Module
PedsQL™HR QoL	Paediatric Quality of Life Inventory Heath Related Quality of Life
PSOM-SNE	Paediatric Stroke Outcome Measure Short Neuro Exam
PTA	Post Traumatic Amnesia
SD	Standard Deviation
SES	Socio Economic Status
SPSS	Statistical Package for the Social Sciences
TBI	Traumatic Brain Injury
WHO	World Health Organization

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Chapter 1
General Introduction

DEFINITION AND EPIDEMIOLOGY OF ACQUIRED BRAIN INJURY (ABI) IN CHILDREN AND YOUTH

Definitions of Acquired Brain Injury (ABI) and children and youth

ABI refers to any post-neonatal damage to the brain, due to an external cause (traumatic brain injury, TBI) or an internal cause (non-traumatic brain injury, NTBI).[1]

According to the World Health Organization[2] children are persons up to and including 14 years and youth persons up to and including 23 years. Within these age groups, preschool children (-5 years), adolescents (13-18 years) and young adults (19-23 years) can be distinguished.

Incidence of ABI

With respect to the incidence of TBI, epidemiological studies in children and youth have so far mainly focused on the age group up to 14 years. In this age group, the reported incidence rates for TBI vary from 70-798 per 100.000 persons per year.[3] Differences among reported rates may be due to differences in classification, inclusion criteria, hospital registrations or national health care systems. Reported rates are probably an underestimation, as it is suggested that mild TBI is unreported or unrecognized in up to half of the cases of head injuries.[4]

Data on the incidence of NTBI are variable as well, and are mainly available for specific causes, including brain tumours (3.5/100.000 in the age group up to 14 years)[5,6] and stroke (2-13/100.000 in the age group up to 14 years).[7]

Overall there is a trend towards an increasing incidence and prevalence of ABI in children and youth over the past decades.[3] This is probably in part related to better registration and also to improvements in medical care.

Causes of ABI

ABI in children and youth may result from events with an external cause (traumatic brain injury, TBI) such as accidents (in traffic, at home or during sports) and violence or from an internal cause (non-traumatic brain injury, NTBI), such as a brain tumour, stroke or infections such as meningitis or encephalitis.[1]

TBI has an acute onset, the onset of NTBI may also be acute (stroke) but is in some cases more gradual (tumour, infection). In the age group up to 4 years old NTBI is most often caused by meningitis; in the age groups from 5 up to 9 and 10 up to14 years old by brain tumours and in the group from 15 up to 19 years by toxic effects of substances.[8] The cause of TBI determines the type of lesion and damage of brain tissue, e.g. more focal or diffuse injuries. The consequences of NTBI can both be local (stroke, tumour), or more diffuse, affecting the entire brain (anoxia, hypoxia or infection).[9] Concerning the causes of TBI and NTBI in children and youth specifically in the Netherlands the information is sparse and incomplete.

Severity of ABI

The severity of ABI is classified as mild, moderate or severe in both TBI and NTBI, however the classification systems are different.[10,11]

Table 1 Classification of severity of injury

	Glasgow Coma Scale (GCS)	Post Traumatic Amnesia (PTA)	Loss Of Consciousness (LOC)
Mild	13-15	<1 day	0-30 minutes
Moderate	9-12	1 to 7 days	30 minutes to 24 hours
Severe	3-8	>7 days	>24 hours

From: Eastvold et al., 2013

In TBI, the classification is usually done during hospital admission, using The Glasgow Coma Scale (GCS)[10] (See Table 1) or the paediatric version of the GCS (PGCS)[11] in preverbal children up to 2 years old (See Table 2) as the gold standard combined with neurological and imaging measures.

Table 2 (Paediatric) Glasgow Coma Scale (GCS and PGCS)

Adult			**Pediatric**	
Spontaneously	4	Best Eye Opening	Spontaneously	4
To verbal stimuli	3		To verbal stimuli	3
To painful stimuli	2		To painful stimuli	2
No eye opening	1		No eye opening	1
Oriented	5	Best Verbal Response	Appropiate coo & cry	5
Confused	4		Irritable cry	4
Inappropriate words	3		Inconsolable crying	3
Incomprehensible	2		Grunts	2
No verbal response	1		No verbal response	1
Obeys commands	6	Best Motor Response	Normal spontaneous	6
Localizes pain	5		Withdraws to touch	5
Withdraws to pain	4		Withdraws to pain	4
Flexion to pain	3		Flexion to pain	3
Extension to pain	2		Extension to pain	2
No motor response	1		No motor response	1

From: Teasdale et al., 1974; Holmes et al., 2005

Moreover, the duration of Post Traumatic Amnesia (PTA) and of loss of consciousness (LOC) as well as other neurological signs are taken into account.[12,13]

In addition to the abovementioned instruments, the King's Outcome Scale for Childhood Head Injury (KOSCHI)[14] and the Glasgow Outcome Scale (GOS)[15] are developed and used to indicate the severity of injury and/or the prognosis in TBI.
Severity of NTBI (Table 3) is usually determined by means of the paediatric modified Rankin Scale (mRS),[16] despite a lack of formal validation in this group of children.

Table 3 Modified Rankin Scale (mRS)

Score	Description
0	No symptoms at all
1	No significant disability despite symptoms; able to carry out all usual duties and activities
2	Slight disability; unable to carry out all previous activities, but able to look after own affairs without assistance
3	Moderate disability; requiring some help, but able to walk without assistance
4	Moderately severe disability; unable to walk without assistance and unable to attend to own bodily needs without assistance
5	Severe disability; bedridden, incontinent and requiring constant nursing care and attention
6	Dead
TOTAL (0-6): _____	

From: Bonita & Beaglehole, 1988

Consequences of ABI in children and youth

With ABI, depending on its nature and severity, multiple neural systems may be involved, resulting in a large variety of potential consequences in body functions and structures. In addition the course of outcome after ABI is highly variable, ranging from a) full recovery, b) persisting and severe impairment, c) absence of impairment initially, with emerging problems over time to d) early slowed development, with catch-up over time.[17]
The complex and intertwined interaction between the health problem (ABI) and its consequences in various health-related domains (body functions and structures, activities and participation, personal and environmental factors) is represented in the International Classification of Functioning, Disability and Health for Children and Youth (ICF-CY) model (Figure 1).[18] Within this comprehensive framework 'Functioning' refers to abilities encompassing body functions (physiological functions of systems) and structures (anatomical parts), activities (execution of actions or tasks by an individual) and participation. Participation is the dynamic result of the complex interactions in the ICF-CY model, and defined as "the nature and extent of a person's involvement in meaningful life situations at home, school, work and community life".[18] Thereby, participation is vital for the development of physical, psychological and social emotional skills and competences, the shaping of identity, the achievement of physical and mental health and well-being.[19] It is conditional to fulfil one's

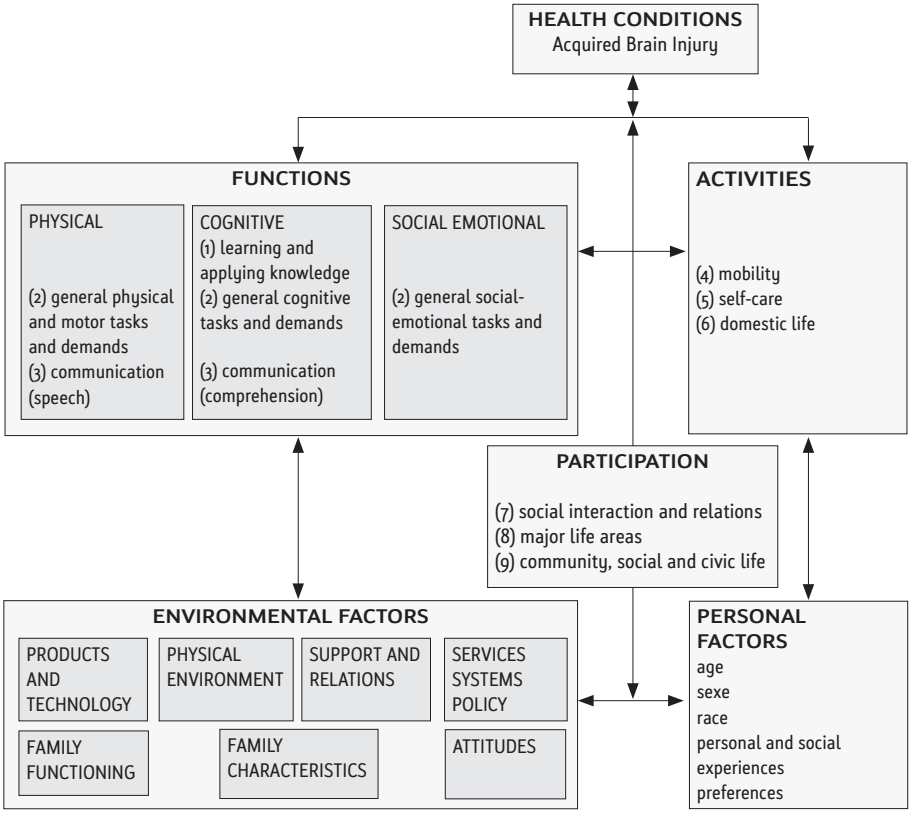
potential as an active participant at home and in the community and associated with positive outcomes in future life.[20]

In addition, the ICF-CY model underscores the influence of personal factors (individual background: e.g. gender, race) and environmental factors (physical, social and attitudinal environment) on body functions and structures and on activities and participation.

Furthermore, 'disability' is an umbrella concept, encompassing impairments of body functions and structures and limitations in activities and participation restrictions.[17,20]

Quality of life (QoL), with the ICF code nd-qol, refers to the general well-being of individuals, including mental, physical and social functioning, and is an important general outcome of ABI as health problem.[20] Overall it is found that consequences of paediatric ABI may reduce QoL, in particular after severe injuries.[21,22] In adolescent TBI survivors reduced QoL is seen in patients with all levels of severity.[23]

Figure 1 The model of the International Classification of Functioning, Disability and Health for Children and Youth (ICF-CY)



Based on: World Health Organization, 2007

Consequences of Traumatic Brain Injury (TBI)

TBI is the leading cause of death and permanent disability among children and youth worldwide.[1,3,4] Overall, the mortality rate in children with TBI is 1%.[4] In TBI the primary injury results immediately from the initial trauma. Complications (secondary injury) include e.g. cerebral hypoxia, hypotension or cerebral oedema. These may occur in the hours and days following the primary injury and cause additional damage.[2,4] Moreover, the physical consequences are associated with the presence or absence of injuries at other parts of the body.[13] Some consequences may be transient, such as those occurring in the post-acute phase (e.g. post traumatic amnesia) or the recovery phase (e.g. temporary post commotional symptoms as headaches, dizziness and irritability).[17] Some symptoms may recover quickly, whereas other problems such as limited energy or cognitive and behavioural consequences often persist at the long term and may impede participation.[25] A small number of children and youth are still in a vegetative or minimal conscious state 1 month after onset of a severe TBI. Worldwide, according to calculations, the actual prevalence was calculated as 49 per million people (PMP, exact numbers are unknown in the Netherlands.[26]

Consequences of paediatric TBI regarding functioning in ICF[2] terms are listed in Table 4.

Table 4 Consequences (limitations) of Traumatic Brain Injury in children and youth, in categories of the International Classification of Functioning, Disability and Health for Children and Youth (ICF-CY)[18]

	PHYSICAL	COGNITIVE	SOCIAL-EMOTIONAL
FUNCTIONS AND STRUCTURES	physical health, seizures taxability/fatigue [30,31] general motor functions, e.g. muscle tone, strength and endurance, coordination,[32] and balance[33] sensory functions[35]	general intellectual functioning,[35] cognitive/mental fatigue[31] memory, attention, speed of information processing, linguistic and praxis abilities[36], cognitive control (inhibition, working memory, flexibility of response)[37] central sensory processing[34] and sensory integration[38]	social cognition/information processing,[40] problem solving[41] specific behavioral / psychiatric disorders (e.g. impulsivity, disinhibition, temper control, mood swings, depression, loss of temper)[4,42]
ACTIVITIES	hip-extension strength, step length[33]; mobility, self care, daily routines[28]	learning and applying knowledge[32]	communicative competences[43] and pragmatic language skills[40]
PARTICIPATION	physical activity and sports[33]	lower school performance, educational attainment and work status[32,39]	social interpersonal interactions, relationships and activities,[4,44] diversity (preference) and intensity (frequency) in recreational activities[45] social competence,[46] social involvement during adolescence and young adulthood,[47,48] perceived quality of life[20,48,49] increased risk for alcohol and drug dependency[50]

Consequences of Non-Traumatic Brain Injury (NTBI)

In general, the death rate after paediatric NTBI is relatively high compared to TBI. In children and youth with stroke, a mortality rate of 16-42% is reported.[27] The occurrence of persisting problems after NTBI is relatively high as well. In children and youth with stroke, long-term consequences are seen in 50-75% of the patients.[27]

Although it is suggested that the consequences of NTBI are often similar to those of TBI,[28] due to differences in their causes and nature the outcome after a TBI cannot be extrapolated to the various aetiologies of NTBI.[29] Consequences of NTBI with respect to body structure and functions and activities and participation after paediatric NTBI are listed in Table 5.

Table 5 Specific consequences of Non-Traumatic Brain Injury in children and youth in categories of the International Classification of Functioning, Disability and Health for Children and Youth (ICF-CY),[18] in addition to Table 4

		PHYSICAL	COGNITIVE	SOCIAL-EMOTIONAL
BODY FUNCTIONS AND STRUCTURES	Brain tumours	growth, puberty, hormone system, sexual functions[5] motor problems (e.g. ataxia , dysarthria, speech problems),[51] impaired sense of smell, impaired hearing, facial paralysis, dizziness, hypoesthesia[52] aphasia[52] visual (field) impairments, double vision, eye movements[5] neurotoxicity[29]	spatial orientation[52]	
	Stroke	hemiparesis[53] visual field impairments, speech[54]	learning difficulties - mental retardation,[59] poor attention[54]	behavioral problems[54]
	Meningitis/ encephalitis	motor deficits, including paralysis, ataxia and hemiparesis; loss of consciousness, seizures; visual and hearing difficulties[55-57]	decreased mental functioning[57,60]	behavioral problems [60,61]
	Anoxic/ hypoxic	poor motor outcome[9] risk of persistent vegetative state (hypoxic injury, e.g. after nearly drowning), seizures[58]	poor outcome, mental retardation (some types of epilepsy)[9]	
ACTIVITIES	Probably comparable with TBI in Table 4 No specific NTBI literature found			
PARTICIPATION		Probably comparable with TBI in Table 4 No specific NTBI literature found	Probably comparable with TBI in Table 4 No specific NTBI literature found	Socializing, wellbeing, quality of life[5,54]

This list is not complete since some conditions are relatively rare, and thus limited information on their consequences is available. An example of such a condition is ADEM (Acute Disseminated Encephalo Myelitis).

Regarding the consequences of paediatric TBI and NTBI it should first be noted that so far, the knowledge on the outcomes of paediatric NTBI is relatively sparse, as the focus of most research in paediatric ABI has been on TBI. Second, the literature on outcomes in children and youth with ABI shows inconsistent results. This variability is due to several reasons: a) studies lack well defined groups with respect to the type and severity of injury; b) there is variation regarding age at the time of injury; c) the number of time points and duration of follow-up is often limited; d) there is large variation in outcome measures; and e) studies usually have small sample sizes, resulting in limited statistical power, and have other methodological flaws.[42,62,63]

Consequences of paediatric ABI on the family

The impact of ABI in youth may also result in family adversity, with high levels of perceived burden, disrupted family systems and unmet support needs.[44] So far, studies on the consequences of family impact after ABI were mainly done in the United States and Australia, and were predominantly focused on TBI. It was found that although many families eventually adapt favourably to the often increased demands of the injury, still clinically significant stress was seen more than 12 months after the trauma in 40-45% of the families with a child with TBI.[64] This observation did not only apply to severe, but also to mild or moderate TBI. It has been suggested that in some cases family members may experience more problems than the child with an ABI.[64]

Due to the unexpected onset of an ABI, the unknown and often not visible consequences and uncertain prognosis, the impact on the family is often delayed until recovery has reached a stable phase and efforts at community reintegration have begun.[38]

Hawley[4] reported sibling stress in 56-33-13% and unmet information need in 83-79-71% of siblings, 2 years after the onset of severe-moderate-mild TBI, respectively. Brothers and sisters were found to suffer from mental stress (changes in mood, problems at school, feeling guilty, worries about recovery/future), changes in family functioning (roles, climate, activities), physical stress (extra tasks, sleeplessness) and chronically increased alertness and responsibility.[64,66] Moreover, it was found that only few families sought support.[67]

Notably, the instruments used to measure the impact of ABI on the family varied widely, again allowing no valid comparison between studies.

> *"Nearly loosing a child was a very traumatic experience as a parent. People telling us how lucky we are that our child is still alive is very depressing, in fact we are still mourning about loosing our child of before the ABI"*
>
> Quote of a parent of a child with ABI

In conclusion, studies on the impact of paediatric ABI on families has so far mainly focused on TBI, with a variety of instruments used to determine its occurrence and severity. The availability of an appropriate instrument for family impact after ABI is important, as it has been previously suggested that measuring and monitoring family impact and functioning should be promoted as long-term patients' outcome is related to family and environmental factors.[66,67]

Determinants of participation after ABI

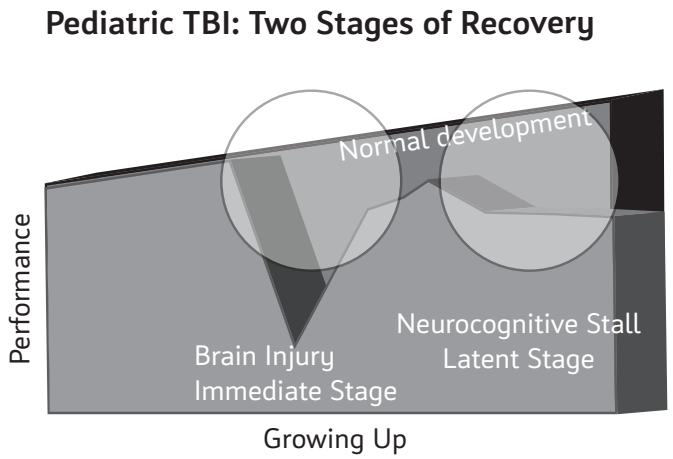
Research in paediatric ABI has long been mainly focussed on physical and cognitive outcomes (body functions and structure) and their determinants, only more recent studies focus on psychosocial outcome,[61] including participation. No systematic literature review study so far specifically addressed the determinants of participation outcomes in both TBI and NTBI. Only some narrative reviews on the outcome of ABI addressed the predictors of outcome.[62,63,68,69] Factors which were reported to be associated most consistently with participation following paediatric ABI included: health conditions (especially severity of injury, neurological complications), body functions and structure (especially movement functions, cognitive functioning, behavioural functioning, mood, mental fatigue), activities (especially communication, self-care), environmental factors (especially family functioning, family nurturing/parenting style, social economic status, acceptance in community, availability of special programs) and personal factors (especially pre-injury behavioural competences, pre-injury cognitive competences).[26,28,32,70] The studies included in these reviews were mainly focused on TBI and employed a large variety of measurement instruments for both predictors as well as outcomes of ABI. In addition, these studies varied with respect to the duration of follow-up.

Injury severity has been identified as an important predictor across all age groups, with more severe ABI being associated with greater problems with respect to motor, cognitive and behavioural functions than the mild group. The latter is consistent with a dose-response relationship between severity of injury and outcome.[32,35] However, several other pre-injury and current personal and environmental factors were found to be strongly associated with outcome as well.[70] It has been suggested that psychosocial outcomes do not always show the same relationship with severity of injury as physical and cognitive outcomes.[71,72]

Age at onset of ABI was found to be a major determinant for outcome of ABI in children and youth.[73] The long-held assumption that 'onset at earlier age means a better prognosis, due to relatively strong plasticity capabilities of the young brain' may have contributed to the general underestimation of the impact of ABI in children and youth.[74] Quite the opposite seems to be true, and this may be due to various reasons: a) brain maturation and development continue throughout childhood into early adulthood;[46] and b) the developmental stage of the brain

during the injury is crucial: growth, maturation and development of the brain interact with injury parameters and impact on acquisition and modification of knowledge, competences and skills and executive functions (e.g. in transitions to higher levels of education, work, social intimacy or living independently).[32,73] This cumulative phenomenon, the interaction between growth, maturation and ABI, is called 'growing into deficit'[46,74] after an immediate phase of recovery children and youth typically experience a decline in outcome that results in plateauing, as opposed to improving of outcome. The so-called "neurocognitive stall" (Figure 2) represents these developmental stage effects on recovery.[75]

Figure 2 The neurocognitive stall



From: Chapman, 2006

In conclusion, participation in children and youth with ABI is still an underrepresented area in the literature.[32,63] More insight into the association between functioning and participation after injury on the one hand and injury characteristics, pre-injury functioning and personal and environmental factors on the other hand is essential to enable the development of tailor-made interventions. For that purpose, more data on the nature of the injury, patterns of recovery and associated factors are needed. In addition, the literature concerning determinants of participation of children and youth has not been reviewed systematically.

Neurorehabilitation, ABI and serious gaming

Neurorehabilitation, i.e. rehabilitation programs for patients with ABI, is driven by plasticity of the brain: every stimulus results in changes in grey (cells) and white (connections) matter, independently of age.[76] Specific knowledge about the mechanisms of recovery of motor and cognitive functions after ABI, however is lacking.[77] Regarding the effectiveness

of neurorehabilitation in children and youth with ABI, systematic reviews[42,78] concluded that the evidence for the effectiveness of interventions to treat motor/neurocognitive/behavioural sequelae is sparse. Nevertheless, consensus statements about the principles of rehabilitation after ABI[79] include the recommendation that rehabilitation should: 1) start as early as possible,[71] (although the length of time since onset of the ABI should not be an exclusion criterion;[79] 2) be targeted, enjoyable, varied and tailor-made, with focus on the client's own real-world circumstances (e. g. daily living activities) to improve generalization, transfer and participation,[73] using and teaching of adaptive cognitive strategies;[79] 3) include interdisciplinary psycho-education, training and support in a systematic, structured and repetitive manner, with patients as active participants in goal setting and monitoring of progress[79] and be family-centered, by including and empowering parents and siblings.[80]
Neurorehabilitation, based on above-mentioned principles, can be enhanced by computer-based training. The latter is, in addition to conventional rehabilitation strategies, considered to be a promising tool. Some evidence for its effect has been demonstrated with gaming with commercial 'off the shelf' consoles'.[81] A systematic review of six high quality RCTs in adults after stroke provides evidence that computer-based cognitive rehabilitation is effective with respect to the improvement of overall cognitive functions, especially memory, thinking operations, executive functions and orientation were measured, after stroke.[82] Other recent studies showed effects of cognitive gaming on working memory in adults after stroke.[83]
A review of computer-based cognitive rehabilitation in children and youth has not been found. Overall, the authors of clinical studies on gaming, undertaken in children and youth with ABI, underscore the importance of more, large scale, methodical solid studies on the effect of neurocognitive outcome of gaming in rehabilitation after ABI in different age groups.[84]

The aim of this thesis

ABI in children and youth relatively often results in death or pervasive, lifelong problems in daily life at home, in school/work and community. Long-term consequences of ABI in children and youth on participation and family functioning and their determinants have been under researched. Current gaps concerning the knowledge on ABI in children and youth include:

- The incidence of ABI in children and youth in the Netherlands.
- The impact on participation and the family.
- Evaluation of effective rehabilitation strategies, in particular serious gaming.

This thesis therefore aims:

- To determine the occurrence and causes of ABI in children and youth in the Netherlands.
- To review the literature on participation of children and youth with ABI and on factors associated with participation.

- To translate, adapt and validate an instrument to measure and monitor participation after paediatric ABI into the Dutch language.
- To evaluate family impact in a cohort of children and youth with ABI and family.
- To evaluate the potential of gaming on improvement of physical, cognitive and social functioning of children and youth with ABI by means of a pilot study.

Outline of this thesis

- **Chapter 1** gives an overview of the literature on ABI in children and youth.
- **Chapters 2 and 3** describe a multicentre, retrospective cohort study on the incidence and causes of paediatric ABI in the Netherlands.
- **Chapter 4** presents the results of a systematic review on determinants of participation of children and youth with ABI.
- **Chapter 5** describes the translation and cross-cultural adaptation and validation of the Child and Family Functioning Survey (CFFS), an instrument to measure and monitor participation after ABI, into the Dutch language.
- The impact of ABI on the family is the focus of **Chapter 6**.
- **Chapter 7** describes a pilot study on the effect of gaming to improve functioning in children and youth with ABI.
- **In Chapter 8** the findings of the studies presented in this thesis are summarized and discussed.

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2

Chapter 2
Youth with Acquired Brain Injury in The Netherlands: a multi-centre study

A.J. de Kloet MSc[1,2], S.R. Hilberink, PhD[3], E. Peeters MD, PhD[4], C.E. Catsman-BerrevoetsMD, PhD[5], M.E. Roebroeck PhD[1,3], T.P.M. Vliet Vlieland MD, PhD[1,6]

[1] Sophia Rehabilitation, The Hague, The Netherlands
[2] The Hague University of Applied Sciences, The Hague, The Netherlands
[3] Erasmus Medical Centre, Department of Rehabilitation Medicine and Physiotherapy, Rotterdam, The Netherlands
[4] Haga Hospital and Medical Center Haaglanden, Department of Paediatric Neurology, The Hague, The Netherlands
[5] Erasmus Medical Centre - Sophia, Department of Paediatric Neurology, Rotterdam, The Netherlands
[6] Department of Orthopaedics, Leiden University Medical Center, Leiden, The Netherlands

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ABSTRACT

Aim To describe the occurrence and causes of acquired brain injury (ABI), including traumatic brain injury (TBI) and non-traumatic brain injury (NTBI), among Dutch youth and estimate incidence rates from the data.

Patients Aged 1 month-24 years, hospital diagnosed with ABI in 2008 or 2009.

Methods In three major hospitals in the southwest region of the Netherlands patients with ABI were retrospectively identified by means of diagnosis codes and specific search terms.

Results One thousand eight hundred and ninety-two patients were included: 1476 with TBI and 416 with NTBI. Causes of TBI and NTBI varied among the age groups 0-4, 5-14 and 15-24 years, with accidents (in traffic or at home) being the most common cause of TBI and hypoxic-ischemic events for NTBI, in all groups. The estimated yearly incidence rates per 100 000 for mild-moderate-severe TBI were 271.2-15.4-2.3 (0-14 years) and 261.6-27.0-7.9 (15-24 years), for mild-moderate-severe NTBI 95.7-11.8-1.3 (0-14 years) and 73.8-6.1-1.6 (15-24 years), respectively.

Conclusion More than 15% of TBI and NTBI in children and youth is classified as moderate or severe, with causes of TBI and NTBI varying among age groups. Based on the occurrence of ABI in three hospitals, the estimated incidence of ABI in children and youth in the southwest region of the Netherlands is substantial.

INTRODUCTION

Acquired brain injury (ABI) in children, youth and young adults may result from events with an external cause (traumatic brain injury, TBI) or internal cause (non-traumatic brain injury, NTBI) such as a brain tumour, stroke or infections such as meningitis or encephalitis.[1]

ABI in children and youth has been designated as a neglected area in medicine[2] and a 'silent epidemic'.[3] TBI is considered to be the most common cause of death or disability among children, youth and young adults.[4] Epidemiological studies in youth have mainly focused on TBI in the age group up to 14 years, reporting annual rates varying from 70 to 798 per 100 000 persons per year in the age group 0-14 years.[4-12]

Data on the incidence of NTBI in children, youth and young adults are only available for specific causes. The reported incidence of stroke varied from 2.1 (Hong Kong)[13] and 2.7 (USA)[14] to 13.0 (France)[15] per 100 000 persons per year in the age group 0-14 years. The incidence of brain tumours varies in the literature from 2.8 (USA)[16] to 25 (UK)[17] per 100 000 persons per year in the age group 0-14 years. To our knowledge, data on the incidence of TBI and NTBI taking the age group of 15-24 years and older into account are not yet available.

Concerning the causes of ABI, several studies have focused on accidents as the cause of TBI in children and youth,[3,5,6,8,9,12] with a number of other studies addressing specific causes as: shaken baby syndrome,[18] violence[19] or alcohol intoxication.[20] All of these studies included different age groups.

More exact figures on the incidence and outcome of ABI resulting from all possible causes in children and youth are needed to raise awareness on the large number of young patients with ABI. These data will help to underscore the need of facilitation and planning of prevention, screening and the provision of care, including both educational facilities as well as rehabilitation care, with a focus on social and societal participation.[21-26] The availability and provision of care for patients with ABI was found to be highly variable and a considerable proportion of cases appear to remain undiagnosed and thus may not receive adequate treatment and follow-up.[1,12,22-26]

Given the lack of knowledge on ABI in children, youth and young adults, the aim of this study was to determine the occurrence and causes of TBI and NTBI in children and youth up to 24 years of age. An additional aim was to estimate the incidence rates for the southwest region of the Netherlands.

METHODS

Design

This study was a multicentre, retrospective hospital-based cohort study. Part of this study, including data from patients with TBI from one centre (Erasmus University Medical Centre in Rotterdam, the Netherlands) in a different time period (2007 and 2008) has been recently published.[27]

The present study was done using a cohort in 2008 and 2009 in three large tertiary care hospitals in two large cities in the southwest region of the Netherlands, including TBI as well as NTBI. The hospitals involved were a university hospital (Erasmus University Medical Centre, Rotterdam, including the Sophia Children's Hospital) and two large teaching hospitals (Haga Hospital, including the Juliana Children's Hospital, The Hague and Medical Centre Haaglanden, The Hague).

This study was approved by the medical ethical committee (METC) of the Erasmus University Medical Centre Rotterdam (MEC-2009-440).

Patients

Patients aged 1 month-24 years with a diagnosis of ABI who presented between 1 January 2008 and 31 December 2009 were retospectively identified in one of the three hospitals.

For this purpose, we used the electronic medical databases of the Intensive Care Units and all outpatient and inpatient wards.

Patients were first selected by age and subsequently a search was performed using diagnosis codes (diagnosis treatment combination (DBC)-codes) and search terms related to ABI. DBC-codes are used in the Netherlands to specify finances in health care. They are derived from the International Statistical Classification of Diseases and Related Health Problems (ICD-codes).[28] The computer-based search strategy included the following terms found in the medical records: minor head injury, traumatic brain injury, concussion, skull/brain trauma, neurological trauma, epilepsy, brain tumour, stroke, infections (meningitis/ encephalitis), post anoxia and otherwise (non-traumatic diagnosis).

Fatal injuries, i.e. patients that died after an incident before arrival at the hospital, were not included in our study. Patients with TBI categorized as Trauma Capitis (abnormalities of the skull without brain symptoms) were recorded but excluded from this study. If patients appeared to have repetitive head injuries, only the first incident was included, to assure an independent sample. The selection procedure was identically performed in all hospitals, except for the patients aged 15-24 years of age with NTBI, of whom the medical records of the University Medical Centre in Rotterdam were not available for this study.

Data collection

This study collected characteristics of patients with ABI for the age groups 0-14 en 15-24 years of age, to facilitate comparisons with the international literature. In addition, the youngest age group was split in two subgroups to describe the causes of ABI. This subdivision is based on general accepted developmental stages and corresponds reasonably with transitions in school systems and hospital care: preschool children (0-4 years), children (5-14 years) and youth (15-24 years).

Data were collected from the selected patient files by four trained research assistants under supervision of the principal investigator, using a standardized registration form including sociodemographic and disease characteristics. Data were registered anonymously.

Sociodemographic data

Gender was recorded and age in years at presentation was calculated using the date of birth and the date of ABI diagnosis recorded in the patient file. Postal code was recorded to determine whether patients were living in the referral area of the hospitals.

Severity

Severity of TBI was scored using the description at the time of presentation in the emergency room, as scores at the site of trauma were usually not available. The Glasgow Coma Scale (GCS)[29] was used in patients older than 2 years of age and the paediatric version of the GCS was used in young pre-verbal children (2 years or younger).[30] TBI was considered mild if the GCS was 13-15, moderate if the GCS was 9-12 or severe if the GCS was <9.[31]

The severity of NTBI, determined at the time of discharge after the first admission to the hospital for this particular problem, was scored by means of an adapted version of the modified paediatric Rankin Scale (mRS)[32] (school performance not taken into consideration):

1. Mild injury: no limitations (mRS 0,1).
2. Moderate injury: mild motor impairments and/or mild problems with learning (mRS 2,3).
3. Severe injury: severe motor impairments and/or severe problems with learning (mRS 4,5).

In addition, mRS 6 was used in case of death during hospitalization.

Causes

For TBI the following causes of injury were registered: 1. traffic accident, 2. accident at home, 3. sport accident, 4. accident at (pre)school, 5. accident playing outdoors, 6. (suspicion of) physical abuse, 7. fall under influence of alcohol or drugs intoxication, 8. fall under influence of epileptic seizure or syncope or 9. unknown.

For NTBI, the following causes were recorded: 1. tumour, 2. meningitis or encephalitis, 3. stroke, 4. ADEM (Acute Disseminated Encephalo Myelitis), MS (Multiple Sclerosis) or acute CNS (Central Nervous System) demyelinating disease otherwise, 5. hypoxic-ischemic, or 6.

otherwise. All relatively rare causes, e.g. Hashimoto encephalopathy and missing causes were classified as 'otherwise'.

Estimated incidence rates

In order to estimate incidence rates, we proportionally assigned missing data regarding severity of TBI (13 cases) and NTBI (54 cases) to a category of severity, according to known valid percentages and calculated the mean number of patients per year (average of 2008 and 2009). We divided the number of patients identified by the number of age-matched young people of the population living in the referral areas of the hospitals, and the result was multiplied by 100 000. The total number of young people (0-14 years and 15-24 years) living in the referral areas in 2008 and 2009 was extracted from data of the research departments of the hospitals, the Regional and Central Institutes of Statistics.[33-36] For this purpose, the variation for three levels of care provided (standard, specialized and intensive care) and the referral areas of other hospitals in both cities were taken into account. The following figures were used as the denominator:

For standard care (mild TBI, NTBI): Haga and MCH The Hague combined (0-14 years: 84 014; 15-24 years: 59 641),[35] the Erasmus University Hospital Medical Centre Rotterdam (0-14 years: 42 456; 15-24 years: 34 684.[34]

- For specialised care (moderate TBI, NTBI): Haga and MCH combined (0-14 years: 136 112; 15-24 years: 90 904),[34] the Erasmus University Hospital Medical Centre Rotterdam (0-14 years: 90 995; 15-24 years: 74 347).[33]
- Intensive care (severe TBI, NTBI): for 0-14 years old the referral areas of Rotterdam and The Hague were combined, due to the supra-regional function of both children hospitals (0-14 years: 415 034);[33-36] Haga The Hague: 15-24 years: 126 886),[34] the Erasmus University Hospital Medical Centre Rotterdam (15-24 years: 177 195.[33]

As one hospital did not supply data of people in age group 15-24 years with NTBI, results on NTBI in 15-24 years old were registered and analysed in the The Hague cohort only.

To extrapolate results to the Dutch population we calculated using the number of inhabitants on January 1st, 2009; 2 915 000 (0-14 years), 2 015 000 (15-24 years).[36]

Statistical analyses

The study used SPSS statistical software, version 17[37] to analyse the data.

Using percentages, characteristics of the patients and ABI were described separately for the age groups 0-14 and 15-24 years of age. To describe the causes of TBI, the youngest age group was split in two subgroups: pre-school children (0-4 years) and school children (5-14 years). Using the Chi-Square test differences in gender, severity and causes of ABI were determined for the two ages groups, for both TBI and NTBI. To adjust for the large number of tests performed, the level of significance α was set at 0.001.

Confidence intervals for the registered incidence rates were calculated according to the (recommended) Wilson method, using Confidence Interval Analysis (CIA) (2.0.0); 2000 (Trevor R. Bryant).

RESULTS

In total 3930 patients were diagnosed with head injury with or without brain symptoms or NTBI in the electronic registries of the three hospitals in 2008 and 2009.
Of these patients 2036 were excluded because they were diagnosed with trauma capitis without brain symptoms. Two other patients were excluded because they were referred from The Hague to Rotterdam and were registered twice.
Hence, the sample consisted of 1892 patients with TBI or NTBI, including 35 patients who died during hospitalization (16 patients with a diagnosis of TBI and 19 with a diagnosis of NTBI).

Characteristics of patients with TBI and NTBI
The characteristics of the patients are shown in Table 1.

Table 1 Patient characteristic for youth with ABI in 2008 and 2009, in 3 major hospitals in The Hague and Rotterdam, broken down into two age groups

Characteristic	TBI			NTBI		
Age	0-14 yrs	15-24 yrs	p-value	0-14 yrs	15-24 yrs[a]	p-value
Number of included patients	842	634		313	103	
Gender Male	473 (56.2%)	454 (71.6%)	**p<0.001**	185 (59.1%)	55 (53.4%)	p=0.31
Severity[b]						
Mild	726 (86.2%)	489 (77.1%)	**p<0.001**	215 (68.7%)	75 (72.8%)	p=0.24
Moderate	74 (8.8%)	94 (14.8%)		41 (13.1%)	9 (8.8%)	
Severe	37 (4.4%)	43 (6.8%)		19 (6.1%)	3 (2.9%)	
Missing	5 (0.6%)	8 (1.3%)		38 (12.1%)	16 (15.5%)	

[a] based only on cohort The Hague
[b] severity of TBI at presentation in the emergency room; severity of NTBI at discharge from the hospital

Overall, TBI occurred more frequently than NTBI in all age groups. In both patient groups with TBI and NTBI the majority of patients were male. In the patients with TBI there was a difference among age groups regarding gender, with more male patients in the 15-24 year old group as compared with the 0-14 year old group. With respect to severity, the large majority of cases were mild: 82.4% and 81.4% in TBI and NTBI, respectively. In the TBI group, the frequency of mild TBI was higher in the younger group as compared with the older age group. In the NTBI group the age groups did not differ with respect to severity.
Table 2 shows that overall traffic accidents and accidents at home were the most common causes of TBI and hypoxic-ischemic incidents for NTBI.

Table 2 Distribution of causes of Traumatic Brain Injury and Non-Traumatic Brain Injury for 3 age categories

TBI causes frequency (%) n=1422[a]	**1: 0-4 years**	**2: 5-14 years**	**3: 15-24 years**	**p-value**
traffic accident	31 (8.1)	136 (30.1)	237 (40.0)	<.001
accident at home	268 (72.6)	66 (13.1)	36 (5.9)	<.001
sports accident	0 (0.0)	77 (16.6)	59 (10.3)	<.001
accident at (pre)school	15 (4.2)	36 (8.2)	22 (3.6)	.003
accident playing outdoor	51 (13.5)	104 (24.1)	27 (4.3)	<.001
(suspicion of) abuse	4 (0.8)	33 (5.8)	147 (25.6)	<.001
fall under influence alcohol/drugs	0 (0.0)	1 (0.2)	58 (9.5)	<.001
collaps cause unknown	1 (0.3)	9 (1.9)	4 (0.8)	.06

NTBI causes frequency (%) n=313[b]	**1: 0-4 years**	**2: 5-14 years**		
tumour	21 (14.4)	44 (27.5)		.004
meningitis/encephalitis	60 (32.5)	21 (13.1)		<.001
stroke	13 (8.7)	10 (4.5)		.14
neurological disorders otherwise	4 (2.5)	2 (2.0)		.75
hypoxic-ischemic	65 (39.4)	71 (47.7)		.12
otherwise	4 (2.5)	12 (5.2)		.21

[a] cause unknown excluded
[b] NTBI 15-24 years cannot be compared with other age groups: based on cohort The Hague only

In patients with TBI aged 0-4 years, accidents in or around the house were the most common, whereas in patients aged 5-14 and 15-24 years traffic accidents were the most frequent cause. The proportion of patients in whom suspicion of abuse and a fall under influence of

alcohol and/or drugs were recorded as the cause of TBI seemed to increase with age.
Table 2 shows that the differences between the three age groups were significant (df=2; p<0.001) for all causes of TBI except for collapse with unknown cause.
With respect to the causes of NTBI, meningitis and encephalitis were relatively frequent in the 0-4 year old group, whereas brain tumours showed a peak in 5-14 year old group. Stroke occurred with a relatively similar frequency in the three age groups. The differences between the age groups 0-4 and 5-14 years were significant (df=2; p<0.001) for the causes tumour, meningitis/ encephalitis and otherwise. Table 3 shows the estimated incidence rate for TBI and NTBI in the southwest region of the Netherlands, based on different referral areas for standard, special and intensive care.

Table 3 Estimated annual incidence with the 95% Confidence Interval (per 100.000) of Acquired Brain Injury in youth up to 24 years in the south-western region of the Netherlands broken down in two age groups

	Traumatic Brain Injury (TBI)			**Non-traumatic Brain Injury (NTBI)**		
	Estimated incidence rate based on all data	Estimated incidence rate based on The Hague data	Estimated incidence rate based on Rotterdam data	Estimated incidence rate based on all data	Estimated incidence rate based on The Hague data	Estimated incidence rate based on Rotterdam data
0-14 yrs	288.9			108.8		
Mild	271.2	324.4 (288.7-365.8)	217.9 (178.9-268.3)	95.7	99.4 (80.8-123.8)	91.9 (67.2-125.5)
Moderate	15.4	20.9 (14.8-30.6)	9.9 (5.2-18.8)	11.8	4.4 (2.0-9.6)	19.2 (12.5-31.3)
Severe	2.3	0.6 (0.2-2.1)	3.9 (2.4-6.3)	1.3	1.0 (0.5-2.8)[b]	1.5 (0.7-3.2)
15-24 yrs	296.5			81.5[a]		
Mild	261.6	256.5 (219.0-300.5)	266.7 (218.9-328.3)	73.8	73.8 (55.0-99.0)	
Moderate	27.0	41.8 (30.5-57.4)	12.1 (6.4-23.0)	6.1	6.1 (3.0-14.4)	
Severe	7.9	6.7 (3.7-13.5)	9.0 (5.6-14.7)	1.6	1.6 (0.4-5.7)	

[a] based on cohort The Hague 15-24 years only

[b] Intensive care for severe TBI and NTBI 0-14 years in cohorts The Hague and Rotterdam in 1 specialised hospital (Erasmus/Sophia)

Bold point estimations are summed to produce an estimation of the total relative incidence of TBI and NTBI per age group. Extrapolating these estimated incidence rates to absolute numbers in the Dutch population[36] this would imply that more than 12 000 (0-14 years) and 7000 (15-24 years) have a hospital-based diagnosis of TBI or NTBI in the Netherlands each year.

DISCUSSION

This multicentre study shows that the incidence of ABI in patients up to 24 years of age in the southwest region of the Netherlands is substantial, with about 1.6-7.9% of both TBI and NTBI being severe. Causes of ABI were found to vary largely among age groups.

With respect to the causes of TBI our study demonstrated differences in the distribution of causes among age groups. Our study showed in particular a higher percentage (suspicion of) physical abuse in 15-24 years old compared to Guerrero (24.9% vs 8.2%).[6] In the age group 0-4 years we registered (suspicion of) physical abuse as the cause in 0.8% of cases, a lower percentage than reported in other studies,[18] especially referring to Shaken Baby Syndrome.[38] These findings stress that health care providers working at Emergency Room Services and Intensive Care Units should be more alert to the signs and symptoms of abusive head injury; physical abuse should be a standard issue of registration.

Andersson[9] et al. reported frequencies of causes for TBI in children between 7-12 years of age in the western part of Sweden, including accidents during playing outdoors (school, public place, playground) (39%), in traffic (14%), during sports (12%), or at home (5%). This study finds a similar ranking with slightly different proportions in 0-14 year old group, but striking differences between 0-4 and 5-14 year old groups. These results underline the need to tailor prevention of TBI to different age groups according to risk factor based strategies. Regarding the planning of the follow-up of patients with TBI, it should be noted that no evidence was found to suggest a threshold of injury severity below which the risk of late sequelae could safely be discounted.[39] Taking into account the most common causes, prevention should be targeted to accidents at and around home in children younger than 5 years of age, to traffic accidents in primary school children (5-14 years old) and at the usage of alcohol and drugs in youth in secondary or high school (15-24 years old). In addition, the results indicate that awareness and prevention of physical abuse is important in all age groups. In the youngest age group we noticed that inadequate fixation in a car seat, chair or stroller was frequently the cause of mild TBI. Raising awareness in parents and care takers of such risk factors for TBI in the very young is warranted.

Regarding the incidence of ABI, incidence rates were estimated using number of persons in the same age range in the referral areas of the hospitals involved, which can then be compared with rates reported in the literature. For TBI, the estimated incidence rates from the present study (mild 271.2-moderate 15.4-severe 2.3 per 100 000/year) for children aged 0-14 years of age are similar to recent figures from the United Kingdom (280 per 100 000/year),[7] whereas earlier studies reported somewhat lower rates in the Netherlands (243 per 100 000).[8] Higher rates were found in Estonia (369/100 000/year, 0-14 years of age)[11] and Germany (581/100 000/year, 0-14 years of age).[12] Langeois[3] found an incidence rate of 798.8 per 100 000/year (USA, 2004) in TBI 0-14 years of age, but included head injury without brain symptoms as well.

For youth aged 15-24 years of age no comparable data were found in the literature. Regarding the incidence of NTBI in children and youth, the estimated incidence rates from the current study are lower than those of TBI, but still considerable. As in the literature data on the incidence of NTBI in children, youth and young adults are only available for specific causes, no direct comparisons with the present study can be made. Given the scarcity of data on NTBI, the challenge for the future is to gain more insight into the incidence of NTBI in children and youth. The results of the current study suggest that NTBI is a substantial group and should be integrated in ABI policy, education, innovation and research. Differences in estimated incidence rates between the present study and previous studies may be explained by differences in definitions of ABI, classification and methodology. These results underscore the need for experts in this field to initiate consensus meetings and support the process of attaining international consensus. Through this consensus guidelines can be developed and implemented worldwide.

This study has a number of limitations. First, differences in estimated incidence rates were found between the hospitals in two cities. This may be explained by differences in classification of Trauma Capitis and mild TBI as the criteria for Trauma Capitis, mild or moderate TBI are not solidly distinctive or undisputed. The higher number of patients 0-14 years of age with severe TBI in the Rotterdam cohort 0-14 years of age can be explained by the presence of an Intensive Care Unit for children in the Erasmus University Hospital Medical Centre Rotterdam/Sophia Children's Hospital.

The estimation of the magnitude of the source population is arbitrary, hospital-based data about referral areas for ABI up to 24 years were not complete. It should be noted that there are differences between the estimated incidence rates in the present study and those reported in a previous publication presenting only the data on TBI from one region (Rotterdam).[27] In the previous study the estimation was based on a cohort in 2007-2008, with regional statistics, whereas in the present study concerning 2008-2009 more accurate (i.e. distinction in age groups; adherent general practitioners for standard care) data were used to define referral areas.

Moreover, the data were gathered retrospectively. Therefore it is conceivable that data were incomplete or classifications were inconsistent. To diminish observer bias in this study a standardized registration form and trained research assistants were used. To account for variations in incidence, cases were registered over 2 years. Another limitation was that the results in the NTBI 15-24 years of age group were based only on data from hospitals in The Hague.

Although we gathered data from three hospitals, these were all situated in urban regions: The Hague as city with metropolitan region Haaglanden, Rotterdam as city with metropolitan region Rijnmond. The incidence of TBI may be different in rural areas, e.g. because of a different traffic density. The number of hospital registered mild TBI cases may be higher

than in a rural area, where the general practitioner will manage most cases of mild TBI. Furthermore, the cities of Rotterdam and The Hague appeal to students and tourists for study, work and leisure time. However, a postal code check showed that no more than 2% of the included group with moderate TBI and NTBI in both cities had a postal code out of the referral area. It is assumed that a similar percentage of youth from inside the referral area will be diagnosed with ABI yearly in a hospital outside the referral area. Finally, this is a hospital-based and not a population based study. Patients with relatively mild TBI may not always be seen in a hospital, and for a minority of mild NTBI this may also be the case leading to an underestimation of incidence. Brown estimated the 'undiagnosed' incidence of mild TBI to be 3-5 times higher than the diagnosed incidence.[40] Despite the limitations, the results of this study give more insight into the incidence of children and youth with ABI in the southwest region of the Netherlands and may help to facilitate and stimulate planning of prevention, screening and the provision of care, including both educational facilities as well as rehabilitation care for this group.
Considering the incidence of ABI in youth, awareness for this problem should be enlarged, affecting healthcare and society in general. Preventive measures should be taken. Taking into account the enlarged risk for long term health problems, with consequences for psycho-social functioning, participation and quality of life for youth and their families, health policy needs urgent attention.

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Declaration of Interest

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Chapter 3
The incidence of traumatic brain injury in young people in the catchment area of the University Hospital Rotterdam, the Netherlands.

E. Daniëlle van Pelt[1], Arend J. de Kloet[2], Sander R. Hilberink[3], Susanne A.M.Lambregts[3], Els Peeters[4], Marije E. Roebroeck[3], Coriene E. Catsman-Berrevoets[1]

[1] Erasmus University Hospital/Sophia Children's Hospital, Department of Paediatric Neurology
[2] Sophia Rehabilitation and The Hague University, The Hague, The Netherlands
[3] Erasmus University Hospital, Department of Rehabilitation Medicine and Physiotherapy, Rotterdam, The Netherlands
[4] Haga Hospital and Medical Centre Haaglanden, Department of Neurology, The Hague, The Netherlands

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ABSTRACT

Background Traumatic brain injury (TBI) is in the developed countries the most common cause of death and disability in childhood.

Aim The purpose of this study is to estimate the incidence of TBI for children and young people in an urbanized region of the Netherlands and to describe relevant characteristics of this group.

Methods Patients, aged 1 month-24 years who presented with traumatic brain injury at the Erasmus Medical Centre (including the Sophia Children's Hospital) in 2007 and 2008 were included in a retrospective study. Data were collected by means of diagnosis codes and search terms for TBI in patient records. The incidence of TBI in the different referral areas of the EMC for standard, specialised and intensive patient care was estimated.

Results 472 patients met the inclusion criteria. The severity of the Injury was classified as mild in 342 patients, moderate in 50 patients and severe in 80 patients. The total incidence of traumatic brain injury in the referral area of the Erasmus Medical Centre was estimated at 113.9 young people per 100.000. The incidence for mild traumatic brain injury was estimated at 104.4 young people, for moderate 6.1 and for severe 3.4 young people per 100.000.

Conclusion The ratio for mild, moderate and severe traumatic brain injury in children and young people was 33.7-1.8-1.In the mild TBI group almost 17% of the patients reported sequelae. The finding that 42% of them had a normal brain CT scan at admission underwrites the necessity of careful follow up of children and young people with mild TBI.

INTRODUCTION

Traumatic brain injury (TBI) is in the developed countries an important public health problem and the most common cause of death and disability in childhood.[1,2] Epidemiological data on TBI in the Netherlands are out of date and incomplete.[3] Studies on the incidence of TBI are difficult to compare because they are based on different definitions and inclusion criteria.[4] They may include the total population,[1,3] or children 0-14 years.[5-8] Some studies only estimate the incidence rate for hospitalised children,[6-10] or use strict criteria for TBI.[11] In a previous Dutch study, the annual incidence rate of traumatic skull and brain injuries was estimated at 836 people per 100.000.[3] In this study 242.4 per 100.000 people were children aged < 15 years. More exact figures are urgently needed in order to be able to estimate the need of post TBI intervention facilities, both at the level of education and rehabilitation care. In recent years, it has become clear that especially in the group of children, adolescents and young adults with mild TBI acquired cognitive deficits are not always diagnosed.[12] Diagnosis of neuropsychological deficits after brain injury is important because they have negative influence on emotional, behavioural and social functioning. Consequently, they may impair school and professional careers as well as quality of life of the victims.[13-16] Plasticity of the brain is an important concept in infants and children, which to a certain extent enables them to reorganise and recover after injury.[17] More recently, evidence arose that a pro-active community based intervention program ameliorates the integration of children with TBI in the community.[18] It is necessary to be aware of the number of young people with TBI who would be eligible for entering such a program before such a proactive approach is introduced in the Netherlands. The purpose of this study is to estimate the annual incidence of TBI for young people in an urbanised region of the Netherlands and to describe relevant characteristics of this group such as severity of brain injury, patient characteristics and present policy concerning clinical observation and follow-up.

METHODS

We retrospectively identified children and young people, aged 1 month-24 years with traumatic injury to the skull who presented in 2007 and 2008 at the Erasmus University Hospital Rotterdam, which includes the Sophia Children's Hospital. We have chosen this age range because in the Netherlands, paediatric rehabilitation specialists offer cognitive rehabilitation programs to children, adolescents and young people in transition to adulthood up to the age of 24 years. We searched the hospital medical database by diagnosis codes (DBC-codes, in Dutch: diagnose-behandel-combinatie) and by search terms in the patient

reports for TBI. DBC-codes are used in the Netherlands to specify finances in health care. They are derived from the International Statistical Classification of Diseases and Related Health Problems (ICD-codes).[19] In the patient reports, a computer-based search strategy was performed with the following terms: minor head injury, traumatic brain injury, concussion, skull/brain trauma, neurological trauma. Two additional databases were consulted to check the completeness of the data collection for TBI patients i.e. Sophia emergency ward database in which the reason for visiting the emergency department is prospectively noted and the Sophia intensive care unit database. This study was approved by the medical ethical committee (METC) of our hospital.

Inclusion criteria

We identified all patients aged 1 month-24 years (i.e. young people) who presented with traumatic injury to the skull and subdivided them in the following categories: 1. injury to the skull without signs and/or symptoms of brain injury at presentation. 2. Injury to the skull with signs and/or symptoms of brain injury at presentation. Criteria for brain injury were a history or observed loss of consciousness after a head trauma, and/or post traumatic amnesia, and/or abnormalities at neurological examination, and/or acute traumatic abnormalities on scan images of the brain. Young people with signs and/or symptoms of TBI were included in our study. Severity of TBI was scored using the Glasgow Coma Scale score at presentation in the emergency room (ER) as mild (GCS 13-15), moderate (GCS 9-12) or severe (GCS < 9).[20] The exact time lapse between trauma and admission could not be certified in most cases. The paediatric version of the GCS was used in young preverbal children (2 years or younger).[21] Based on CT or MRI images, we distinguished between abnormalities of the skull (fractures) and abnormalities of the brain (haematoma, contusion, ischemic, diffuse axonal injury (DAI) with or without skull fractures (facial fractures not included)).

Data collection

Information concerning date of the incident, age and gender was derived from the digital or paper patient files. Patients were subdivided into four groups matching preschool (0-3 yrs), primary education (4-11 yrs), secondary education (12-18 yrs) and young adults (19-24 yrs). We also collected data on severity of TBI, circumstances of injury (1. traffic, 2. at home, 3. outdoors, sub activities: a. playing outdoors, b. sports, 4. school/work and 5. 'other causes of injury', sub activities: a. (suspicion of) physical abuse, b. fall under influence of alcohol or drugs intoxication, c. epileptic seizure or syncope). In addition, we derived data on hospital care: imaging type and results (1. no abnormalities, 2. skull fracture, 3. hematoma, 4. brain contusion and combinations of intracerebral injuries), hospitalisation (yes/no, duration), type of care after discharge from the hospital (i.e. 1. outpatient follow-up in paediatrics,

(paediatric) neurology, (neuro)surgery, 2. outpatient rehabilitation care, 3. outpatient follow up by other than previously mentioned medical specialists). We also collected data on clinical course, outcome, fatal injuries and long-term physical and/or cognitive complaints after injury (yes/no/unknown). The following complications (i.e. clinical deterioration due to new pathological changes following TBI) were found in the study group: (increase of) haemorrhage, epileptic seizures, deterioration of GCS-score, growing skull fracture, CNS infection, disorders in plasma sodium levels or intracranial high pressure) (yes/no).

Analyses

We used SPSS statistical software (IBM Company, version 15) to analyse the collected data. We performed multiple frequency analysis to study patient characteristics for severity of brain injury, cause of injury, hospitalisation and follow-up. For proportions, we calculated 95% confidence intervals. For the comparison and analysis of proportions, we used Chi-Square tests. One-way-ANOVA and Kruskal Wallis tests were used for analysis of means and medians respectively. All the performed statistical analyses were 2-tailed tested. One person was included twice in our database because he had an injury to the skull with signs of brain injury on two separate occasions. We excluded the second incident from our data to assure an independent sample for our statistical analysis.

Incidence data

Annual incidence was calculated based on the number of young people aged 0-24 years living in the referral areas of the Erasmus University Hospital, which differ for levels of standard, specialized and intensive care. The Erasmus University Hospital provides standard care for the city of Rotterdam (approximately 163.837 inhabitants 0-24 years). For specialised care the hospital serves the region Rotterdam-Rijnmond (approximately 407.050 inhabitants 0-24 years). Intensive care is provided for the South-West region of the Netherlands (approximately 1.183.747 inhabitants 0-24 years).[22] We extracted the mean number of young people (0-24 yrs) living in these regions in 2007 and 2008 from publications of the Dutch Office of Statistics.[23] In order to calculate annual incidence rates, we divided the number of young people who visited our hospital with TBI in one year by the number of young people living in its different referral areas. In order to calculate the number of patients in our study not living in the Erasmus University Hospital referral area, we checked the ZIP codes for a random sample of 100 TBI patients.

RESULTS

Patient characteristics

In 2007 and 2008, 734 young people presented at our hospital with a head trauma of which 472 patients with TBI could be included in our study. Patient characteristics are presented in Table 1.

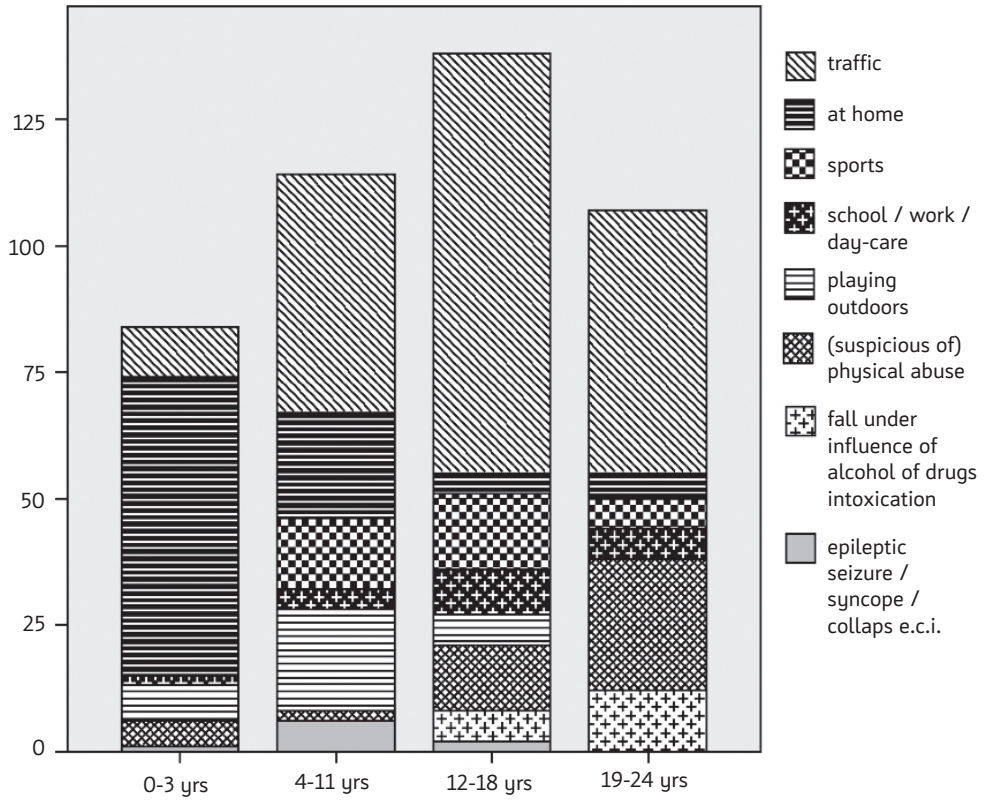
Table 1 Patient characteristics for the total patient group with traumatic brain injury

Factor (n = 472)	Number	Percent	95% CI
Gender			
Male	317	67.2%	62.9-71.4%
Female	155	32.8%	28.6-37.1%
Age groups			
0-3 yrs	95	20.1%	16.5-23.8%
4-11 yrs	121	25.6%	21.7-29.6%
12-18 yrs	140	29.7%	25.5-34.1%
19-24 yrs	116	24.6%	20.7-28.5%
Cause of injury			
1. Traffic	192	40.7%	36.2-45.1%
2. At home	89	18.9%	15.3-22.4%
3. Sports	35	7.4%	5.1-9.8%
4. School/work/day-care	21	4.4%	2.6-6.3%
5. Playing outdoors	33	7.0%	4.7-9.3%
6. (suspicious of) physical abuse	46	9.7%	7.1-12.4%
7. fall under influence of alcohol or intoxication	18	3.8%	2.1-5.5%
otherwise	9	1.9%	0.7-3.1%
8. epileptic seizure of syncope or collaps e.c.i.	29	6.1%	4.0-8.3%
9. event unknown			
Additional imaging	398	84.3%	81.0-87.6%
Normal results	228	57.3%	52.4-62.1%
Abnormal results	170	42.7%	37.9-47.6%
Hospitalisation	343	72.7%	68.6-76.7%
Post-care	240	50.8%	46.3-55.4%
Complications	47	10.0%	7.3-12.8%
Fatal Injury	24	5.1%	3.1-7.1%

One out of three patients was female. The mean age at TBI was 12.0 years (SD 7.5). The causes of injury differed between age groups ($\chi^2 = 229.19$, df = 12, $p<0.001$). In children 0-3 years, the cause of injury was most frequently accidents at home. In children 4-11 years, more accidents occurred during sports and playing outdoors. Children 12-18 years were more often involved in traffic accidents. In young adults, accidents were more often caused by

other injuries, of which the categories physical abuse (22.4%, 95% CI 14.8-30.0%) and falls associated with alcohol intoxication (10.3%, 95% CI 4.8-19.9%) were prominent (Figure 1).

Figure 1 Stacked bar chart representing causes of injury per age group in 472 young people with traumatic brain injury



Based on GCS at presentation at the ER, 342 patients (72.5%: 95% CI 68.4-76.5%) presented with mild TBI. 50 patients (10.6%: 95% CI 7.8-13.4%) had a moderate TBI and 80 patients (16.9%: 95% CI 13.6-20.3%) were classified as severe TBI. The mean ages of the children with mild (mean 11.7 years, SD 7.5) and moderate (mean 10.6 years, SD 7.7) brain injury did not differ but patients with severe brain injury (mean 13.9 years, SD 6.9) were older ($F = 3.96$, $df = 2$, $p = 0.020$). Sixteen patients in the severe TBI group (20%) recovered remarkably fast. These children (mean age 10.9 years, SD 6.1) were all initially admitted to the Intensive Care Unit and in need of artificial respiratory support and subsequently completely recovered neurologically within several hours.

Incidence data

The annual incidence of mild TBI calculated from the 2007-2008 cohort was estimated at 104.4 patients per 100.000 young people 1 month-24 yrs old in the city Rotterdam. The annual incidence of moderate TBI in this two-year period was estimated at 6.1 per 100.000 young people in the Rotterdam-Rijnmond area. The annual incidence of severe TBI was estimated at 3.4 per 100.000 young people in the South-West region of the Netherlands. The total annual incidence of TBI in the catchment area of the Erasmus University Hospital was calculated at 113.9 per 100.000 young people. The annual incidence of admission to the hospital was 74.5 per 100.000 young people and the estimated annual incidence of fatal TBI was 1.5 per 100.000 young people. In order to compare our data with those from the literature in the group of children under 15 years of age the annual incidence of TBI in children aged 1 month-15 years from this cohort are represented in Table 2.[1,3,4,5,7,8,9,10,11]

Table 2 Summary of data from studies on the incidence of TBI in children and young adults

Study (ref)	Inclusion Criteria	Annual Incidence of TBI
Present study	TBI patients aged 0-14 years	130.3 per 100.000 children 0-14 years 111.6 mild TBI per 100.000 children 0-14 years 5.9 moderate TBI 100.000 children 0-14 years 2.8 severe TBI 100.000 children 0-14 years 1.3 deaths per 100.000 children 0-14 years
Langois et al, 2004 and 2005, USA[1,5]	ICD-codes for TBI and minor head injury: children aged 0-14 years	798.8 per 100.000 children 0-14 years 4.5 deaths per 100.000 children 0-14 years 63.0 hospitalisations per 100.000 children 0-14 years
Meerhof et al, 1997, the Netherlands[3]	TBI and minor head injury in total population	242.7 per 100.000 children 0-14 years
Kraus et al, 1990, USA[4]	Hospitalised TBI patients aged 0-14 years and 0-19 years	230 hospitalisations per 100.000 children 0-14 years 219.4 hospitalisations per 100.000 children 0-19 years 10.0 deaths per 100.000 children 0-19 years
Hawley et al, 2003, United Kingdom[7]	> 24 h hospitalized TBI patients aged 0-14 years	280 per 100.000 children aged 0-14 years
Ventsel et al, 2007, Estonia[8]	TBI patients aged 0-14 years	369 per 100.000 children aged 0-14 years 3.1 deaths per 100.000 children 0-14 years
Reid et al, 2001, USA[9]	TBI deaths and hospitalisations in patients aged 0-19 years	73.5 per 100.000 children 0-19 years 9.3 deaths per 100.000 children 0-19 years
Schneier et al, 2006, USA[10]	Hospitalised TBI patients aged 0-16 years	70 per 100.000 children 0-16 years
Emanuelson et al, 1997, Sweden[11]	TBI patients aged 0-17 years with TBI including one of the following criteria: > 1 hour loss of consciousness; clinical, neurophysiological or neuroradiological evidence of brain contusion	12 per 100.000 children 0-17 years

Clinical details

Evaluation and management of the patients with TBI in our hospital is carried out according to the guidelines of the Dutch Society of Neurology.[24] In Table 3 clinical parameters of the identified TBI patients are presented.

Table 3 Clinical parameters of the patients with Traumatic Brain Injury (n = 472)

	Mild TBI (n = 342)		**Moderate TBI (n=50)**		**Severe TBI (n=80)**	
Mean age (SD)	11.7 (7.5)		10.6 (7.7)		13.9 (6.9)	
Imaging performed (n)[a]	271	79.2%	49	98%	78	97.5%
Hospitalisation (n)[a]	213	62.3%	50	98%	80	100%
Median days (IQR))	1 (1-3)		3 (1-7)		7 (2-19)	
Outpatient care (n)[b]	**143**	**42.1%**	**41**	**82%**	**56**	**96.6%**
Outpatient clinic (neurology, neurosurgery, paediatrics)	97	68.3%	23	56.1%	17	30.4%
Rehabilitation therapy	13	9.2%	16	39%	36	64.3%
Other medical specialist	32	22.5%	2	4.9%	3	5.4%
Complication (n)[a]	9	2.6%	9	18%	29	36.3 %
Fatal injury (n)	2		-		22	
Reported Long-term cognitive symptoms (n)[a]						
Yes	24	16.8%	18	43.9%	35	62.5%
No	39	27.3%	10	24.4%	7	12.5%
Unknown	80	55.9%	13	41.7%	14	25%

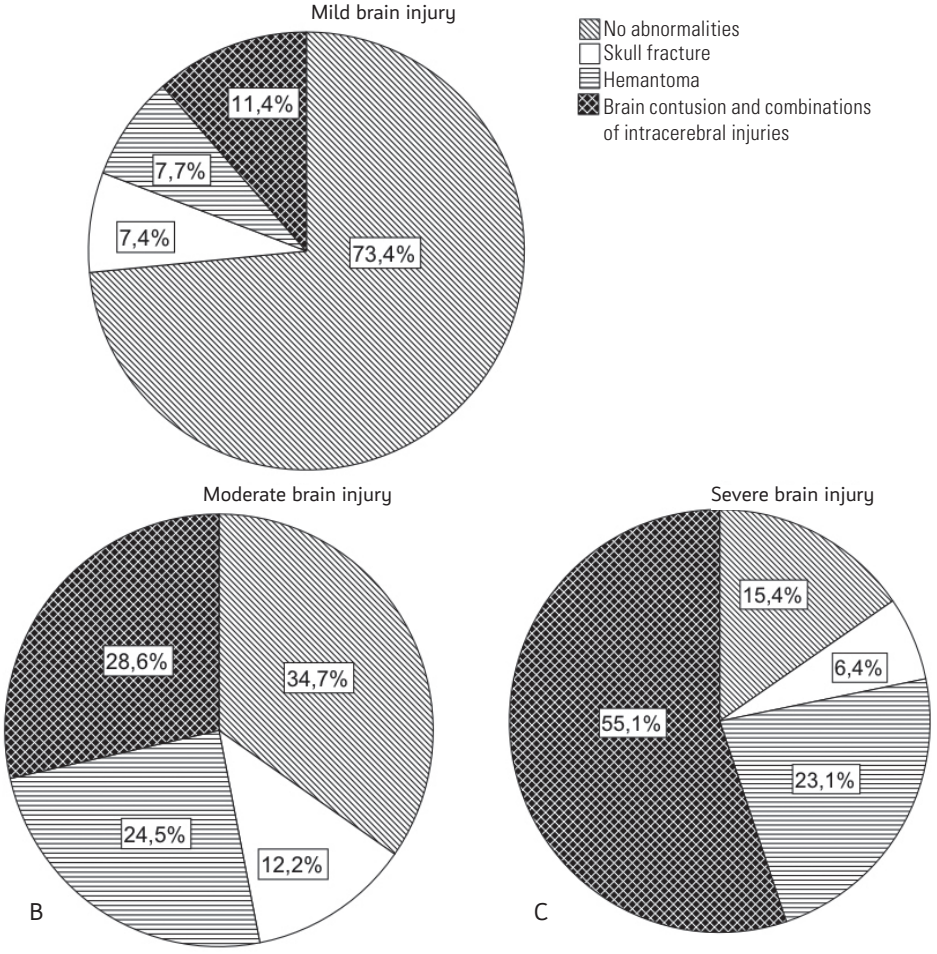
Legend: n = number of patients, SD = standard deviation. IQR = inter quartile range.

[a] percentage calculated as a proportion of the subgroups respectively mild, moderate and severe TBI.

[b] percentages calculated as a proportion of the patients who received outpatient care after discharge from the hospital (bold figures) in the subgroups with mild, moderate and severe TBI. Figures for outpatient care and reported long-term cognitive symptoms are corrected for fatal injuries and these figures only include survivors. Percentages for long-term symptoms are calculated as a percentage of the patients who received post-care in the categories of mild, moderate and severe traumatic brain injury.

In 398 patients (84.3%) a brain CT scan (394 patients) or MRI scan was performed. In the group classified as severe TBI, one child died before a CT scan could be performed. In one child in the severe TBI group and one child in the moderate TBI group, GCS normalised so fast after admission to the ER that sedation would have been needed to make a brain CT scan. For this reason they were admitted to the neurological ward for intensive 24 hour observation without radiological evaluation. In the mild TBI group, 271 children (79.2%) had a brain CT scan following the guidelines for patients with mild TBI of the Dutch Society of Neurology.[24] Traumatic abnormalities at neuro-imaging were found in 72 (26.6%) of these children (Figure 2).

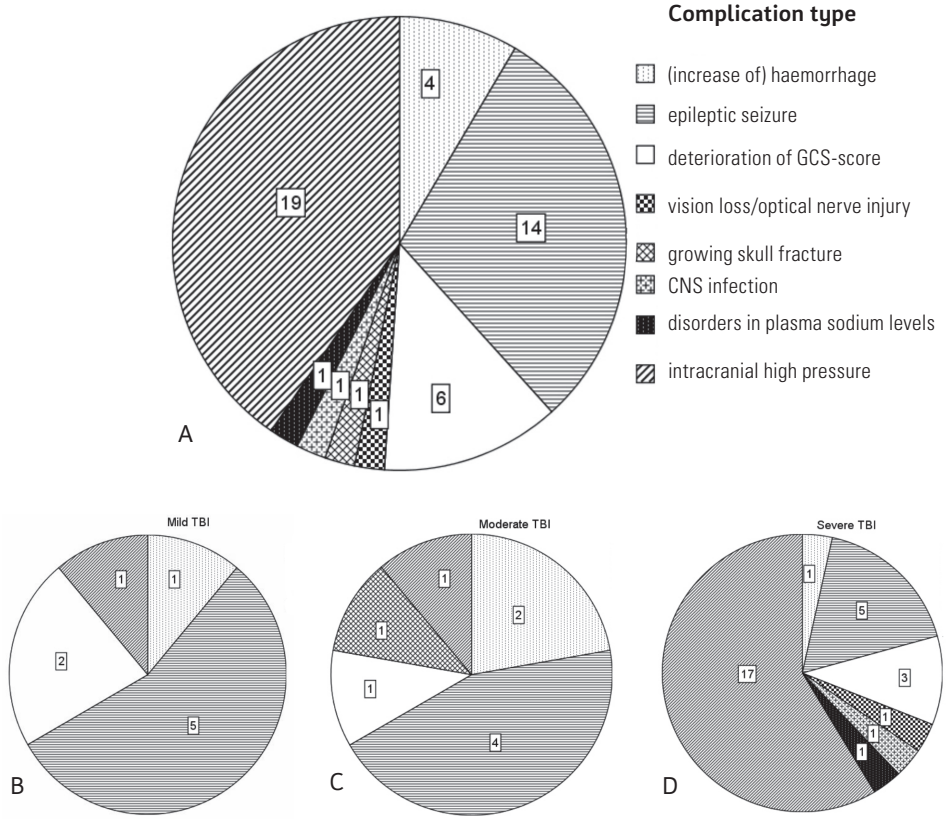
Figure 2 Pie charts representing results of cerebral CT or MRI imaging in 398 patients with traumatic brain injury: A: mild traumatic brain injury, B: moderate traumatic brain injury: C. severe traumatic brain injury



The ratio for abnormalities at neuro-imaging was 4.3 out of 10 images. In comparison to the patients with mild TBI, patients classified as having moderate or severe TBI more frequently showed abnormalities on neuro-imaging ($\chi^2 = 95.06$, df = 2, $p<0.001$) (Table 4). Of all included patients, 343 (72.7%) were admitted to the hospital. The 129 children that were not admitted were all classified as mild TBI patients. 78 of them (60%) had a normal brain CT scan which contributed to the decision to send them home. Patients with severe brain injury were hospitalised for a median 7 days (IQR 2-9) versus 3 days (IQR 1-7) for moderate and 1 day (IQR 1-3) for mild TBI ($\chi^2 = 53.78$, df = 2, $p<0.001$) (Table 4). Patients with TBI caused by traffic

accidents were significantly more often admitted to the hospital in comparison to the other patients ($\chi^2 = 23.03$, df = 4, $p<0.001$) (Table 4): 83.9% of them were hospitalised versus 74.2% of the patients with accidents at home, 63.2% by accidents outside, 71.4% by accidents at school/work and 58.3% by 'other causes of injury'. After discharge, patients with severe TBI were significantly more frequent enrolled in outpatient facilities compared to patients with mild or moderate TBI ($\chi^2 = 41.99$, df = 2, $p<0.001$) (Table 4). The type of outpatient care for mild, moderate and severe brain injured patients differed. Outpatient care for patients with mild TBI was limited to outpatient visits or visits to other medical specialists (Table 3). Patients with severe TBI enrolled rehabilitation treatment programs significantly more frequent than patients with mild or moderate TBI ($\chi^2 = 68.78$, df = 4, $p<0.001$) (Table 4). In patients with severe TBI a significantly larger number of complications occurred during the clinical course (Table 3) ($\chi^2 = 85{,}50$, df = 2, $p<0.001$). In Figure 3, patient counts for type of complications in young people with mild, moderate en severe TBI are presented.

Figure 3 Pie charts with patient counts for type of complications: A total TBI group, B mild TBI, C moderate TBI and D severe TBI



Twenty-four patients (5.1%: 95% CI3.1-7.1%) died of which 22 patients had severe TBI (14 patients with polytrauma). The two other patients were initially classified as having mild TBI based on their GCS score at presentation. One was a haemophilia patient who died due to progressive intracerebral haematoma, despite maximal treatment with factor VIII. The other patient died of diffuse delayed cerebral oedema, after a relatively mild trauma. Nineteen deadly injuries (79.2%) were caused by traffic accidents. Patients with severe TBI had significantly more persisting long term physical and cognitive symptoms in comparison to moderate or mild TBI patients ($\chi^2 = 21.75$, df = 2, $p<0.001$) (Table 4).

Table 4 Chi-squared contingency table with parameters that reached statistical significance when compared with Chi-squared test

Cause of injury	Age group	
Accidents at home Sports and playing outdoors Traffic accidents Other causes	0-3 years 4-11 years 12-18 years 19-24 years	$\chi^2 = 229.19$, df = 12, $p < 0.001$
Neuroimaging more frequently abnormal	Moderate and severe TBI vs mild TBI	$\chi^2 = 95.06$, df = 2, $p < 0.001$
More frequently admitted to the hospital	Victims of traffic accidents vs all other causes of TBI	$\chi^2 = 23.03$, df = 4, $p < 0.001$
More frequently enroled in outpatient facilities	Severe TBI vs mild and moderate TBI	$\chi^2 = 41.99$, df = 2, $p < 0.001$
Higher number of complications	Severe TBI vs mild and moderate TBI	$\chi^2 = 85.50$, df = 2, $p < 0.001$
Longer duration of hospitalisation	Severe TBI vs mild and moderate TBI	$\chi^2 = 53.78$, df = 2, $p < 0.001$
More persisting long term physical and cognitive problems	Severe TBI vs mild and moderate TBI	$\chi^2 = 21.75$, df = 2, $p < 0.001$

The mean age of patients who reported long-term cognitive sequelae was significantly higher (13.2 years, SD 6.7) than of patients who did not (8.9 years, SD 6.9) ($F = 5.93$, df = 2, $p = 0.003$).

DISCUSSION

We performed an extensive search strategy for patients with a newly acquired TBI in our hospital. A search strategy by ICD-codes alone may be incomplete.[25] The data collection in this study is more accurate because additional cases were identified by the search terms in the patient reports and supplemental data bases. We estimated the mean total incidence of TBI in the catchment area of the Erasmus University Hospital in 2007-2008 as 113.9 cases per 100.000 children and young adults. In a previous Dutch study the incidence of

traumatic skull and brain injury was estimated 836 people per 100.000, of which were 242.7 children aged <15 years per 100.000 persons.[3] In the USA, the incidence of TBI is estimated 798.8 children 0-14 years per 100.000 annually between 1995 and 2001.[1,5] A comparison of annual incidences found in other studies is difficult, because in many of them minor head injuries without brain involvement were included and because different search strategies were used.[3-11] Our estimated hospitalisation rate of 74.5 cases per 100.000 children and young adults aged 0-24 years agrees with estimated incidence for TBI hospitalisation in two earlier studies.[9,10] The Erasmus University Hospital is a tertiary care centre and young people with moderate or severe TBI from the defined regions are all referred to our hospital. Because the data were calculated with different denominators, the estimations of incidence of severe and moderate TBI are not clouded by the academic ratio of severity of TBI. The estimated incidence of mild TBI is however a minimum incidence for Rotterdam, because we do not exactly know how many children present with mild TBI at the emergency rooms of the three smaller hospitals in Rotterdam, or how many patients did not present at a hospital at all. Rotterdam is a large city that appeals to students and tourists for study, work and leisure time. In agreement with findings in the previous Dutch study in which at random sample 21% of the patients did not live in the hospital's referral area we found that 29% (27% mild TBI, 2% moderate TBI) of the patients did not live (at the moment of data collection) in the referral areas of our hospital.[3] This finding would mean that our estimated annual incidences are too high. However, the latter finding may well be balanced by the number of children with TBI who presented at one of the smaller hospitals in Rotterdam or were admitted to hospitals elsewhere while visiting other cities. Although if we exclude the patients who did not live in the hospitals referral area, we can calculate the minimum annual incidence for mild TBI at 74.2 per 100.000 young people. The minimum incidence for moderate TBI is calculated at 6.0 per 100.000 young people. At random sample only 2% of the patients with moderate TBI and none with severe TBI did not live in the hospitals catchments area.

A difference in causes of injury for the age groups is expected, because the children in the different age groups also have different activities of interest. As expected traffic is the most common cause of severe TBI and fatal injuries.[26,27] The finding that in patients with severe TBI mean age is significantly higher is explained by the more risky behaviour of young adolescents who more often participate in traffic, drink alcohol and are involved in brawls. The latter two age related factors are also responsible for the high rate of adolescents and young adults with (suspicion of) abusive head trauma. The GCS as measure of the severity of the TBI is an important tool to predict outcome. However, in some patients use of alcohol may have influenced the classification of severity of the trauma.[20] For example one of the included patients was hospitalised on an ICU with a GCS <9 and alcohol intoxication and perhaps should have been included in the mild TBI group. On the other hand 16 patients

with an initial low GCS score recovered remarkably fast confirming that GCS score does not always accurately predict the outcome of severe TBI in children.[28,29] CNS imaging was performed in 398 of the TBI patients (84.3%). In the Octopus study was demonstrated that in children older than 6 years with mild TBI, clinical observation was equally safe as discharge from the hospital after a normal brain CT. In contrast what might be expected, the large number of CT scans in children with mild TBI (60%) did not reduce admission to the hospital. Of the children with normal findings on brain CT scan only 39% was sent home after evaluation versus 72% of the children that did not have a CT scan at all. This was explained by the fact that 50% of the children with mild TBI who had a CT scan were either younger than 6 years, had other traumatic abnormalities that necessitated admission or did not have a competent carer at home.[30]

In the present study 24 children died. The incidence for fatal TBI was estimated 1.5 cases per 100.000 children and young adults in 2007 en 2008. The fatal outcome of TBI is almost for certain an underestimation because approximately the same number never reaches a hospital and dies at the scene of the incident.[26,27] Fourteen of the 22 patients with severe TBI who died were polytrauma patients (63.6%). In these patients extra-cranial causes may have contributed to the fatal course. Two patients in this study who died of a fatal brain injury were initially classified as mild TBI. One patient had as evident risk factor haemophilia.[31] The other patient, a three year old girl died due to delayed cerebral oedema after a trivial head trauma. This particular clinical course has been described in patients with a mutation in the calcium channels with sporadic hemiplegic migraine.[32,33] Regretfully, this was not assessed in this particular patient. Our observations support recent findings that in patients with mild and moderately severe traumatic brain injury the GCS has a limited value to predict survival or death.[34,35]

Data on long-term sequelae were not complete because not all patients with TBI received care after discharge from the hospital. Some patients had follow-up by other medical specialists than neurologists or neurosurgeons or in other hospitals and rehabilitation centres. In the patients who did report on presence or absence of long-term symptoms, mean age of the children that did report cognitive symptoms was higher than of the patients that did not. This may be explained by the older children being more capable to express long-term sequelae than younger children. 16.8% of the mild TBI patients who had follow up (n = 143) reported long-term cognitive sequelae. An important finding is that 42.0% of these young people had no abnormalities on brain CT-scan at admission. Our findings are in agreement with those of a British postal questionnaire survey in which approximately 20% of children with mild TBI suffered from sequelae such as poor concentration, personality change and educational problems after TBI.[36] Recently it has become clear that for the group of children and young adults with mild TBI the need for diagnosis and rehabilitation treatment of acquired brain injury sequelae is underestimated. Cognitive rehabilitation programs are rarely offered to

children with mild or moderate TBI.[12] Extrapolating our data to the Dutch population would mean that each year approximately 470 children with mild or moderate TBI would benefit from such a program, apart from the children who would be identified as needing more intensive rehabilitation programs.[12,17]

CONCLUSIONS

We estimated that in the catchment area of the Erasmus University Hospital the mean total incidence of TBI in 2007-2008, in children and young people 1 month-24 years of age was 113.9 cases per 100.000; mild TBI 104.4 cases per 100.000, moderate TBI 6.1 cases per 100.000 and severe TBI 3.4 cases per 100.000 young people. In the mild TBI group almost 17% of the patients reported sequelae. The finding that 42% of them had a normal brain CT scan at admission underwrites the necessity of careful follow up of children and young people with mild TBI.

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4

Chapter 4
Determinants of participation of youth with Acquired Brain Injury: a systematic review

A.J. de Kloet[1,2], R.Gijzen[3], L.W.Braga[4], J.J.L. Meesters[1,5], J.W.Schoones[5], T.P.M. Vliet Vlieland[1,5]

[1] Sophia Rehabilitation, The Hague, The Netherlands
[2] The Hague University of Applied Sciences, The Hague, The Netherlands
[3] Vilans, Knowledge Centre for Chronic Care, Utrecht, The Netherlands
[4] Sarah Network of Rehabilitation Hospitals, Rio de Janeiro, Brazil
[5] Leiden University Medical Centre, Leiden, The Netherlands

Submitted

ABSTRACT

Objectives Participation is considerably restricted in children and adolescents with acquired brain injury (ABI) as compared to their healthy peers. This systematic review aims to identify which factors are associated with participation in children and adolescents with ABI.

Methods A systematic search in Medline and various other electronic databases from January 2001 to November 2012 was performed. All clinical studies describing determinants of participation at least one year after the diagnosis of ABI by means of one or more predefined instruments in patients up to 18 years of age were included. Extracted data included study characteristics, patient characteristics, participation outcome and determinants of participation (categorized into: health conditions (including characteristics of ABI), body functions and structures, activities, personal factors and environmental factors). The methodological quality of the studies was evaluated based on three quality aspects (selection, information and statistical analysis bias) and scored as low, moderate or high.

Results Five studies, using an explicit participation outcome measure were selected after review, including a total of 1172 patients, with a follow-up ranging from 1 up to 84 months. Three studies included patients with a traumatic or a non-traumatic brain injury and 2 studies with only patients with TBI. The factors which were most consistently found to be associated with more problems in one or more dimensions of participation were greater severity of ABI, problems in movement functions, cognitive functioning, behavioural functioning and sensory functioning, problems in accessibility and design of the physical environment. In addition, a more supportive nurturing and parenting style, higher household income, more acceptance and support in the community, more availability of special programs and special services were associated with less participation problems. The overall methodological quality of the included studies was moderate in all 5 studies.

Conclusion This systematic review shows that only a few, moderate quality, studies on the determinants of participation after ABI using recommended explicit measurement instruments are available. Several factors in the ICF components health condition, body functions and structures and environmental factors were consistently found to be associated with participation. More methodologically sound studies using the recommended explicit outcome measures, a standardized set of potential determinants and long term follow-up are suggested to increase the knowledge on participation in children and youth with ABI.

INTRODUCTION

Acquired brain injury (ABI) refers to any damage to the brain that occurs after birth,[1] and may have traumatic (traumatic brain injury, TBI) or non-traumatic causes (non-traumatic brain injury, NTBI). Among children and adolescents ABI is a common condition, as well as the leading cause of death[2] and permanent functional limitations in functioning.[3-10]

So far, studies on the outcome of TBI in children and adolescents have been mainly concerned with physical, cognitive and behavioural functioning and to a lesser extent with participation.

According to the International Classification of Functioning, Disability and Health (ICF) of the World Health Organization (WHO),[11] participation can be defined as the nature and extent of a person's involvement in meaningful life situations at home, school, work and community life.[3]

Regarding the extent and nature of participation restrictions a few literature reviews on participation outcome after paediatric ABI are available, including one on behavioural outcome and adaptive functioning,[4] one on community integration interventions[8] and two narrative reviews on participation outcome measures.[9,10] Overall it was found that significantly more children and adolescents with ABI had limitations in social relations, peer social-play at school and engagement in organized community, social and civic areas of life than their healthy peers.

Most studies included in these reviews were focused on TBI and/or the age group up to 15 years old. Moreover, some of the studies concerned small populations ($n < 50$), had a specific focus within participation (participation at home or at school or in recreational time) and/or a follow-up time of one year or less.[4,8-10] As far as the determinants of participation after paediatric ABI are concerned, the literature has thus far not been systematically summarized. In a number of studies addressing the following factors were reported to be significantly associated with participation restrictions after ABI: greater injury severity;[3,5,6,12,13] bilateral injury and frontal end temporal lesions;[14] presence of neurological complications;[3,15] physical, cognitive and social emotional impairments;[15] limited pre-injury competences;[6,16] pre-injury psychiatric disorders;[13] younger age at injury;[3] worse pre-injury or actual family functioning;[12] lower socio economic status;[16] restrictions in physical, social and attitudinal environment;[3] and limited availability of adequate information, programs/services.[17] Given the absence of a systematic synthesis of the literature on participation determinants after paediatric ABI the aim of the present study was to systematically review the literature on factors associated with participation after paediatric TBI and NTBI.

METHODS

Search Strategy

In cooperation with a trained librarian (J.W.S.) a search strategy was composed (see Appendix 1). The search strategy consisted of a combination of two main concepts: Participation (social participation, participation in leisure time, community, school, domestic life, interpersonal interactions and relationships, major life areas, community, social and civic life); and Acquired Brain Injury (e.g. Traumatic Brain Injury; Stroke; Brain Tumour), and was restricted to children and youth in the age group up to 18 years old: children (0-12 years), adolescents (13-18 years), youth (15-23 years), or paediatrics (0-18 years).[18] The search strategy was developed for PubMed and subsequently adapted for use in other databases, including EMBASE (OVID version), Web of Science, COCHRANE Library, CINAHL (EbscoHost version), PsycINFO (EbscoHost-version), Academic Search Premier and ScienceDirect. Original clinical studies, irrespective of the study design, were selected. Restrictions included in the electronic search pertained to the language (papers in English) and studies in humans. The search was performed on November 12, 2012.

Data collection and analysis

We defined 4 steps in the selection of studies, data extraction and analysis. All steps were performed by three of the authors independently (A.J.K., R.G., J.M.). In case of disagreement about the selection or data extraction, consensus was reached through discussion. If consensus between the two authors was not achieved, a final decision was made by a third author (T.V.V.).

Step 1: Screening of titles and abstracts

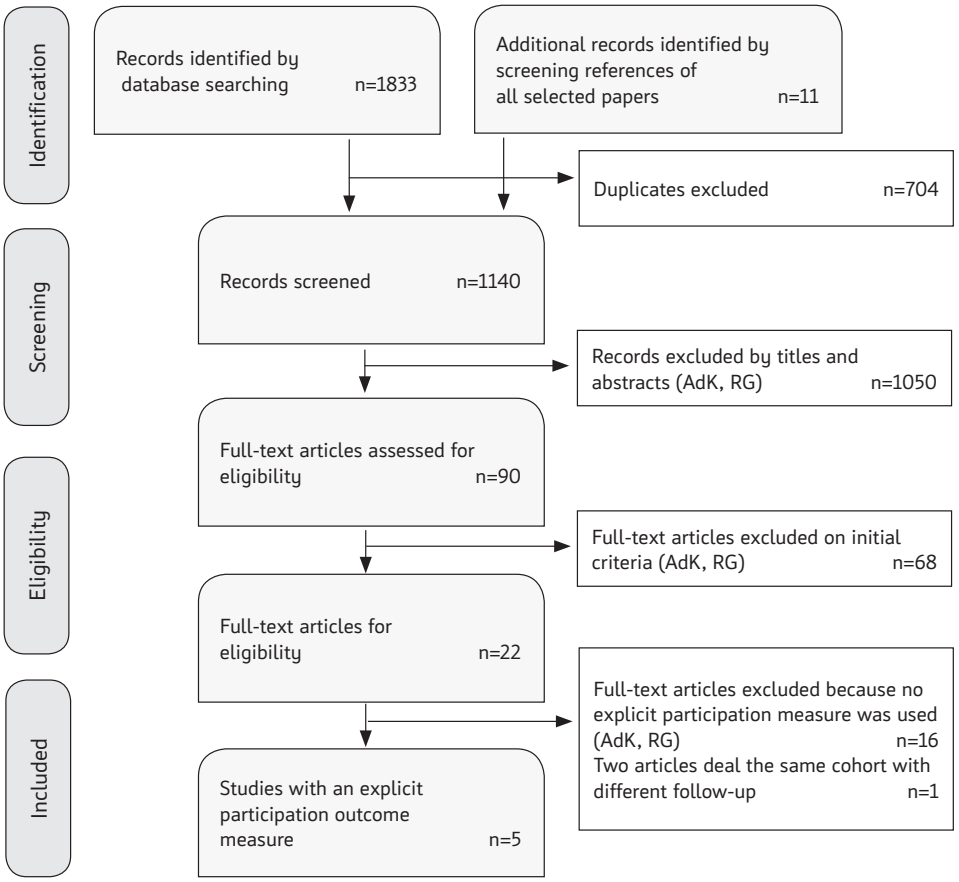
First, all duplicates in the results of the electronic search were removed. The remaining titles and abstracts were included if the following criteria were met: (1) original clinical study with at least 10 patients; (2) providing of quantitative information on participation (irrespective of the outcome measure) at least 12 months after the diagnosis. Comprehensive outcome measures, such as quality of life instruments, were only considered to be participation measures if the participation was described as a separate dimension; and (3) describing factors associated with participation at least 12 months after the diagnosis. In case a study also included adult patients also, it was only selected if results on the participants in the age group 0-18 years old were reported separately. Studies which were solely aimed at the methodological properties of specific measurement instruments were excluded.

Step 2: Selection of full-text papers

Titles and abstracts identified as potentially eligible were selected for full-article review (see figure 1). If an abstract was not available, the full-text paper was requested. For the screening

of the full-text papers the abovementioned criteria were again used. In Step 2, two additional inclusion criteria were used to be able to compare and summarize results: (4) using at least one instrument to measure participation which is included in one or more published lists of recommended explicit measurement instruments for participation in children with ABI (see Appendix 2)[9,12,19] and (5) using the results of at least one recommended explicit outcome measure as dependent variable in the data analysis.

Figure 1 Flow Chart



Finally, the references of all selected papers and systematic reviews included in the yield of the search strategy were checked for potentially eligible studies that were not identified in the original search strategy. The titles and abstracts of these references were screened using the abovementioned selection procedure.

If one study was described in several papers, the various papers were considered as one study, with multiple references.

Step 3: Data extraction

For all selected full-text papers the following study characteristics were systematically extracted: title, first author, year of publication, country where the study was conducted, study design (retrospective, prospective or cross-sectional) and duration of follow-up. The patient characteristics registered were: the number of subjects in the study, diagnosis, inclusion criteria, time since onset of ABI and socio-demographic characteristics (age, sex) were registered.

For the participation outcome, we noted the time of the follow-up assessment and the instruments used to measure participation.[9,19] In addition, the reported actual results on participation outcome regarding these participation measures were extracted.

For the determinants of participation, variables were categorized according to the ICF-CY[11] in Health Condition (e.g. injury characteristics; code hc); Body Functions and Structures (physiological functions of systems and structure or anatomical parts; code b); Activities (execution of an action or task by an individual; code d); Environmental Factors (physical, social and attitudinal environment; code e); and Personal Factors (individual background, e.g. gender, race; code p). Determinants were categorized to the most precise ICF component (e.g. b Body Functions), chapter (e.g. b1 Mental Functions) or category (e.g. b126 Temperament and personality functions)[11] according to the established ICF linking rules,[20] if they were associated with one or more dimensions of participation in social interactions and relations, major life areas and community, social and civic life. In the prospective studies data extraction of results of analyses of associations between potential determinants and participation outcome were based on data of the final (follow-up) assessment. Factors were rated as being consistently associated with participation if a statistically significant association was found in more than 1 study and no statistically significant associations in the opposite direction were seen.

Step 4: Assessment of methodological quality

To assess the methodological quality of the included studies, we used a quality checklist employed in similar reviews but in other patient groups,[21] which was based on items described in a review of tools for quality assessment[22] and on a review of the quality of prognostic studies in systematic reviews.[23] Two authors independently assessed the quality of each study by scoring 15 items, divided into three categories: a) selection bias (items 1-6); b) information bias (items 7-18) and c) statistical analysis of potential determinants of participation (items 19-23). 'No information found' was reported as question mark and scored as 'bias or unclear'. Bias was considered present if more than 2 of the items within a category pointed in this direction. Particular emphasis was placed on the employment of a multivariate analysis of potential

determinants of participation. Finally, quality was rated high when no bias was scored in all 3 categories, moderate with bias in 1 or 2 and low with bias in all 3 categories.

RESULTS

Figure 1 presents the selection of studies. The initial electronic database search yielded 1833 records, wherein 11 records were added after screening the references of systematic reviews resulting from the initial search. After excluding 704 records which appeared in multiple databases, 1140 unique records were evaluated, based on title and abstract. Subsequently, with the first selection in step 1, 1050 records were excluded because they did not meet the inclusion criteria, and 90 full text papers were retrieved. In step 2, it was found that 22 full-text papers met the first 3 inclusion criteria.[24-45] After applying inclusion criteria (4) and (5), 16 studies were excluded as they did not comprise an explicit participation measure. The characteristics of these studies are presented in Appendix 3.
Finally, 6 papers meeting all inclusion criteria were selected. Two of these 6 papers concerned the same study[25,42] with only a different follow-up. The study with the longest follow-up was included in the review, thus finally 5 studies were included.[26,29,32,41,42]

Study characteristics

The characteristics of the 5 included studies[26,29,32,41,42] are presented in Table 1. Four studies[26,29,41,42] were from the North Americas, whereas one[32] was executed in Australia. Three studies had a cross-sectional design,[26,32,41] the other 2 studies had a prospective design.[29,42] Two studies[41,42] were concerned with TBI only, whereas the other 3 studies[26,29,32] included both patients with TBI and NTBI. Five different age ranges were used in 5 studies, varying in length from 12 to 19 years. One study[42] included children under the age of 4, whereas all studies included patients up to at least 18 years old. The number of (follow-up) measurements varied from 1 to 5, the time since the onset of injury ranged from 1 up to 84 months in all 5 studies. In one of the two prospective studies[42] the follow-up was up to 36 months after the onset of ABI. In one study the outcome of patients with TBI or NTBI were compared with healthy controls.[42]

Participation outcome

In table 1 the measurement instruments employed in the 5 selected studies are presented. The explicit participation measures included the Child and Adolescent Scale of Participation (CASP)[26,32,41,42] and the Children's Assessment of Participation and Enjoyment (CAPE).[29]
Two of the three cross-sectional studies both using the CASP, found that, depending on age group, 30-73%[26] and 25-75%[32] of children and youth were restricted in at least 1 participation domain (at home, at school or in community).

Table 1 *Characteristics of 5 studies (6 papers), using explicit participation outcome measures, on determinants of participation after paediatric acquired brain injury*

First author, country	Study design	Year of publication	Number of patients (TBI/NTBI/ controls)	Diagnosis	Follow-up post injury in months (range)	Participation measure		
						Explicit ABI[a]	Explicit general[a]	Implicit[b]
Bedell, USA[26]	Cross-sectional	2004	60 (38/22/0)	TBI + NTBI	42 (4-80)	CASP		PEDI, CASE
Wells, Canada[41]	Cross-sectional	2009	30 (30/0/0)	TBI	30 (12-60)	CASP		CASE
Galvin, Australia[32]	Cross-sectional	2010	20 (12/8/0)	TBI + NTBI	25 (4-84)	CASP		CASE
Rivara, USA[42]	Prospective	2012	926 (729/0/197)	TBI	1-3-12-24-36	CASP		ABAS-II, PedsQL, CASE, FAD
Anaby, Canada[29]	Prospective	2012	136 (113/23/0)	TBI + NTBI	8-12		CAPE	FAD, CASE

[a] according to Bedell, et al, 2007; van Tol, et al, 2011;

[b] according to Bedell, et al, 2007; van Tol, et al, 2011; Mc Cauley, et al, 2011

CASP=Child and Adolescent Scale of Participation; CAPE=Children's Assessment of Participation and Enjoyment; ABAS II=Adaptive Behaviour Assessment System - Second Edition; CASE=Child and Adolescent Scale of Environment; FAD=Family Assessment Device; FBII=Family Burden of Injury Interview; PEDI=Paediatric Evaluation of Disability Inventory (social functioning scale); PedsQL=Paediatric Quality of Life inventory (social subscale).

Participation restrictions were seen in social relations (50-80% at home, 55-80% with friends or at school, 65-80% in community), in major life areas (55-70% in educational activities, 50-65% in work activities) and structured community, social and civic life (47-60% in household activities, 30-45% in shop-manage money activities, 65-71% in managing daily schedule, 46-60% in using transportation), where all patients were missing adequate support and attitudes in environment.[41] Mobility or moving around was least restricted in and around home (30%), more problems were experienced in moving around in community (55%).[26, 32,41]

Two studies[29,42] had a prospective design. Rivara,[25,42] using the CASP, found significantly worse total participation scores at all 4 time points compared to a control group with arm injury. Anaby[29] examined the changes in level of participation over 1 year after return to school, using the CAPE to measure participation (social, physical and recreational) in out-of-school activities in children and youth with TBI and NTBI. In that study it was found that intensity (how often a child does an activity) scores were more likely to change over time than diversity (whether a child does an activity) scores.

Determinants of participation

Table 2 shows the results of the reported associations between various potential participation determinants and participation after paediatric ABI. Overall, a range of factors was evaluated, with most of the studies examining multiple independent variables. The dependent variables concerned social participation in play or leisure activities at home (CASP, CAPE), at school (CASP) and in community (CASP, CAPE), as well as participation at school or in work (CASP) and structured events in community, social and civic life (CASP, CAPE). Four studies[26,29,41,42] employed multivariate analyses.

The factors which were most consistently found to be associated with more problems in one or more dimensions of participation in the ICF-CY component Health Condition was a greater severity of ABI.[29,41,42] Type or cause of injury was consistently found not to have an impact on participation.

Concerning Body Functions and Body Structures, problems in movement functions, cognitive functioning, behavioural functioning and sensory functioning were significantly associated with more participation restrictions.

Regarding Environmental factors, problems in accessibility and design of the physical environment were significantly related to more participation restrictions. Moreover, a more supportive nurturing and parenting style, higher household income, more acceptance and support in the community, more availability of special programs and special services were associated with less participation restrictions.

None of the factors in the ICF components Activities and Personal Factors were consistently associated with participation outcome.

Table 2 Results of 5 studies on determinants of participation of children and youth with Acquired Brain Injury

Independent variables				
Health Condition[a]	**Body functions and structure[a]**	**Activities[a]**	**Environmental Factors[a]**	**Personal Factors[a]**
Greater severity of ABI -: 29*, 41*, 42*	MENTAL FUNCTIONS[b] (b140-b189[c]) Problems in cognitive functioning[d] -: 26*, 32 Problems in behavioural functioning -: 26*, 32 Problems in emotional functioning -: 26*	GENERAL TASKS/ROUTINES (d210-d299) Capacity +: 32	PHYSICAL ENVIRONMENT (e210-e299) Problems in accessibility, design -: 26*, 32, 41*	General health problems -: 26*
Type/cause of injury =: 26*, 29*, 32	SENSORY FUNCTIONS AND PAIN (b210-b229) Sensory functioning problems -: 26*, 32	MOBILITY (d410-d499) Capacity +: 32 = 26*	SUPPORT AND RELATIONS (e310-e399) Worse family functioning -: 29* = 42* Supportive nurturing and parenting style +: 32, 41* Higher household income (SES) +: 29*, 42* Higher parental education =: 42*	Younger age (at onset) -: 41* Longer time since onset -: 29* = 26*, 32 Older age (at follow up) -: 42*
Presence of neurological comorbidities =: 42*	VOICE AND SPEECH (b 310-b399) Speech problems -: 26*	SELF-CARE (d510-d599) Capacity +: 26*	ATTITUDES (e410-499) Acceptance and support in community +: 26*, 32, 41*	Race/Ethnicity =: 26*
	MOVEMENT RELATED FUNCTIONS (b710-b729) Problems in movement functions -: 26*, 32		SERVICES, SYSTEMS POLICY (e510-d599) Availability of special programs +: 26*, 32, 41* Availability of special services +: 26*, 32, 41* Length of stay in inpatient rehabilitation = : 26*	

According to the ICF-CY: a=component b=chapter c=code d=category
Relation can be + (positive) , meaning resulting in less participation problems, - (negative) meaning resulting in more participation problems or = (neutral) if relations were studied but not found
* multivariate analysis

Methodological quality of studies

Table 3 summarizes the results of the methodological quality assessment of the 5 included studies.

Table 3 Quality assessment of 5 studies on determinants of participation of children and youth with Acquired Brain Injury

First author, country (search number record)	Selection bias present[a]	Information bias present[a]	Statistical analysis bias present[a]	Total score	Level of quality[b]
Bedell, USA (484)	1	0	0	1/3	M
Wells, Canada (261)	1	0	0	1/3	M
Galvin, Australia (143)	1	0	1	2/3	M
Rivara, USA (55)	1	0	0	1/3	M
Anaby, Canada (36)	1	0	0	1/3	M

[a] 0= no bias present; 1= bias present or unclear

[b] H= high quality: no evidence for selection bias, information bias or analyses bias; M= moderate quality: one or two quality aspects rated as bias present or unclear; L= low quality: all three aspects rated as bias present or unclear

The methodological quality was rated as moderate in all 5 studies, mainly due to selection bias.

DISCUSSION

In this systematic review 5 studies on determinants of participation of children and adolescents after ABI were included, with 2 studies restricted to only TBI, and all studies having a moderate methodological quality.

These 5 studies showed that, 12-84 months after the onset of ABI, 25-80% of children and youth were restricted in at least 1 participation domain, while problems hardly decreased over time. In out-of-school time the intensity (how often a child does an activity) of activities was more likely to change over time than the diversity (whether a child does an activity).

With regard to participation outcome after paediatric ABI, the results of our study are comparable with available reviews:[4,8-10] problems pervasive,[26,32,38] not decreasing over time,[26,34,35,39] manifesting in social interactions and relations,[24-45] as well as in school[25,26,32,41,42] and engagement in organized community, social and civic areas of life.[24-26,29, 32,41,42] Analogy between the reviews, however, is limited due to essential differences, e.g. focus on 1 or several domains of participation.

The factors most consistently associated with one or more dimensions of participation

in social interactions and relations, major life areas and community, social and civic life were: greater severity of ABI, sensory functioning problems (Health Condition); problems in movement functions, cognitive functioning, behaviour (Body Functions and Structure); problems in accessibility and design, higher social economic status and availability of special services en programs (Environmental Factors). No consistently associated factors were found in the ICF categories Activities and Personal Factors.

Results in the studies included in this review concerning the determinants of participation after paediatric ABI (Table 2) are comparable with literature: a greater severity of the injury,[3,5,6,12,13] the presence of impairments of physical, cognitive and behavioural functioning,[15] lower household income,[16] restrictions in physical, social and attitudinal environment.[17] Longer time since onset[7] and worse family functioning[12] were found as associated factor in 1 or more of included studies, but disputed in another. The included studies did not report an impact of the type of injury, length of stay in inpatient rehabilitation,[2] presence of comorbidities and problems in mobility[2] on participation after paediatric ABI.

Our review showed several additional or more specified associated factors, e.g. problems in sensory functioning and acceptance and support in community.

It should be noted that the included five studies differed considerably in participation domain (e.g. at home/school/community or home/community) and the selection of potential determinants (e.g. type of injury, neurological comorbidities, race/ethnicity). Relatively few studies included 'Activities' and 'Personal Factors' in the analysis of determinants of participation after paediatric ABI.

Overall, the methodological quality of the studies was moderate, due to potential bias in all three aspects of the instrument which was applied, with: 3 studies showed selection bias (especially lack of theoretical background or loss of patients in follow-up) and 1 presented statistical analysis bias (especially missing information on missing values). Included studies showed a great variety in age at inclusion, age range, number and time since onset of injury of (follow-up) measurements. It should be noted that some of the studies in our review had a cross-sectional and others a prospective design, so that the potential determinants in some cases were recorded directly after the onset of ABI and the outcome after follow up whereas in other cases all measurements (dependent and independent factors) were done at one time point. For the early identification of patients at risk for participation restrictions, it is important to have predictors which can be measured directly after the onset of ABI. Such predictors can only be derived from prospective studies.

Since there was an absence of systematic reviews of studies focusing on determinants of participation after paediatric ABI, our findings can only be compared with similar syntheses of the literature concerning children with other conditions, such as Cerebral Palsy[48-50] and other physical limitations.[51,52] In these studies participation was found to be associated with a variety of factors as well. Gross motor function, manual ability, limitations in mobility and

communication are reported more consistently as associated with participation after CP[51,52] than after ABI (this review), as well as gender. Unlike after CP and other physical disabilities the present review showed that current (problems in) cognitive functioning and behaviour were associated with more participation restrictions after ABI.

This study has a number of limitations. First, we cannot draw reliable conclusions about causality: several independent factors are mutually influencing each other and moreover they were measured at the same point in time as the dependent factors in the cross-sectional studies. We did not attempt to pool data, as studies were very heterogeneous concerning study designs, patient selection and measurement methods. Inconsistent findings in this systematic review are probably due to large variation in age at inclusion, age range, number and timing of follow-up measurements, definition and focus on domain of participation, selection of instruments.

Another limitation is the limited number of 5 included studies. In the search strategy we included only studies in English, so that potentially eligible studies in other languages may have been missed.

In the selection process neither intervention, nor retrospective studies were found, possibly due to the strict inclusion criteria. Thirdly, only a small sample of children and adolescents with NTBI was included in the 3 selected papers, while determinants of participation outcome after TBI cannot be generalized across various aetiologies and of NTBI.[59] Finally, all studies were performed in Western countries, 4 in the North Americas and 1 in Australia, this limits broader generalization of results as well.

Therefore, we recommend international consensus on the definition of participation and the use of a minimum set of variables potentially related to participation and quality of life outcome, following recommendations of the inter-agency Paediatric TBI Outcomes Workgroup.[19] Then, further development and validation of ABI, domain and age specific participation outcome measures is required. Recently 2 explicit participation outcome measures have been developed as explicit participation outcome measure for children (5-17 years old): the youth report version of the Child and Adolescent Scale of Participation (CASP)[53] and the Participation and Environment Measure for Children and Youth (PEM-CY),[54] the latter for youth with or without disabilities, assessing parent reported participation frequency, extent of involvement, and desire for change in sets of activities typical for the home, school, or community. Similar initiatives are needed to more accurately identify and describe (determinants of) participation in order to augment current knowledge about participation after paediatric ABI and associated factors, and will guide efforts to develop timely and useful interventions for patients and family to maximize participation and quality of life, and minimize secondary problems commonly associated with ABI.[32]

Regarding the classification and interpretation of associated factors, the ICF appeared to be supportive to analyse and describe the studies included in this review, as suggested by

others.[56-58] The ICF model serves to underscore the complexity, interrelated and dynamic nature of participation as well. It should be noted that linking of several ICF categories, e.g. aspects of communication (in b167 or d3), learning (in b1 or d1) and personality (in b126 or personal factors). Moreover, the distinction between general (d710-729) versus complex (d720-729) versus special (d730-779) interpersonal interactions is arbitrary. Some categories require specification regarding to paediatric ABI, e.g. in external factors (ICF code e) and family (e310) could be differentiated in impact and functioning, acceptance and attitudes, educational competencies and skills, communication and worries as specific and associated with functioning and disabilities of the child and adolescent.

CONCLUSION

In this systematic review on determinants of participation after paediatric ABI 5 studies using an explicit participation outcome measure were included, all of moderate quality. Therefore more studies are needed, based on consensus regarding the definition of participation and methods of measurement and on the set of potential determinants to be analysed, including large cohorts of children and youth in all age groups and different cause and severity of injury and employing a methodologically sound analysis.

Declaration of Interest statement

The authors report no conflicts of interest.

Appendix 1. Search Strategy Systematic Review: Determinants of participation among children and adolescents with Acquired Brain Injury (PubMed-version)

(((“Human activities”[majr] OR activity[ti] OR activities[ti]) AND (rehabilitation OR rehabilitat*)) OR ((participation OR “Interpersonal Relations”[majr] OR “Environment”[majr] OR “Social Adjustment”[majr]) AND (rehabilitation OR rehabilitat*)) OR ((participation NOT (“Consumer Participation”[mesh] OR “Patient Participation”[mesh] OR “Refusal to Participate”[mesh] OR “patient participation” OR “consumer participation” OR “client participation”))) OR (“home participation” OR “school participation” OR “social participation” OR “societal participation” OR “society participation” OR “community participation” OR “civic participation” OR “participation outcomes” OR “leisure participation” OR “recreation participation” OR “sports participation” OR “sport participation” OR “Social Participation”[Mesh] OR “Activities of Daily Living”[mesh] OR “Activities of Daily Living” OR “daily life” OR “daily living” OR participat*[ti] OR “Patient Participation”[majr])) AND (“Brain Injuries”[Mesh] OR “Brain Injury” OR “Brain Injuries” OR “Brain Lacerations” OR “Brain Laceration” OR “Cortical Contusion” OR “Cortical Contusions” OR “Post-Traumatic Encephalopathies” OR “Post-Traumatic Encephalopathy” OR “Posttraumatic Encephalopathy” OR “Brain Contusion” OR “Brain Contusions” OR “Traumatic Encephalopathy” OR “Brain Trauma” OR “Brain Traumas” OR “Traumatic Encephalopathies” OR Concussion OR Concussions OR “Contrecoup Injury” OR “Contrecoup Injuries” OR “Post-Concussion Syndrome” OR “Postconcussion Syndrome” OR “Traumatic Brain Hemorrhage” OR “Traumatic Brain Stem Hemorrhage” OR “Traumatic Cerebral Hemorrhage” OR “Traumatic Brain Hemorrhages” OR “Traumatic Cerebral Hemorrhages” OR “Traumatic Cerebral Haemorrhage” OR “Traumatic Cerebral Haemorrhages” OR “Diffuse Axonal Injury” OR “Diffuse Axonal Injuries” OR “Post-Traumatic Epilepsy” OR “Posttraumatic Epilepsy” OR Pneumocephalus OR “Shaken Baby Syndrome”) AND (“Child”[mesh] OR child[tw] OR children OR pediatric OR paediatric OR pediatrics OR paediatrics OR “Adolescent”[mesh] OR adolescence OR adolescent OR adolescents OR “Young Adult”[mesh] OR “young adult” OR “young adults” OR child*[tw] OR schoolchild*[tw] OR infan*[tw] OR adolesc*[tw] OR pediat*[tw] OR paediat*[tw] OR boy[tw] OR boys[tw] OR boyhood[tw] OR girl[tw] OR girls[tw] OR girlhood[tw] OR youth[tw] OR youths[tw] OR teens[tw] OR teenager*[tw] OR puberty[tw] OR preschool*[tw] OR juvenile[tw])

Appendix 2. Variables used in data extraction, according to the ICF-CY

Dependent (outcome) variables	Explicit participation measures; ABI specific Child and Adolescent Scale of Participation, CASP [1,2]
	Explicit participation measures; not ABI specific Assessment of Life Habits for Children, LIFE-H [1] Children's Assessment of Participation and Enjoyment, CAPE [1] School Functioning Assessment, SFA [1]
	(Subsections of) Other scales, Implicit measuring participation; not ABI specific Adaptive Behaviour Assessment System - Second Edition (ABAS-II) Child and Adolescent Scale of Environment, CASE [2] Child Behaviour Check List, CBCL (social competence scale) [1,2] Child Health Questionnaire, CHQ [1] Conflict Behaviour Questionnaire/Interaction Behaviour Questionnaire, CBQ/IBQ [2] Family Assessment Device, FAD [2] Family Burden of Injury Interview, FBII [2] Interpersonal Negotiation Strategies, INS [2] Mayo-Portland Adaptive Inventory-4, MPAI-4 [2] Neuro-Quality of Life, Neuro-QOL (social relations) [2] Patient-Reported Outcomes Measurement Information System, PROMIS (peer relations) [2] Paediatric Evaluation of Disability Inventory, PEDI (social functioning scales) [2] Paediatric Quality of Life inventory, PedsQL (social subscale) [2] Social Skills Rating Scale, SSRS [2] Strengths and Difficulties Questionnaire, SDQ (peer relations and prosocial behaviour) [2] Video Social Inference Test, VSIT [2] Vineland Adaptive Behaviour Scale, VABS-II (socialization scale) [1,2]

[1] recommended participation measures by Bedell, et al, 2007; van Tol, et al, 2011
[2] recommended TBI outcome measures by Mc Cauley, et al, 2011

Appendix 3. Characteristics of 16 studies, using implicit participation outcome measures, with authors' suggestions on factors associated with participation after paediatric acquired brain injury.

First author, country	Study design	Year	Number of patients (TBI/ NTBI/controls)	Diag-nosis	Follow-up post injury in months (range)	Participation measure			Factors associated with participation[c]
						Explicit ABI[a]	Explicit general[a]	Implicit[b]	
Anderson, Australia	Prospective	2001	17 (17/0/35)	TBI	1-12-30	--	--	VABS-II	problems in communication
Janusz, USA	Prospective	2002	75 (75/0/46)	TBI	48 (36-60)	--	--	VABS-II, CBCL, INS	worse social information processing and problem solving
Stancin, USA	Prospective	2002	84 (84/0/50)	TBI	1-6-12-48 (36-60)	--	--	VABS-II, CHQ	worse adaptive skills; usage of medication
Hawley, United Kingdom	Retrospective	2004	67 (67/0/14)	TBI	24	--	--	VABS-II	problems in pre-injury behaviour and cognitive competences
Levin, USA	Cross-sectional	2004	58 (58/0/40)	TBI	36 (8-64)	--	--	VABS-II	location of injury; epilepsy
Yeates, USA	Prospective	2004	109 (109/0/80)	TBI	1-6-12-48 (36-60)	--	--	VABS-II, FAD, CBCL, INS	worse social information processing and problem solving ; problems in pre-injury behaviour and cognitive competences
Anderson, Australia	Prospective	2005	150 (150/0/0)	TBI	1-30	--	--	VABS-II , FBII	higher family burden; problems in pre-injury behaviour and cognitive competences
Aarsen, the Netherlands	Cross-sectional	2006	38 (0/38/0)	NTBI	91 (43-136)	--	--	PEDI, CBCL	presence of neurological comorbidities; worse adaptive skills; presence of mood problems
Anderson, Australia	Prospective	2006	84 (84/0/33)	TBI	1-6-30	--	--	PedsQL, FBII	problems in learning and applying knowledge, in pre-injury behaviour and cognitive competences; worse adaptive skills; higher family burden
Priagatano, USA	Retrospective	2006	60 (60/0/16)	TBI	16 (12-20)	--	--	CBCL	
Catroppa, Australia	Prospective	2008	48 (48/0/17)	TBI	1-6-30-60	--	--	VABS-II	problems in learning and applying knowledge; worse pre-injury family functioning
Levin, USA	Retrospective	2009	52 (52/0/41)	TBI	12	--	--	VABS-II	location of injury; epilepsy; problems in communication
Limond, United Kingdom	Cross-sectional	2009	47 (47/0/0)	TBI	34 (12-60)	--	--	PedsQL, SDQ	presence of mental fatigue
Muscara, Australia	Prospective	2009	36 (36/0/0)	TBI	104 (84-120)	--	--	ABAS-II	
Anderson, Australia	Cross-sectional	2009	124 (124/0/0)	TBI	163 (50-288)	--	--	VABS-II, ABAS-II, SSRS	
Kapapa, Germany	Prospective	2010	24 (24/0/0)	TBI	6-30	--	--	--	problems in daily living skills, in learning and applying knowledge; worse adaptive skills; presence of physical or mental fatigue
Rivara, USA	Prospective	2011	926 (729/0/197)	TBI	1-3-12-24	CASP		ABAS-II, PedsQL, CASE, FAD	

a according to Bedell, et al, 2007; van Tol, et al, 2011; b according to Bedell, et al, 2007; van Tol, et al, 2011; Mc Cauley, et al, 2011; c only factors additional to results in Table 2 are reported here; CASP=Child and Adolescent Scale of Participation; CAPE=Children's Assessment of Participation and Enjoyment ; ABAS II=Adaptive Behaviour Assessment System - Second Edition; CASE=Child and Adolescent Scale of Environment; CBCL=Child Behaviour Check List (social competence scale); CHQ=Child Health Questionnaire; FAD=Family Assessment Device; FBII=Family Burden of Injury Interview; INS=Interpersonal Negotiation Strategies; PEDI=Paediatric Evaluation of Disability Inventory (social functioning scale); PedsQL=Paediatric Quality of Life inventory (social subscale); SDQ=Strengths and Difficulties Questionnaire (peer relations and prosocial behaviour); SSRS= Social Skills Rating Scale, SSRS; VABS II=Vineland Adaptive Behaviour Scale Second Edition (socialization scale).

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5

Chapter 5
Psychometric evaluation of the Dutch language version of the Child and Family Follow-up Survey (CFFS)

Arend J. de Kloet[1,2], Monique A.M. Berger[2], Gary M.Bedell[3], Coriene E.Catsman-Berrevoets[4], Frederike van Markus-Doornbosch[1], Thea P.M. Vliet Vlieland[1,5]

1. Sophia Rehabilitation, The Hague, The Netherlands
2. The Hague University of Applied Sciences, The Hague, The Netherlands
3. Department of Occupational Therapy, Tufts University, Medford, MA, USA
4. Department of Paediatric Neurology, Erasmus University Hospital - Sophia Children's Hospital, Rotterdam, The Netherlands
5. Department of Orthopaedics, Leiden University Medical Centre, Leiden, The Netherlands

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ABSTRACT

Aim The Child and Family Follow-up Survey is developed to monitor long term outcome of children and youth with acquired brain injury (ABI). The aim of the present study was to translate and adapt it into the Dutch language and to evaluate its reliability and validity.

Methods The CFFS includes the Child and Adolescent Scale of Participation (CASP), the Child and Adolescent Factors Inventory (CAFI), and the Child and Adolescent Scale of Environment (CASE). The CFFS was translated into Dutch following international guidelines and adapted. The internal consistency, validity and test-retest reliability were examined among 2 groups of patients (n=140 and n=27) in the age of 5-22 years with ABI and their parents.

Results The translation and adaptation resulted in the CFFS- DLV, Dutch Language Version. The CASP-DLV, CAFI-DLV and CASE-DLV had a good internal consistency, with Cronbach's alpha being 0.95, 0.89 and 0.83, respectively. There were statistically significant correlations among the three CFFS subscale scores. These scores were also significantly correlated with the total scores of the Paediatric Quality of Life Inventory (PedsQL, parent) and the Paediatric Stroke Outcome Measure (PSOM), but not with the domain scores of the Children's Assessment of Participation and Enjoyment (CAPE). The test-retest reliability was good to moderate, with the intra-class correlation coefficients being 0.90 for the CASP-DLV, 0.95 for the CAFI-DLV and 0.68 for the CASE-DLV.

Conclusion The CFFS-DLV, as translation and adaptation of the CFFS into Dutch, proved to be a promising instrument to measure long term outcome of children and youth with ABI. Further research is needed to examine its responsiveness to change and potential in other patient groups.

INTRODUCTION

Acquired brain injury (ABI) in children, adolescents and young adults (-24 years) may result from events with an external cause (traumatic brain injury, TBI) or internal cause (non-traumatic brain injury, NTBI) such as a brain tumour, stroke or infections such as meningitis or encephalitis.[1] The estimated yearly incidence rates in the Netherlands are 585/100 000 and 190/100 000, respectively for TBI and NTBI, with about 15% classified as moderate or severe.[2]

It is generally acknowledged that ABI in children and youth may have a considerable impact on their functioning and quality of life.[3,4,5] Participation, i.e. the nature and extent of a person's involvement in meaningful life situations at home, school, work and community life[6,7] is an important aspect of functioning. However, studies on the nature, incidence and specific patterns of participation problems of children and adolescents with ABI are relatively scarce. The available studies mainly focus on traumatic brain injury (TBI) and in general conclude on the increased occurrence of participation problems in comparison with healthy peers.[8-14]

In the literature, a range of very different instruments is used with respect to participation in children and youth with ABI as outcome measure. Specific and validated measures to assess the extent of ability and disability on the level of activities and participation among children and youth with ABI are needed for clinical care and research, to provide information that will assist decisions about intervention needs, potential intervention effects, and policies that address participation.[15]

The Child and Family Follow-up Survey (CFFS) is a relatively recently developed set of measures to assess long-term outcome regarding young people with ABI.[15-17] It includes the Child and Adolescent Scale of Participation (CASP), the Child and Adolescent Factors Inventory (CAFI), and the Child and Adolescent Scale of Environment (CASE) and is advocated for use as outcome measure in paediatric traumatic brain injury research.[18,19]

So far, in the Netherlands no ABI-specific instrument to monitor outcome on the level of activities and participation, applicable in clinical care and research, is available. Therefore, the aim of this study was (1) to translate and adapt the original English version of the CFFS into a Dutch language version and (2) to evaluate its psychometric qualities in children and youth with ABI in the Netherlands.

METHODS

1. Translation and cross-cultural adaptation of the CFFS

The CFFS

The CFFS[11,16] was developed for young people in the age group 4-21 years with ABI and consists of 5 sections: general information about actual functioning of the young one (section 1), the Child and Adolescent Scale of Participation (CASP) (2), The Child and Adolescent Factors Inventory (CAFI) (3A) and the Child and Adolescent Scale of Environment (CASE) (3B), actual child's needs and support (4A) and the family needs and support (4B), as well as suggestions to improve healthcare policy for youth with ABI and their families (5). The CAFI and the CASE are both included in the same section of the CFFS entitled "Problems experienced in daily life". The CASP, CAFI and CASE are quantitative measures and subject to this psychometric evaluation.

The CASP measures young people's extent of participation and restrictions in home, school and community life situations and activities compared to same-age peers as reported by a parent or caregiver. The CASP contains 20 items divided into four clusters: (1) Home Participation, (2) School Participation, (3) Community Participation and (4) Home and Community Living Activities. The items are rated on a 4-point scale (4=Age expected, 3=Somewhat limited, 2=Very limited, 1=Unable). In addition, an item can be rated as 'not applicable'. CASP summary scores (total and subsection) can be transformed to a 100-point scale by summing the scores from each applicable item, dividing this number by the maximum possible score (variable due to the number of applicable items) and multiplying this by 100. For the present study, the 'Not applicable' response options in the CASP were excluded from the analyses (if patients scored 'Not applicable' this item was not taken into account in the scoring).

The CAFI consists of 15 items focused on health-related problems with cognitive, psychological, physical and sensory functions as a result of the ABI-diagnosis. Each item or problem is rated on a 3-point scale: no problem (1), little problem (2), and big problem (3). CAFI summary scores (total and composite domain) can be calculated by summing the scores of all items, dividing this number by the maximum possible score, and multiplying this by 100. The scores, transformed to a 100-point scale, range from 33 to 100.

The CASE consists of 18 items related to physical, social and attitudinal environmental problems that children and youth may experience at home, school or in the community. Each item or problem is rated on a 3-point scale: No problem (1), little problem (2), big problem (3) or 'Not applicable'. CASE summary scores can be calculated by summing the scores of all items, dividing this sum by the maximum possible score, and multiplying it by 100. The score ranges from 0 to 100. For the present study, the 'Not applicable' response

options in the CASE were counted as 'no problem'. For the CASP a higher score indicates a better level of functioning, whereas for the CAFI and CASE a lower score indicates better levels of functioning.

Its reliability and validity have been established,[20] the CFFS has been translated into 3 other languages: Hebrew, Arabic and traditional Chinese. The CASP was translated in Spanish, French and German as well.[20]

Translation and adaptation of the CFFS

The aim of a linguistic validation is to produce a translated version in a foreign language, which is conceptually equivalent to the original version, as well as clear and easy to understand. The translated instrument should be understood by most respondents in a selected population and should maintain a reading and comprehension level that will be accessible by most respondents, even of a low education level. This aim was achieved by following international guidelines for cross-cultural translation and adaptation,[21,22] which distinguishes 4 steps.

In step 1 a forward translation of the English version of the CFFS into a Dutch version was independently made by two Dutch health care professionals (AdK=Arend de Kloet, CC=Coriene Catsman-Berrevoets). Both of them have Dutch as their mother tongue and are fluent in English, one of them with expertise on the construct under study. The two translations were compared, discrepancies resolved and synthesized into one Dutch provisional version (step 2). Then a professional, independent and bilingual translator (HM=Hanneke Meulenbroek) and a Dutch health care professional with English as mother tongue (FvM=Frederike van Markus-Doornbosch) made a back translation of the provisional Dutch version into the original English language (step 3). In step 4 an expert panel, consisting of the 4 translators, discussed the differences between the back translations and the original English version and checked whether the items had maintained their intended meaning.

2. Validation of the CFFS-DLV

Study design

The validation part of the present study had a cross-sectional design and was conducted in 2011 and 2012. It was approved by the Medical Ethics Committee of the Erasmus University Medical Centre in Rotterdam (MEC 2009-440).

Patients

For the present study recruitment was done among 2 different groups of patients with ABI and their parents (Cohorts 1 and 2). Cohort 1 (n=140) was used to determine internal consistency and validity of the CFFS-DLV and obtained from a larger, multicentre study on

the incidence and long-term follow-up of ABI in the Netherlands.[2] In that study, performed in 2010, 1881 patients aged 0-24 years with a hospital-based diagnosis ABI made in 2008 or 2009 were identified by means of a review of the medical records of the emergency ward databases and the patient administrations of 3 major hospitals: the Erasmus University Hospital in Rotterdam, and the Haga Hospital The Hague and Medical Centre Haaglanden, The Hague.[2] For the patient selection the following diagnoses codes were used: minor head injury, traumatic brain injury, concussion, skull/brain trauma, neurological trauma, epilepsy, brain tumour, stroke, infections (meningitis/encephalitis) and post anoxia. In both cohorts, the following basic characteristics of the participants were registered: age (years), sex, cause (TBI or NTBI) and severity. Severity of TBI was scored using the Glasgow Coma Scale (GCS)[23] or the paediatric version of the GCS[24] at the time of presentation in the emergency room. TBI was considered mild if the GCS was 13-15, moderate if the GCS was 9-12 or severe if the GCS was < 9.[25] The severity of NTBI, determined at the time of discharge after the first admission to the hospital for this particular problem, was scored by means of an adapted version of the modified paediatric Rankin Scale (mRS).[26] In addition, for NTBI, the underlying diagnosis was recorded (epilepsy, brain tumour, stroke, infections (meningitis/ encephalitis), post anoxia or otherwise (non-traumatic diagnosis).

For the present study, initially both the group 4-12 years and the group 13-20 years were stratified for the year of onset (2008 or 2009), type (TBI or NTBI) and severity (mild-moderate-severe) of injury. Four hundred and thirty-three patients were subsequently selected: all severe TBI and NTBI were invited, mild and moderate TBI and NTBI were selected at random via select cases, option select random cases in SPSS[27]. Selected patients were subsequently invited by regular mail to undergo an assessment approximately two years after onset of ABI.
Cohort 2 was used to determine test-retest reliability of the CFFS-DLV and comprised patients with ABI. They were recruited by inviting parents of patients diagnosed with ABI, who were treated at the outpatient clinic of a Rehabilitation Centre because of physical and/ or neuropsychological problems. They were all in the age group between 4 and 22 years and living at home.

Assessment methods

To determine the internal consistency and validity of the CFFS-DLV, the instrument and all other questionnaires were administered once to parents/caregivers of patients in cohort 1, prior to a medical neurological and neuropsychological examination of their child. For the assessment of the reliability, the CFFS-DLV was sent by regular mail to the parents of 35 children and adolescents with ABI (cohort 2). After they returned the questionnaire, a second CFFS-DLV was sent. The maximum time between filling in the first and second CFFS-DLV

was 2 weeks, as 'reasonable compromise between recollection bias and unwanted (on the part of the investigator) clinical change'.[28] In case the questionnaires were not returned, a reminder was sent after 3 weeks for the first administration and after 1 week for the second administration. Children completed the CAPE[29] after the neurological and neuropsychological examination. Socio demographic data of the patients (age, sex) and caregivers (relation to the child) and injury data (type, severity) were obtained from medical records.

Apart from the CFFS, the following questionnaires were administered: The PedsQL (Paediatric Quality of Life Inventory)[25] is an instrument measuring health related quality of life (HRQOL). Up to 40% of children are identified as having poorer quality of life after TBI.[31-33] The PedsQL is previously used or recommended in children after TBI.[18,30, 32, 24, 35] It comprises 23 items, divided over 4 subscales: Physical Functioning, Emotional Functioning, Social Functioning, and School Functioning. To create a Total Scale Score the mean is computed as the sum of all the item scores over the number of items answered. For ease of interpretability, items are reversed scored and linearly transformed to a 0-100 scale, so that higher scores indicate better HRQOL (Health-Related Quality of Life). The subscales include Physical Functioning and Psychosocial Functioning (Emotional, Social and School Functioning), both with a score range of 0-100. The PedsQL has 4 versions: for age categories 5-7, 8-12, 13-18 and 19-23 years old, both with a version for children or youth and for parents. The reliability and validity of the PedsQL is well demonstrated in several school[36] and clinical populations, e.g. children and adolescents with Cerebral Palsy and cancer.[37,38] The PedsQL Total and subscale scores were chosen as core outcome to determine concurrent validity of the CFFS-DLV. For the present study, only the parent version of the PedsQl was used to determine concurrent validity with the CFFS-DLV, given that the CFFS is a parent-reported measure.

The PSOM (Paediatric Stroke Outcome Measure)[39] measures neurological outcome regarding 5 areas of functioning: right sensorimotor, left sensorimotor, language production, language comprehension, and cognitive/behavioural. An overall Deficit Severity Score (DSS) of normal-mild-moderate-severe, as indicator of actual level of functioning is based on the combination of these scores, with a score range of 0-10. The PSOM was found to be a valid and reliable outcome measure in paediatric stroke.[40]

The CAPE (Children's Assessment of Participation and Enjoyment)[28] measures self-reported participation in recreation and leisure activities outside school activities. There are three levels of scoring for the CAPE: overall participation scores, scale scores for five types of activities (recreational, active physical, social, skill-based, self-improvement) on five dimensions of participation: diversity, intensity, experienced pleasure, with whom and where. The CAPE was found to be reliable and valid in children and adolescents (6-18 years old) with physical disabilities.[28,41] For the present study, only the diversity ('which activities does the child do') and intensity ('how often does a child do activities') dimensions of the CAPE were taken into account.

Analysis

Comparisons of the socio demographic characteristics and the CFFS-DLV scores between cohorts 1 and 2 were done by means of the Mann-Whitney U test or Chi-Square test, where appropriate. Internal consistency of the CASP-DLV, CAFI-DLV, and CASE-DLV was determined by computing Cronbach's alpha using the data from cohort 1.

'Better and best level of functioning' and 'worse and worst level of functioning' were determined by counting the number of respondents with a highest or lowest possible score on the CASP-DLV, CAFI-DLV and CASE-DLV. For the CASP, a higher score indicates a better level of functioning, whereas for the CAFI and CASE a lower score indicates a better level of functioning.

Concurrent validity was determined by means of Spearman Rank Correlation Coefficients (r) between CASP-DLV, CAFI-DLV, CASE-DLV on the one side and PedsQL, PSOM, and CAPE on the other side. We expected that the correlations would be moderate to strong, especially between CASP-DLV and PedsQL and CAFI-DLV and PSOM. In general, r<0.40 is considered as weak correlation, r=0.41-0.60 moderate, r=0.61-0.80 good and r >0.81excellent.[37] To examine if age would affect concurrent validity, the correlations of the CASP-DLV, CAFI-DLV and CASE-DLV total scores and the PedsQL parent version were repeated for patients in the age groups 5-14 and 15-22 separately.

Intra Class Correlation Coefficients (ICC) were computed to investigate the test-retest reliability[38] of the CFFS-DLV, using the total scores of the CASP-DLV, CAFI-DLV and CASE-DLV from cohort 2. Differences between the initial test and retest scores were analysed by computing the difference with the 95% confidence interval and by applying the Wilcoxon-Signed-Rank test.

RESULTS

Review expert panel

The expert panel found no items to be irrelevant in the Dutch culture. However, the three parents who completed the CFFS-DLV suggested to briefly explain the term 'participation' in the introduction and improve the translation of the word 'community' into the Dutch language. These suggestions were discussed with the expert panel and agreed upon. Furthermore the expert panel had no remarks regarding the readability and clarity of the questionnaire.

In addition, the expert panel suggested 2 aspects which were considered relevant but currently not included the CAFI: 'planning and organizing' (e.g. being on time, cleaning room) and 'language comprehension' (e.g. understanding of written or spoken language). The expert panel also noted 'Preferred activities in leisure time?' as missing in the open ended items in part 2 (child) and 4B (family). These comments were passed on to the original developer of the CFFS.

Patients

Two hundred and forty-seven (56%) patients responded to the invitation by regular mail to undergo an assessment approximately two years after the onset of ABI. Non-response was partly due to inaccuracy of the address information: of 68 patients the Patient Information Form was returned with 'wrong address'. Of the 247 responders, 147 children and parents agreed to participate. Main reasons not to participate were 'too burdensome', 'not interested due to lack of problems or lack of time' and comorbidity (psychiatric). Of these 147 participants, 135 completed the CFFS-DLV and at least one other questionnaire. In total 114 children underwent a neurological examination on an outpatient clinic of the participating hospitals, including the PSOM and 65 of them gave consent for a home visit to administer additional questionnaires.

With respect to cohort 2, 27 of the 35 invited patients returned two questionnaires (cohort 2). The clinical characteristics of the participants in cohorts 1 and 2 are shown in Table I.

Overall, cohort 1 counted more male patients (52% vs. 33%) and more patients diagnosed with 'mild' ABI (75% vs. 22%) than cohort 2.

Table I Characteristics of patients with acquired brain injury in a study on the validation of the Child and Family Functioning Survey (-Dutch Language Version)

		Cohort 1 (n=140)	Cohort 2 (n=27)	p-value[1]
Age, years; median (range)		14 (5-22)	16 (7-22)	0.016
Male sex; number (percentage)		73 (52.1)	18 (33.3)	0.129
Cause and severity;				
Traumatic	Total; number (percentage of total ABI)	106 (76)	17 (63)	0.170
	Mild; number (percentage of total TBI)	79 (75)	3 (18)	
	Moderate	12 (11)	5 (29)	
	Severe	13 (12)	9 (53)	
	Unknown	2 (2)	0 (0)	
Non-traumatic	Total; number (percentage of total ABI)	34 (24)	10 (37)	<0.001
	Mild; number (percentage of total TBI)	26 (76)	3 (30)	
	Moderate	7 (21)	1 (10)	
	Severe	1 (3)	6 (60)	
	Unknown	0 (0)	0 (0)	
Respondents	number (percentage) mother/father/ other/patient/unknown;	94 (67) / 25 (18)/ 1 (1) / 2 (1) / 18 (13)	24 (89) / 1 (4) / 2 (7) / 0 (0) / 0 (0)	
CFFS-DLV[2] parent reported; median (range)				
CASP[2]	Total (range 0-100)	98.8 (30.0-100)	82.5 (40.0-100)	<0.001
	Home (0-100)	100.0 (29.2-100)	83.3 (54.2-100)	<0.001
	Community (0-100)	100.0 (25.0-100)	75.0 (37.5-100)	<0.001
	School (0-100)	100.0 (20.0-100)	85.0 (0.0-100)	<0.001
	Home & Community Living (0-100)	100.0 (20.0-100)	85.0 (25.0-100)	0.001
CAFI[3]	Total (33-100)	37.8 (33.3-84.4)	58.9 (35.6-86.7)	<0.001
CASE[3]	Total (0-100)	33.3 (33.3-59.3)	39.8 (33.3-64.8)	<0.001
PedsQL[2]	parent reported; median (range) (n = 135)			
	Total (0-100)	83.7 (40.8-100.0)		
	Physical (0-100)	93.8 (18.8-100.0)		
	Psychosocial (0-100)	78.6 (36.7-100.0)		
PSOM[2]	professional reported (0-4.5); median (range) (n = 107)	0.5 (0.0-4.5)		
CAPE[2]	child reported; mean (standard deviation) (n=65)			
	Diversity (0-55)	27.0 (15.0-40.0)		
	Intensity (1-7)	2.4 (1.5-3.8)		

[1] p-value of Mann-Whitney U test or Chi Square test

[2] CFFS-DLV= Child and Family Functioning Survey (-Dutch Language Version); CASP= Child and Adolescent Scale of Participation; CAFI= Child and Adolescent Factors Inventory ; CASE=Child and Adolescent Scale of Environment; PedsQl= Paediatric Quality of Life Inventory; PSOM= Paediatric Stroke Outcome Measure; CAPE= Children's Assessment of Participation and Enjoyment

Internal consistency and floor and ceiling effects

Using the data from cohort 1, Cronbach's alpha was 0.95 for the CASP-DLV, 0.89 for the CAFI-DLV and 0.83 for the CASE-DLV. The mutual correlations between CASP-CAFI and CAFI-CASE were moderate (-0.43 and 0.55, respectively) and between CASP-CASE low (-0.24). The average total scores of cohort 1 were significantly better than those of cohort 2 (CASP-DLV 92.4 versus 79.5, CAFI-DLV 39.6 versus 58.9 and CASE-DLV 34.6 versus 42.9) (all p-values <0.001, Mann-Whitney U test). Table II shows that for the CASP-DLV the best level of functioning (highest score) was seen in 63 (45%) of the patients in cohort 1.

Table II Numbers (%) of patients with a highest or lowest possible score[1] on the CASP-DLV, CAFI-DLV and CASE-DLV[2] total scores

	highest possible score		lowest possible score	
	COHORT 1	COHORT 2	COHORT 1	COHORT 2
CASP-DLV (0-100)	63 (45)	3 (11)	1 (0.7)	1 (3.7)
CAFI-DLV (33-100)	0 (0)	1 (3.7)	46 (32.9)	1 (3.7)
CASE-DLV (0-100)	0 (0)	2 (7.4)	66 (47.1)	1 (3.7)

[1] for the CASP a higher score indicates a better level of functioning, whereas for the CAFI and CASE a lower score indicates a better levels of functioning

[2] CASP-DLV= Child and Adolescent Scale of Participation (-Dutch Language Version); CAFI-DLV= Child and Adolescent Factors Inventory (-Dutch Language Version); CASE-DLV= Child and Adolescent Scale of Environment (-Dutch Language Version)

Overall, the CASP-DLV, CAFI-DLV and CASE-DLV total scores showed significant correlations with the parent version of the PedsQL (total score) and the PSOM (total score). The Spearman rank correlation coefficients of the domain scores of the CASP-DLV, CAFI-DLV and CASE-DLV with the PedsQL (total score) varied from 0.33 to 0.64 (all p-values <0.05). The correlations between CASP-DLV and PedsQL and CAFI-DLV and PSOM were, in contrast with what we suspected, not relatively higher. Repetition of the analysis for the correlations of the CASP, CAFI and CASE total scores with the PedsQL parents for the age groups 5-14 years and 15-22 years separately showed overall similar results in both age groups, with slightly stronger associations in the older patient group. Neither the CASP-DLV, CAFI -DLV nor CASE-DLV total or subscale scores were associated with the CAPE dimension scores diversity or intensity.

Concurrent validity

Table III shows the correlations between the CASP-DLV, CAFI-DLV and CASE-DLV and other measures of functioning, participation and environmental factors.

Table III Concurrent validity of the CFFS-DLV[1]

	Parent reported		Patient reported	
	PedsQL parents total (n=135)	PSOM medical neurological (n=114)	CAPE patient participation diversity (n=64)	CAPE patient participation intensity (n=64)
CASP[1] total	0.451*	-0.497*	0.082	0.050
CASP home	0.382*	-0.557*		
CASP community	0.410*	-0.444*		
CASP school	0.416*	-0.523*		
CASP home & community living	0.330*	-0.309**		
CAFI[1] total	-0.738*	0.396*	-0.035	-0.045
CAFI cognitive	-0.635*	0.286**		
CAFI psychological	-0.634*	0.328*		
CAFI physical	-0.593*	0.313*		
CAFI sensory	-0.515*	0.304*		
CASE[1] total	-0.626*	0.480*	0.032	0.072

* Correlation is significant at the 0.001 level (2-tailed)

** Correlation is significant at the 0.05 level (2-tailed)

1 CFFS-DLV= Child and Family Functioning Survey (-Dutch Language Version); CASP= Child and Adolescent Scale of Participation; CAFI= Child and Adolescent Factors Inventory; CASE= Child and Adolescent Scale of Environment; PedsQl= Paediatric Quality of Life Inventory; PSOM= Paediatric Stroke Outcome Measure; CAPE= Children's Assessment of Participation and Enjoyment

Reliability

Table IV shows the CFFS test-retest results for cohort 2.

The best levels of functioning for the CAFI-DLV and CASE-DLV (lowest scores) were seen in 46 (33%) and 66 (47%) in cohort 1, respectively.

Table IV Test-retest reliability of the CASP-DLV, CAFI-DLV and CASE-DLV[1] total scores

variable	Median score (range) 1st administration	Median score (range) 2nd administration	Mean difference (95% CI) Paired t-test	P value Wilcoxon[1]	ICC[2] (95% CI)
CASP-DLV[3]	82.5 (40.0-100.0)	78.8 (42.5-100.0)	2.3 (-1.7 to 6.2)	0.415	0.90 (.079-.096)
CAFI-DLV[3]	55.6 (35.6-86.7)	53.3 (33.3-82.2)	1.5 (-0.8 to 3.7)	0.189	0.95 (.089-.098)
CASE-DLV[3]	39.8 (33.3-64.8)	40.7 (33.3-55.6)	0.8 (-2.0 to 3.7)	0.632	0.81 (.533-.916)

1 significant at the 0.01 level; ICC average measures

2 ICC= Intraclass Correlation Coefficient; CI= Confidence Interval

3 CASP-DLV= Child and Adolescent Scale of Participation (-Dutch Language Version); CAFI-DLV= Child and Adolescent Factors Inventory (-Dutch Language Version); CASE-DLV= Child and Adolescent Scale of Environment (-Dutch Language Version)

Overall, there were no statistically significant differences between the first and the second measurement. Test-retest reliability was found to be high for the CASP-DLV and CAFI-DLV and moderate for the CASE-DLV.

DISCUSSION

This study showed that translation of the original English version of the CFFS into the Dutch language (CFFS-DLV) did not compromise the psychometric qualities of this survey, which is developed to monitor long term outcome of children and youth with ABI.

The results of this study are largely in line with those obtained in a study performed by Bedell[16], who was the developer of the CFFS. Bedell[16] included patients with a range of disabling conditions (n=260) as well as without disabilities (n=53). Regarding test-retest reliability Bedell[16] reported similar results for the CASP (0.94 vs. 0.90 in the present study) and CASE (0.75 vs. 0.81 in the present study) and somewhat less favourable results for the CAFI (0.68 vs. 0.95 in the present study). The internal consistency of the CASP, CAFI and CASE as reported by Bedell[16] was high (Cronbach's alpha 0.96, 0.86 and 0.91, respectively) and comparable to our study (0.95, 0.89 and 0.83 respectively). With respect to validity, in the previous study correlations with the Paediatric Evaluation of Disability Inventory (PEDI)[44] were computed, with the correlation coefficients being 0.75, 0.31 and 0.31 for the CASP, CAFI and CASE, respectively. In contrast, in our study the PedsQL (parents version) was used for comparison, yielding a weaker correlation for the CASP (0.45) and stronger correlations for the CAFI and CASE (0.74 and 0.63, respectively).

Concerning the mutual correlations among the CASP, CAFI and CASE, the correlation coefficients varied between 0.24 and 0.55 in the present study and 0.55-0.58 in the previous study.[16] These associations underline the interdependence of limitations on the level of participation (CASP), body functions and structures (CAFI) and environmental factors (CASE) in this patient group.[13,16]

Our additional effort to compare the parent-reported health-related problems with functions (CAFI-DLV) with a professional's score (PSOM), a stroke specific outcome measure, resulted in evidence for concurrent validity.

The incomplete associations between the CAFI-DLV, PSOM and PedsQL, each with a somewhat different scope or perspective, indicate that the three instruments can be used supplementary to each other in measuring the (impact of) limitations in body structure and functions, activities and participation in children and adolescents with ABI and their families. Previous research,[28,41] demonstrated relations between the CAPE scores with level of impairments and environmental problems in children with Cerebral Palsy. The absence of an association of the CASP with the CAPE as seen in the present study could possibly be

explained by the CASP focusing on participation restrictions (in broad categories) whereas the CAPE measures the range, diversity and frequency of participation (in discrete activities), which may be different aspects. The range and how often one participates may be based on factors such as child/family preferences and family resources. In addition, the 55 CAPE-items require reading, language and (sustained) attention skills, that are frequently limited after ABI, and the single version may not fit all age ranges.[45] Finally, important contemporary activities, such as social media and gaming, are lacking. Moreover, the perspectives of parents and children with respect to participation may be different. Indeed, overall better correlations of the CAPE with other outcome measures were seen in previous studies (Lawson, Anaby) in which the CAPE was compared only with child-reported instruments.
A further examination of the CAPE in research in ABI, for example in relation to the PedsQL and PSOM was advocated.

A relatively high proportion of patients with the best or worst possible score limits the discriminative qualities of a questionnaire, for example with respect to its sensitivity to change. In this study, the CFFS-DLV demonstrated high percentages of patients with the best possible score for the CASP-DLV, CAFI-DLV and CASE-DLV. This result is likely to be explained by the selection of patients, yielding a population with predominantly mild ABI, not requiring treatment. Further research in larger cohorts with children and adolescents with clinically significant symptoms of ABI at different time points across recovery is required to evaluate the potential of the CASP-DLV, CAFI-DLV and CASE-DLV to detect improvement or regression over time.

Parents are important observers,[46,47] however may be limited in their ability to value the mental state and experience of participation restrictions and quality of life of another person, despite the fact that they live closely together. In monitoring outcome at the level of participation it is recommended to merge different perspectives, due to discrepancies regarding the assessment of participation of children and youth with ABI between patients, parents or caregivers and professionals.[45,46] A youth version of the CASP (CASP-Y)[48] for the age group 8-21 years has recently been validated and will be considered in the future research projects to gain children's perspectives about their own participation. In accordance with Galvin[11] the addition of supplement for an 'outside family observer' (teacher, colleague, friend) as well, to get a more comprehensive impression of the functioning of the child seems useful. A selection of CFFS-DLV items (part 4A: items 3,4,5; 4B: 2,3; 5: 1,2) can be used for this purpose. Moreover, a mixed method design, integrating more qualitative and quantitative information, as suggested by van Tol et al.[49] may be a next step in participation studies in ABI. In addition to closed questions, open-ended questions such as in the CFFS part 1 (personal situation), 4 (family impact) and 5 (actual needs and concerns) or an interview[50] could enable parents to describe the situation more precisely and specifically. Personalised information is meaningful for clinicians to improve understanding of parents perspective but

requires qualitatively (or content) analyses if used in research.

This study has a number of limitations. First, the generalizability of the results is limited by the sample size of n= 108 and n=27 for the validity and reliability studies, respectively. Moreover, the characteristics of the patients included in the two cohorts differed significantly. The largest cohort included children who were not referred for treatment of ABI and accordingly comprised relatively many children with no or few consequences of ABI, whereas in the smaller cohort the patients were recruited from the rehabilitation setting, with the majority of children having severe ABI. Given these differences, it remains unclear whether the results obtained within one of the cohorts can be generalised to the other cohort. To overcome these shortcomings, a larger scale and longitudinal study including sufficient numbers and proportions of children with mild, moderate and severe ABI would be needed. Such a design would not only allow for a further examination of the measurement properties as studied in the present project, but also of the responsiveness to change on the group and individual level.

Another limitation was the use of the PSOM-SNE,[39] which was, although commonly used in clinical practice after non-stroke NTBI and TBI and recommended as outcome measure,[40,51,52] primarily designed to assess medical neurological functioning of children and youth after stroke. Despite this shortcoming, it was used in the absence of a specific instrument for these populations.

Moreover, no specific instrument measuring participation was available as gold standard for comparison with the CFFS-DLV. In fact the CASP (participation), CAFI (functions) and CASE (environmental factors) have different scopes. Finally, the sensitivity to change of the CFFS has not been studied yet. Finally, although the majority of parent-responders were mothers, it cannot be ruled out that the results of this study are influenced by the type of respondent (mother, father or guardian). To further examine this effect, a different study design and study size would be needed.

In conclusion, the CFFS-DLV is a promising instrument to measure long term outcome of young people with ABI in the Netherlands and Dutch-speaking Belgium. However, larger, prospective studies are needed to confirm and further explore its measurement properties.

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Declaration of interest

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6

Chapter 6
Family Impact of Acquired Brain Injury in children and youth

A.J. de Kloet[1,2], S.A.M. Lambregts[3], M.A.M. Berger[1], F. van Markus-Doornbosch[2], R. Wolterbeek[4], T.P.M. Vliet Vlieland[2,5]

1. The Hague University of Applied Sciences, The Hague, The Netherlands
2. Sophia Rehabilitation, The Hague, The Netherlands
3. Revant Rehabilitation Centre, Breda, The Netherlands
4. Department of Medical Statistics, Leiden University Medical Centre, Leiden, The Netherlands
5. Department of Orthopaedics, Leiden University Medical Centre, Leiden, The Netherlands

Submitted

ABSTRACT

Objective To assess the impact of Acquired Brain Injury (ABI) in children and youth on the family and explore factors associated with the extent of family impact.

Design Follow-up study.

Setting General hospital, rehabilitation care and the community.

Participants A cohort sample of parents of children and youth, 24-30 months after the diagnosis ABI was made in a general hospital. The inclusion criteria were age 4-20 years at onset of ABI. The patients of whom the parents were included in this study had an age range of 6-22.

Interventions Not applicable.

Main outcome measures Family impact was measured with the Pediatric Quality of Life Inventory Family Impact Module (PedsQL™FIM). Additional assessments included the PedsQL™General Core and Multiple Fatigue Scales, the Paediatric Stroke Outcome Measure Short Neuro Exam (PSOM-SNE), the Child & Family Follow-up Survey (CFFS) and sociodemographic and disease characteristics.

Results The parents of 108 patients participated in the study. The median age of the patients was 13 years (range 5-22), with 60 patients (56%) being male. The cause of ABI was traumatic (TBI) in 81 patients (75%) and non-traumatic in 27 patients (25%). At the time of diagnosis 19/81 (23%) and 5/27 (19%) were classified as moderate or severe in the TBI and NTBI groups, respectively.In the total group of patients with TBI and NTBI family impact was found to be associated with the severity and type of injury and the presence of child health problems before the ABI.

Conclusion Two years after ABI, the impact on the family as measured by the PedsQL™FIM was considerable. The extent of family impact was associated with characteristics of ABI as well as the health status of the child before ABI.

INTRODUCTION

Acquired brain injury (ABI) refers to any damage to the brain that occurs after birth, due to a traumatic (TBI) or non-traumatic (NTBI) cause. In children and youth the yearly incidence of ABI is substantial, with estimated incidence rates for the age group 0-24 years in the Netherlands being 585 per 100.000 for TBI and 190 per 100.000 for NTBI,[1] similar to incidence rates reported in the international literature.[2-4] Overall it is found that TBI may have a considerable impact on the patients' functioning[5,6] and quality of life[7-9] although the results regarding the impact of severity of TBI on quality of life were conflicting.

There are various studies reporting on the occurrence of problems in patients' functioning after NTBI in comparison with their healthy peers, such as in children with stroke[10,11] and brain tumours.[12] Moreover, the literature suggests that the long-term outcome is also related to family and environmental factors (including family cohesion, resources, social support, socioeconomic status).[13-17] Vice versa, family functioning can be influenced by the consequences of pediatric ABI, with negative effects on coping, problem-solving and communication of parents,[15,17,18] reflected by increased rates of family disruption, divorce and disfunctioning of brothers or sisters[19,20] after ABI. Although many families eventually adapt favorably to the often increased demands of the situation after injury, clinically significant stress was found in approximately 40% of families more than 12 months after onset of paediatric TBI.[2,21]

Regarding the factors related to the extent of family impact, injury severity, functional impairment, health problems, behavioral changes and emotional problems after ABI, were found to have a significant association to family functioning.[14,19,22-24]

So far, studies on family impact after ABI have only been done in the United States and Australia, and were primarily focused on TBI. In addition to a relatively large variety in inclusion criteria and time since onset of injury, these studies used various instruments to measure family impact. Specific measures for family burden or impact of trauma and/or pediatric chronic health conditions, include the Impact on Family Scale (IFS),[25] Parenting Stress Index Short Form (PSI/SF),[26] Family Burden of Injury[14,27] and The Family Impact Module (PedsQL™FIM) of the Paediatric Quality of Life Inventory Interview (FBII) (PedsQL™4.0).[28] The PedsQL™FIM appears to be a useful instrument, as it includes the physical, emotional, social and cognitive functioning of parents. These domains were found to be negatively influenced after paediatric ABI in the literature.[18,21,29,30] Moreover the PedsQL™FIM is available in multiple languages including Dutch, was designed as multidimensional measure of the impact of pediatric chronic health conditions. The PedsQL™FIM showed good psychometric properties in parents of children with complex chronic health problems[28] and cancer[31] and was used in studies on children with Duchenne,[32] a diversity of disabilities[33] and chronic pain.[34]

So far, the PedsQL™FIM has not been used in studies on the family impact of ABI. The aim of the present study was therefore to determine the impact of paediatric TBI and NTBI on families in the Netherlands, 24-30 months after diagnosis, using the PedsQL™FIM.
Secondary aim was to determine associations between sociodemographic characteristics (patient and family characteristics), ABI characteristics and actual functioning on the one hand, and the family impact as measured with the PedsQL™FIM on the other hand.

METHODS

Design and setting

This study on family impact was part of a larger, multicentre, hospital-based study on the incidence of ABI in the Netherlands.[1] In that study, performed in 2010, 1892 patients aged 0-24 years, with a first hospital-based diagnosis ABI made in 2008 or 2009, were identified by means of a review of the medical records of the emergency ward databases and the patient admission registries of 3 major hospitals in the Netherlands (Erasmus University Medical Centre in Rotterdam, Haga Hospital, The Hague and Medical Centre Haaglanden, The Hague). In a follow-up study we aimed to determine the health status approximately 2 years after onset of ABI. The present study on family impact is part of the follow-up study. The study (including the follow-up) was approved by the medical ethical committee (METC) of the Erasmus University Medical Centre Rotterdam (METC-2009-440). All parents and patients, as required by law from 18 years, participating in the follow-up assessment gave written informed consent.

Participants

For the larger study patients were selected from the registries of the participating hospitals using the following causes of injury for TBI: accident (e.g. in traffic, at home, in sports), (suspicion of) physical abuse and fall under influence of alcohol or drugs intoxication. For NTBI, the following causes were recorded: tumour, meningitis or encephalitis, stroke, ADEM (Acute Disseminated Encephalo Myelitis), MS (Multiple Sclerosis) or acute CNS (Central Nervous System) demyelinating disease and hypoxia-ischemia.
Patients were excluded if they were diagnosed with trauma capitis (minor head injury without brain symptoms). Inclusion criteria for the follow-up study were: age at onset ABI 4-20 years and ability to understand and complete questionnaires in Dutch. To select patients for the follow-up study in this article the total group of participants was categorized by age (4-12 or 13-20 years), year of onset (2008 or 2009), type (TBI or NTBI) and severity of injury (mild-moderate-severe), yielding 24 subgroups in total. Aiming at a total number of 400 patients to be invited for follow-up with a predicted response of 50%, 18-20 patients per subgroup

were selected. Within each subgroup, participants were at random selected using 'select cases, option select random sample of cases' in the statistical software program Statistical Package for Social Sciences (SPSS).[35] This procedure yielded a selection of 433 patients. These patients and/or their parents were subsequently approached by mail to participate in the study.

Assessments

Of all patients participating in the larger study, the age at onset, gender, year of onset, the type of injury (TBI or NTBI) and the severity had been extracted from the medical records. The severity of TBI was determined by means of the Glasgow Coma Scale (GCS) at hospital admission. According to the GCS, the severity of TBI was considered mild if the GCS was 13-15, moderate if the GCS was 9-12 or severe if the GCS was <9.[36] The severity of NTBI was determined at the time of discharge after the first admission to the hospital for this particular problem, and was scored by means of an adapted version of the modified paediatric Rankin Scale (mRS)[10,37] (school performance not taken into consideration): (1) Mild injury: no limitations (mRS 0, 1);(2) Moderate injury: mild motor impairments and/or mild problems with learning (mRS 2, 3); (3) Severe injury: severe motor impairments and/or severe problems with learning (mRS 4, 5). In addition, mRS 6 was used in cases of death during admission.

The questionnaires were in part completed at home and in part during the visit for the examination. Within 1-3 months after informed consent was given and in the week before the examination of the child in an outpatient rehabilitation clinic, parents received 4 questionnaires to be completed at home: the Child & Family Follow-up Survey (CFFS),[38] the Paediatric Quality of Life General Core Scale,[39] the PedsQL™FIM[28] and the PedsQL Multidimensional Fatigue Scale[40] (average duration 45 minutes). Subsequently, about 1 week later, the child was examined in an outpatient rehabilitation clinic. During the visit for the examination parents were interviewed by trained assessors. The structured interview included questions on the presence of physical and/or mental health problems of the parents before the ABI and/or at present (2 questions, yes/no) and/or the presence of physical and/or mental problems of the child before the ABI and/or at present (2 questions, yes/no) (4 questions in total, yes/no).

Family impact

The 36-item PedsQL™FIM yields a Parent Health Related Quality of Life (HRQoL) Summary Score (the Physical, Emotional, Social, and Cognitive Functioning Subscales; 20 items), a Family Functioning Summary Score (Daily Activities and Family Relationships Subscales; 8 items), Communication Subscale score (3 items) and a Worry Subscale score (5 items), as well as a Total Score. Higher subscale, summary and total scores indicate better functioning. If more than 50% of the items in the scale were missing, the Subcale Score was not

computed. Although there are other strategies for inputting missing values, this computation is consistent with the previous PedsQL™FIM peer-reviewed publications, as well as other well-established HRQOL measures.[41]

Overall functioning and fatigue

Two other modules of the Paediatric Quality of Life Inventory (PedsQL™4.0), pertaining to the child's health status, and both available in a Dutch language version, were used:

a. The General Core Scale,[39,42] which measures physical (8 items), emotional (5), social (5) and school functioning (5). In this study parent report versions for children 5-7, 8-12 and 13-18 years old were used.
b. The Multidimensional Fatigue Scale,[40] designed as a child self-report and parent proxy-report generic symptom-specific instrument to measure general fatigue (6 items), sleep (6) and cognitive fatigue (6) in children. The overall functioning and fatigue scores range from 0-100, with higher scores indicating better functioning). In this study the parent version was used.

Neurological functioning

The Paediatric Stroke Outcome Measure Short Neuro Exam (PSOM-SNE) was used for the neurological functioning,[43] It includes 5 areas of functioning: right sensorimotor, left sensorimotor, language production, language comprehension, and cognitive/behavioural. An overall Deficit Severity Score (DSS) of normal-mild-moderate-severe, as indicator of actual level of functioning is based on the combination of these scores, with a score range of 0-10. Lower scores indicate better functioning (less negative impact).

Participation and Environmental factors

The Child & Family Follow-up Survey (CFFS),[38,44] comprising the Child and Adolescent Scale of Participation (CASP), The Child and Adolescent Factors Inventory (CAFI) and the Child and Adolescent Scale of Environment (CASE) was used.

For both the CAFI and the CASE, higher scores indicate a greater number of problems, a greater impact of problems or a combination of the two.

Statistical analysis

Characteristics of patients and parents were analysed using descriptive statistics. All continuous variables were, according to their distribution, expressed as mean with standard deviation or median with score range.

Comparisons of sociodemographic and injury characteristics of participants in the present follow-up study as compared to those of all invited patients were done by means of the Mann-Whitney-U test.

To determine which factors were associated with family impact, the mean PedsQL™FIM Total Score, HRQoL and Family Functioning Summary Scales and the two Subscales Scores Communication and Worry were compared between subgroups of patients. Subgroups were made for the following variables: Characteristics before or at onset of ABI (sociodemographic: patient age and gender; educational level parents and single or double parent household; presence of health problems before ABI; injury characteristics: type, severity); functioning 2 years after onset of ABI (actual neurological functioning, activities and participation, fatigue, quality of life). For continuous variables, subgroups were made were made according to the mean (low/high). Comparisons of family impact scores between subgroups were done by means of independent t-tests for continuous variables or one way Analysis of Variance (ANOVA) for categorical variables.

Then, separate univariable models were used for each independent variable, again using the PedsQL™FIM Total Score, HRQoL and Family Functioning Summary Scales and the two Subscales Scores Communication and Worry as dependent variables.

Next, baseline characteristics (before or at onset of ABI) were fitted in linear multivariable regression models as independent or predictor variables, with the PedsQL™FIM Total Score as the dependent variable. The variables which were not significantly associated with this outcome were dropped from the model, after a stepwise check. Results were presented as regression coefficients and explained variance.

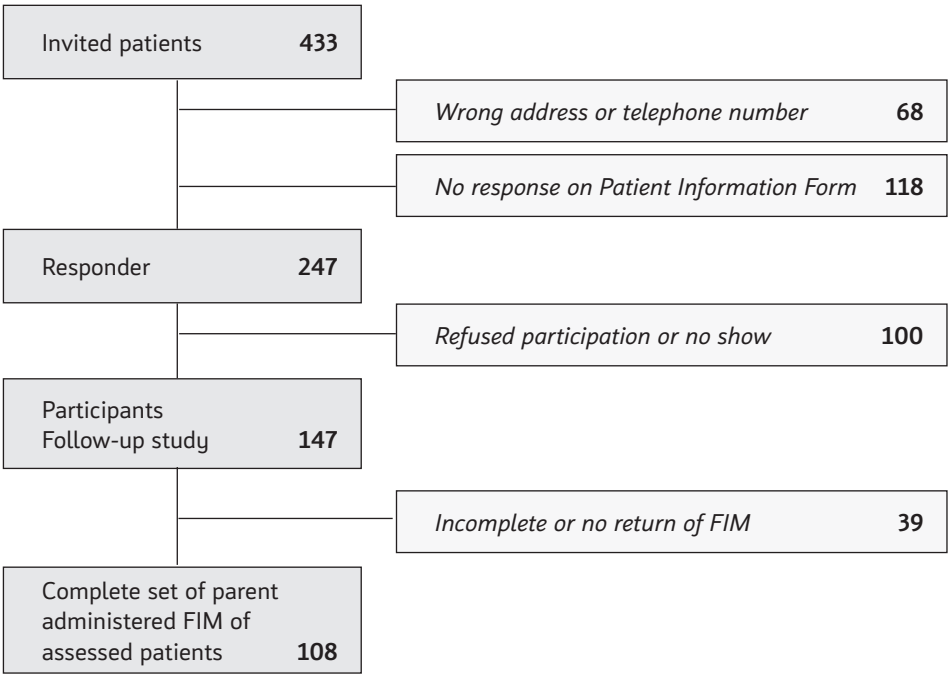
The sample size of n=108 supports the number of analyses conducted. The use of different classification systems for severity in TBI and NTBI warranted the need to conduct the analyses separately in those subgroups. As this categorization yielded a relatively small number of patients in the various categories of severity, we also combined TBI and NTBI to examine the impact of severity on family impact. In addition, for all analyses, a p-value less than 0.05 was adopted as the criterion for statistical significance. All data were analysed using SPSS version 21.0 software.[35] Missing values were processed according to instructions of each questionnaire.

RESULTS

Participants

The flow of patients is presented in Figure 1. In total, 147 participants were included in the present follow-up study. Of those, a total of 108 (60%) parents filled in the PedsQL™FIM. Eighty-one (75%) of the patients had TBI, with 62 (77%) being classified as mild and 19 (23 %) as moderate/severe. There were 27 patients with NTBI (25%), of whom 22 (81%) were classified as mild and 5 (19 %) as moderate/severe.

Figure 1 Flow chart recruitment



Regarding the presence of health problems among parents, the numbers (%) of parents reporting the presence of mental or physical health problems were 26 (22%) before ABI and 27 (23%) at present. For the presence of health problems among children, these numbers (%) were 23 (26%) before ABI and 36 (38%) at present.
Comparisons between participants in the follow-up study (n=147) and all invited patients (n=433) showed no significant differences regarding the distribution in age groups and types of injury. However, among the participants the proportion of patients with mild TBI was somewhat lower than in the total group (84 (78%) versus 359 (83%)).

Table 1 shows the characteristics of the 108 included participants with ABI and their parents. In the TBI group (75% of participants) the severity ratio mild: moderate/severe was 77:23. In the NTBI group (25%) the severity ratio mild: moderate/severe was 81:19. In the total ABI group 27 cases (26 %) reported pre-injury health problems versus 39 cases (38%) with health problems 2 years after onset of ABI. Parents reported a low educational level in 13 cases (13%) versus intermediate in 40 (40%) and high in 47 (47%) cases. Being a single parent household was reported by 31 (30%) parents.

Table 1 Characteristics of patients with Acquired Brain Injury and their parents in a study on family impact approximately 2 years after onset

		Cohort (n=108)
Age in years; median (range)		13 (5-22)
	Age Group ≤ 14 years old; number (%)	65 (60)
	Sexe, male; number (%)	60 (56)
Cause and severity		
Traumatic[1]	Total; number (% of total ABI)	81 (75)
	Mild; number (% of total TBI)	62 (77)
	Moderate/ Severe; number (% of total TBI)	19 (23)
Non-traumatic[2]	Total; number (% of total ABI)	27 (25)
	Mild; number (% of total NTBI)	22 (81)
	Moderate/ Severe; number (% of total NTBI)	5 (19)
Pre-injury physical or mental health problems; number (%) (n=104)		27 (26)
Actual physical or mental health problems; number (%) (n=103)		39 (38)
Educational level of parents; number (%) (n = 100)		
Low[3]		13 (13)
Intermediate		40 (40)
High		47 (47)
Single parent household; number (%) (n=102)		31 (30)

[1] determined by means of the Glasgow Coma Scale (GCS) at hospital admission
[2] determined by means of a disability scale based on the Modified Rankin Scale (mRS) at hospital discharge
[3] low (pre-vocational practical education or less), intermediate (pre-vocational theoretical education and upper secondary vocational education) or high (secondary education, higher education and/or university level education)

Family Impact after pediatric ABI

Regarding the PedsQL™FIM Total Score and the Summary Scores Parent Health Related Quality of Life Score and Family Functioning, the median scores varied from 81.7-85.4, with comparable score ranges (Table 2). The median scores for the Subscales Communication and Worry were 100 and 90, respectively.

In addition to the data presented in Table 2, the highest possible score, meaning no problems, was reported by 12 parents (11%) for the PedsQL™FIM Total Score, 26 parents (24%) for the Parent Health Related Quality of Life Score and 27 parents (25%) for the Family Functioning Score. The lowest possible score, meaning maximal family impact, was only reported once (1%), for the Subscale Worry.

Table 2 Scores on parent reported questionnaires and neurological outcome (PSOM) approximately 2 years after onset of ABI

Family Impact	Peds QL FIM-DLV ; median (range)	
	Total (range 0-100) n=108	82.9 (33.6 -100)
	Parent HR QoL (range 0-100) n=107	85.4 (33.5 -100)
	Family functioning (range 0-100) n=107	81.7 (30.8 -100)
	Communication (range 0-100) n=107	100.0 (33.3 -100)
	Worry (range 0-100) n=106	90.0 (0 -100)
Quality of Life	PedsQL General Core Scale-DLV; median (range) n=105	
	Total (0-100)	79.3 (40.8 -100)
Fatigue	PedsQL Fatigue-DLV; median (range) n=83	
	Total (0-100)	77.8 (36.1-100)
	Cognitive fatigue (0-100)	70.8 (37.5-100)
Activities and Participation	CFFS-DLV; median (range)	
	CASP Total (0-100) participation problems n=104	97.5 (42.5 -100)
	CAFI Total (33.3-100) limitations in functions n=107	40.0 (33.3-67.5)
	CASE Total (0-100) environmental limitations n=93	33.3 (33.3-59.3)
Actual functioning	PSOM professional reported; median (range) (0-10)	0.5 (0 -7)

The correlations of the PedsQL™FIM Total Score with the Parent Health Related Quality of Life Summary Score (r=0.971) and the Family Functioning Summary Score idem (r=0.879) were high ($p < 0.01$). The mutual correlation between the Summary Scores Parent Health Related Quality of Life parents and Family Functioning was 0.871, and significant at the 0.01 level (2-tailed).

Table 3 shows the results of the univariable analysis with the PedsQL™FIM Total Score, Summary and Subscale Scores as dependent variables and sociodemographic, pre-injury and injury characteristics and actual functioning ad independent variables. For the independent variables, patients were divided in subgroups according to fixed categories for nominal variables or by the mean score for numeric variables.

The FIM Communication and Worry Subscales were significantly different between younger and older patients, with lower scores in older patients. There was a significant difference between the FIM Total and Parent Health Related Quality of Life Summary Score and Family Functioning Summary Scores and the two Subscale Scores Communication and Worry in subgroups of patients with and without health problems before ABI, and between the TBI and NTBI groups.

Table 3 Results of univariable analysis of Total, Summary and Subscale Scores on PedsQL™FIM as dependent variables, related to baseline characteristics at onset (sociodemographic, pre-injury health, injury characteristics) and results at follow-up (actual functioning) approximately 2 years after onset of ABI, as independent or predictor variables*

	Predictor Variables		Family Impact Total Score	Quality of Life Summary Score	Family Functioning Summary Score	Communi-cation Subscale Score	Worry Subscale Score
Socio-demographic Characteristics	Age (at Onset)	≤14 y (N=65) †	82.8 (16.9)	84.4 (17.7)	79.8 (18.5)	89.3 (17.5)	81.9 (22.5)
		>14 y (N=63)	76.7 (18.8)	78.2(19.5)	77.0 (20.8)	77.5 (24.2)	70.8 (27.9)
	Sex	Male †	81.3 (16.9)	82.8 (17.3)	80.2 (18.2)	85,4 (20.2)	76.1 (24.6)
		Female	79.3 (19.1)	80.8 (20.1)	76.7 (20.8)	83.5 (22.5)	79.2 (26.3)
	Educational Level Parents	Low (N=11) †	75.7 (16.3)	77.8 (17.0	77.6 (20.5)	82.1 (22.0)	63.8 (28.6)
		Intermediate (N=40)	78.7 (16.9)	79.3 (18.3)	77.9 (19.3)	86.1 (19.9)	78.0 (23.1)
		High (N=47)	82.7 (19.9)	85.3 (19.6)	79.3 (20.6)	84.6 (22.4)	79.3 (26.8)
	Single Parent Household	Yes (N=31) †	77.0 (17.7)	78.3 (19.2)	76.5 (19.0)	85.2 (20.0)	72.7 (28.0)
		No (N=71)	82.4 (17.8)	84.2 (18.0)	79.9 (19.9)	85.7 (21.2)	79.6 (24.6)
Pre-injury Functioning	Health Problems	Yes (N=27) †	71.1 (21.7)	72.7 (23.5)	71.2 (22.0)	83.3 (26.0)	65.4 (25.9)
		No (N =77)	83.4 (15.5)	84.9 (15.8)	81.3 (18.0)	88.6 (17.7)	82.0 (24.1)
Injury Characteristics	Type of Injury	TBI (N=81) †	83.6 (16.1)	85.1 (17.2)	80.8 (18.3)	89.7 (17.1)	83.2 (21.6)
		NTBI (N 27)	70.8 (19.6)	72.6 (19.7)	72.3 (21.4)	69.4 (24.7)	60.7 (28.0)
	Severity of Injury	Mild (N=84) †	81.8 (16.2)	83.4 (16.8)	79.8 (18.2)	84.9 (20.3)	79.5 (22.8)
		Moderate/ severe (N=24)	75.6 (22.5)	76.8 (23.4)	74.8 (23.0)	83.3 (20.3)	70.6 (31.9)
	Severity TBI	Mild TBI (N=62)	84.1 (15.4)	85.8 (16.2)	80.4 (18.3)	88.5 (17.9)	84.6 (18.6)
		Moderate/ severe TBI (N=19)	82.0 (18.7)	82.7 (20.3)	82.0 (18.6)	93.4 (14.3)	78.9 (29.5)
	Severity NTBI	Mild NTBI (N=22)	75.5 (17.0)	76.7 (17.1)	78.0 (18.1)	75.0 (23.7)	65.9 (27.7)
		Moderate/ severe NTBI (N=5)	50.1 (18.3)	54.4 (22.0)	47.2 (16.9)	45.0 (9.5)	38.8 (18.1)

	Predictor Variables		Family Impact Total Score	Quality of Life Summary Score	Family Functioning Summary Score	Communi-cation Subscale Score	Worry Subscale Score
Actual Functioning	PSOM-SNE §	Low (=0) (N=43) ‡	85.1 (15.3)	86.6 (16.7)	81.7 (17.4)	89.8 (17.3)	85.9 (20.8)
		High (>0) (N=63)	76.5 (19.0)	78.1 (19.3)	76.1 (20.7)	80.2 (23.1)	70.5 (26.6)
	CASP	Low (≤97) (N=51) ‡	74.8 (17.8)	76.9 (18.5)	72.9 (19.7)	78.5 (22.8)	70.3 (26.4)
		High (>97) N=53)	85.2 (16.8)	86.3 (18.0)	83.6 (17.8)	90.3 (17.4)	83.9 (23.2)
	CAFI §	Low (≤40) (N=59) ‡	88.7 (12.2)	89.8 (12.8)	85.6 (15.8)	95.2 (11.7)	90.0 (18.1)
		High (>40) (N=48)	69.9 (18.4)	72.1 (20.1)	69.5 (19.9)	70.9 (22.7)	61.3 (24.3)
	CASE	Low (≤33) (N=53) ‡	88.6 (13.1)	89.4 (13.4)	86.6 (16.0)	92.6 (16.2)	89.2 (19.6)
		High (>33) (N=50)	71.1 (18.6)	73.4 (20.4)	69.8 (19.6)	75.5 (22.7)	64.0 (24.9)
	PedsQL QoL	Low (≤80) (N=53) ‡	69.9 (17.8)	71.8 (19.2)	70.2 (19.6)	74.9 (23.4)	61.8 (26.0)
		High (>80) (N=52)	91.3 (100)	92.9 (9.9)	87.1 (15.5)	95.4 (10.6)	92.9 (12.6)
	PedsQL Fatigue	Low (≤78) (N=42) ‡	68.8 (17.5)	70.3 (18.7)	69.0 (20.1)	76.6 (23.4)	60.9 (26.9)
		High (>78) (N=41)	93.1 (7.8)	95.0 (6.8)	88.7 (13.5)	97.2 (6.9)	94.0 (12.4)

* all variables are expressed as mean SD; high score indicates better functioning, except for §: high score indicates bigger problem
† group split in categories or ‡ group split in categories by median score
Dark gray cells indicate significant difference between groups, tested by t-test and One war ANOVA (for Educational level parents)

Moreover, for the total group of ABI the severity of injury was associated with family functioning. This association was seen in the NTBI subgroup as well, but not in the TBI subgroup.
Moreover, almost all measures of functioning and participation at follow-up participation (CAPE, CASP), environmental factors (CAFI), fatigue (PedsQL™Fatigue) and quality of life (PedsQL HR QoL). Similar results were found for neurological functioning (PSOM), except for the association with the Summary Score on Family Functioning, which did not

reach statistical significance. There was no indication of possible collinearity among the independent variables to be entered in the multivariable model (sociodemographics: patient age and gender; educational level parents and single or double parent household; presence of health problems before and after ABI; injury characteristics: type, severity) (tolerance values of all variables > 0.2). Table 4 shows that in a multivariable model the type of ABI (NTBI > TBI), severity (moderate/severe > mild) , and the presence of health problems before ABI were associated with more family impact, according to the PedsQL™FIM Total Score, with the final model accounting for 21.4% of the variance. As the type of injury (TBI or NTBI) was included in the model, no analyses for TBI and NTBI separately were done to examine the impact of severity on the PedsQL™FIM Total Score within subgroups of ABI. Sex (p=0.929), age (p=0.655), single parent household (p=0.356) and parents' educational level (p=0.426) were not significantly associated with family impact.

Table 4 Results of multivariable regression analysis, with Total Score on the PedsQL™FIM as dependent variable, approximately 2 years after onset of ABI, related to significant predictive baseline characteristics at onset of ABI

		Regression coefficient B	Significance level*	95% Confidence Interval	
				Lower Bound	Upper Bound
Intercept		54.929	.000	44.394	65.464
Pre-injury health problems	No	12.628	.001	5.250	20.007
	Yes	0[a]	.	.	.
Type of injury	TBI	11.740	.002	4.445	19.035
	NTBI	0[a]	.	.	.
Severity of injury	Mild	9.140	.020	1.449	16.830
	Moderate/ Severe	0[a]	.	.	.
		R^2 = .214			

* $p < 0.05$

[a] this parameter is set to zero because it is redundant

DISCUSSION

In a selected group of children and youth with ABI, with relatively many children with mild TBI or NTBI and only few being treated for consequences of ABI, the impact on the family as measured by the PedsQL™FIM was considerable.

The results of our study suggest that the PedsQLTM FIM is a promising, multidimensional instrument to measure family functioning, parental health related quality of life, communication and worries after pediatric ABI, with high mutual correlations between Total, Summary and Subscale Scores. The Subscales Communication and Worries are additional to other specific family impact measures.[25,26] The availability of an appropriate

instrument to measure and monitor family impact and functioning after ABI is important, as has been previously suggested in the literature.[13-17] Subsequently, the development and implementation of specific family centered interventions in rehabilitation and chronic care for youth with ABI has been advocated.[45,46,47]

The results of the univariable analysis showed that functioning 2 years after ABI was associated with the PedsQL™FIM Total Score (Family Impact), Summary Scores (parents' Quality of Life and Family Functioning) and Subscale Sores (Communication and Worries).

This is in line with other studies concerning patients' actual functioning (in our study measured with PSOM, CAFI),[14,22] participation (CASP), quality of life (PedsQL HR QL)[18,30] and environmental factors (CASE).[16,17] Our results support the importance of (measuring) fatigue as associated with family impact, just as others published on fatigue after pediatric ABI related to general health-related problems[23] and sleep problems.[24] Similar to other studies[14,48] it was found that current health problems of children were found to impact family functioning after ABI. The variables concerning actual functioning were not entered into the multivariable prediction model, as they concerned the outcome of ABI rather than its starting point.

The prediction model of family functioning after ABI using only sociodemographic, pre-injury and injury characteristics, showed that the presence of NTBI, a greater severity of either TBI or NTBI and the presence of pre-injury health problems were associated with more family impact. These findings are largely in line with the literature.[5,6,14,49] However, the impact of the type of ABI on family impact has been scarcely studied, as most studies were so far done among specific diagnosis groups. The finding that NTBI had a greater impact on family functioning than TBI. This difference may be due to the different nature of the two types of ABI, with TBI having a transient and/or steady course in many patients, whereas the underlying conditions in NTBI may have other consequences, such as side effects of medical treatment and risk of recurrence or relapse.[10,12]

In our study 'younger age at onset' was not significantly associated (r=0.655) with family impact. This is surprising, as younger age at onset, has been previously associated with poorer outcomes in the literature.[13,27] A potential explanation may be the so called 'growing into deficit' theory.[49] This theory implies that children and youth may experience a decline in functioning later on in their development, when brain development is supposed to support age-specific cognitive and behavioral competences that are required for more complex demands,[50] e.g. in transitions to higher levels of education, work, social intimacy or living independently. In contrast with the literature, we found 3 baseline characteristics being not significantly associated with family impact: parents' educational level,[14,15] single parent household,[15] and sex.[50]

Several limitations of our study should be noted. First, the generalizability of the results is probably limited by the selection of the cohort. Patient recruitment was done in hospitals and not in the rehabilitation setting. Therefore, the population consisted of patients with

predominantly mild ABI, not requiring treatment. The results are therefore not generalizable to groups of patients with ABI who are currently treated for the consequences.[5,6,38] According to literature[51,52] approximately 20% of children with mild TBI is hindered by consequences after 3 and 10% after 12 months, respectively. Differences with other studies may be explained by these limitations. The relatively high number of non-responders may be a confounder. This is likely due to the relatively high percentage of children and youth without consequences after a mild ABI. Another reason for non-response could be that the invitation for participating in the study was sent by mail two years after the hospital based diagnosis. We did not systematically record the reasons for non-participation. Some of the non-response was due to wrong addresses, and is probably random. Although response bias cannot be excluded, the characteristics of the patients at hospital admission or discharge in the present study are fairly similar to those of the larger population, which was described in a previous publication.[44] The relatively low response resulted in an overall small sample size, which may have limited the statistical power of the study.

Another limitation is time since onset: 2 years after the hospital based diagnoses is a relatively long period in which many other factors may influence outcomes such as family functioning as well, and for parents it is a long period to reflect on.

Another limitation is the difference in the classification systems and time points used for severity grading between TBI and NTBI employed in the present study. For this reason we did analyses within the two subgroups separately. The association between severity and FIM appeared to be stronger in NTBI than in TBI. Despite the observation that the impact of severity on family functioning remained in the multivariable model including the type of ABI as a separate independent variable, it could be hypothesized that severity as determined at hospital admission is a better predictor for future functioning in NTBI than in TBI. This finding underscores the need to take the differences between the two types of ABI, as well as the classification systems for their severity, always into account when conducting research in this area. Another limitation concerning the assessment of neurological functioning was that we used the PSOM, which has only been found to be a reliable and valid measure in paediatric stroke, but not in other forms of NTBI or in TBI. However, at the time the study was designed, it was considered the best available quantitative instrument providing a standardized neurological assessment in all diagnosis groups.

Finally, a limitation of the study relates to the interpretation of the magnitude of the observed PedsQL™FIM scores in the group of patients with ABI. To our knowledge, there is no literature on this subject in this patient group available yet. Future studies are needed to define the Minimal Clinically Important Difference (MCID) of the PedsQL™ FIM, the difference in scores that can be interpreted as clinically meaningful, in children with ABI.

To overcome these shortcomings, a larger scale and longitudinal study including sufficient numbers and proportions of children with mild, moderate and severe ABI would be needed.

CONCLUSION

Family impact following a diagnosis of paediatric ABI involves risks of long-term psychosocial problems for parents and families, partly due to the specific consequences of pediatric ABI. The results of this study support the importance of the systematic monitoring of family impact to enable tailor-made psycho-education, follow-up and support for parents, brothers and sisters. The PedsQL™FIM appears to be an appropriate, multidimensional instrument for measuring and monitoring family impact after pediatric TBI and NTBI. Further research on family impact after ABI is required to further elucidate associated factors and examine the utility of cumulative risk index.[53]

Declaration of Interest statement

The authors report no conflicts of interest. The authors alone are responsible for the content and writing of the paper.

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7

Chapter 7
Gaming supports youth with acquired brain injury? A pilot study

A.J. de Kloet[1,2], M.A.M. Berger[2], I.M.A.J. Verhoeven[3], K. van Stein Callenfels[2], T.P.M. Vliet Vlieland[1,4]

1. Sophia Rehabilitation, The Hague, The Netherlands
2. The Hague University of Applied Sciences, The Hague, The Netherlands
3. Technical University, Delft, The Netherlands
4. Department of Orthopaedics, Leiden University Medical Centre, Leiden, The Netherlands

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ABSTRACT

Aim To explore the effects of usage of the Nintendo Wii on physical, cognitive and social functioning in patients with acquired brain injury (ABI).

Methods This multicentre, observational proof-of-concept study included children, adolescents and young adults with ABI aged 6-29 years. A standardized, yet individually tailored 12-week intervention with the Nintendo Wii was delivered by trained instructors. The treatment goals were set on an individual basis and included targets regarding physical, mental and/or social functioning. Outcome assessments were done at baseline and after 12 weeks, and included: the average number of minutes per week of recreational physical activity; the CAPE (Children's Assessment of Participation and Enjoyment); the ANT (Amsterdam Neuropsychological Tasks); the achievement of individual treatment goals (Goal Attainment Scaling); and quality of life (PedsQL; Paediatric Quality of Life Inventory). Statistical analyses included paired t-tests or Wilcoxon-Signed-Rank tests.

Results Fifty patients were included, (31 boys and 19 girls; mean age 17.1 years (SD 4.4)), of whom 45 (90%) completed the study. Significant changes of the amount of physical activity, speed of information processing, attention, response inhibition and visual-motor coordination ($p<0.05$) were seen after 12 weeks, whereas there were no differences in CAPE or PedsQL scores. Two-thirds of the patients reported an improvement of the main treatment goal.

Conclusion This study supports the potential benefits of gaming in children and youth with ABI.

INTRODUCTION

The incidence of acquired brain damage (ABI) in people aged up to 25 years old in the Netherlands is substantial, with about 19 000 new cases per year[1,2.] International incidence rates for traumatic brain injury in the age group 0-14 years vary, due to differences in definition, inclusion criteria and methodology, from 280[3] to 798[4] per 100 000 persons per year.

Patients with ABI experience motor problems as well as cognitive, behavioural and emotional limitations. These consequences often have a significant and long-standing impact on activities of daily living and participation in society, such as difficulty in achieving and maintaining employment and social relationships.[5,6,7] Moreover, it was found that young patients with ABI are less involved in leisure activities than their peers, their activities are more passive, home-based and lack variety.[5] Patients have labelled social isolation as their most disabling limitation in activities and participation and as their major problem.[8,9]

Regarding the effectiveness of rehabilitation of children and youth with ABI, systematic reviews[10,11] concluded that the evidence for the effectiveness of interventions to treat neurocognitive sequelae is sparse. Interventions that proved to be effective in individual clinical studies included the ATAG (Amsterdam Trainingsprogramma Aandacht Geheugen voor kinderen; Training program Attention and Memory for children),[12] a structured and attractive program of 20 weeks daily training of sustained, focused attention, mental tracking and memory, and the SARAH-program,[13] a family based program, focused on improving family problem solving, relationships and associated child's behaviour.

In addition to conventional rehabilitation strategies, virtual reality (VR) and gaming, especially commercial 'off the shelf' consoles, are more and more acknowledged to be promising therapeutic interventions to improve learning and performance of motor skills in patients with ABI.[14] Recently, two systematic reviews evaluating the effects of virtual reality and interactive video gaming in patients after stroke were published.[15,16] One review[15] included 5 randomized clinical trials and 7 observational studies with 11 of the 12 studies showing a benefit of virtual reality for selected outcome. The other review[16] found limited evidence that the use of virtual reality and interactive video gaming may be beneficial in improving arm function and Activities of Daily Living (ADL) function when compared with the same dose of conventional therapy. Moreover, insufficient evidence was found for the effectiveness of virtual reality and interactive video gaming on grip strength or gait speed. The latter review also concluded that there are few studies evaluating the use of commercial gaming consoles, such as the Nintendo Wii. In the two reviews, two studies using the Nintendo Wii were included,[17,18] both reporting positive effects on motor functioning. A recent study published after the inclusion period of the 2 aforementioned reviews found a significant improvement in static and dynamic balance using easy Balance Virtual Rehabilitation (eBaViR), a system

based on the Wii Balance Board, in adult patients with ABI including stroke.[19] Specifically in children and youth with ABI the potential effectiveness of the Nintendo Wii on visual-perceptual processing, postural control, and functional mobility was described in a case series including adolescents and children with cerebral palsy.[20]

In conclusion, the currently available literature suggests that the available studies on the Nintendo Wii in ABI are sparse, have mainly focused on motor outcome measures, adults, and count small samples. The aim of the present study was therefore to explore the effect of the usage of the Nintendo Wii in children, adolescents and young adults with ABI on variables effecting body functions, activities, participation and overall quality of life. Being a proof-of-concept study, we hypothesized that gaming with the Wii may have a positive effect on physical, cognitive and social functioning in this patient group.

PATIENTS AND METHODS

Design

This multicentre, observational study was carried out from February to June 2010 in three centres in the Netherlands (Sophia Rehabilitation, The Hague; De Hoogstraat Rehabilitation, Utrecht and Mariendael, Arnhem). These centres provide rehabilitative services and/or special education for children and youth with physical disabilities and chronic diseases.

Patients who were eligible for the study were invited by their medical specialist to participate in the study. If they were interested, they received information from one of the therapists or teachers who were involved in the project. After this introduction, all patients / students and their parents (patients under the age of 16 years) received an information leaflet about the project. This study was approved by the medical ethical committee of the Leiden University Medical Centre. All participants / patients gave written informed consent. In addition, all participants signed a contract for the loan of a Nintendo Wii set for the duration of the study.

Patients

Inclusion criteria were: Having ABI according to the Diagnosis Treatment Combination-coding of the medical registries of Sophia Rehabilitation, De Hoogstraat or Mariendael, with the diagnosis verified by their treating rehabilitation specialist; age from 6 to 29 years; and being a patient or a student at the time of inclusion in one of the participating institutions.

Fifty-eight children, adolescents and young adults, registered as patient or student in one of the three centres, were informed about the study and received general information. Fifty-one of them showed interest and were invited for the screening. All 51 patients were found to be eligible for the study. After the screening one patient declined participation, so that 50 patients were finally included.

Excluded were patients who: would not be able to play with the Nintendo Wii due to e.g. lack of coordination, poor physical or mental condition; had a risk of falling due to insufficient balance and/or inadequate motor response; had excessive disinhibition (sensory or behavioural); or had impaired sensory processing (visual-auditory disruption), as judged by the treating rehabilitation specialist.

Intervention

The 12-week intervention consisted of two training sessions (60 minutes each) regarding the use of the Nintendo Wii, delivered by a trained physical therapist, occupational therapist or a teacher from the special school which participated in the study. Assessments were conducted before (baseline) and directly after the intervention (follow-up at 12 weeks).

At the first training session, an inventory of the participant's three main limitations regarding their daily functioning was made by means of the 'personal profile', a semi-structured interview comprising the following domains: gross motor activities (seven categories) and fine motor activities (five categories), information processing (three categories), communication (six categories), self-confidence, social participation and daily physical activity (each one category).

Subsequently, three Nintendo Wii games were assigned, matching the individual treatment goals and by taking into account the individual's motor and cognitive limitations and interest. This was done by using a fixed, digital protocol, which was called TherapWii (available at www.TherapWii.nl). This protocol included a list of common treatment goals in patients with ABI which are linked to 16 different Nintendo Wii games, each game consisting of several sub-games. For example, the goal "improving balance" was linked to six games (i.e. Wii Fit, Sports, Sports Resort, EA Sports, Samba de Amigo and Kororinpa), more specifically to 57 sub-games (e.g. Single Leg Extension and Ski Jump of the game Wii Fit). The protocol was developed by an expert group including four physical therapists, two occupational therapists, two teachers and two neuropsychologists, all with ample experience in the treatment of children and youth with ABI. After the first training session the participant was able to connect and start the console, create a personal profile and play the three assigned games (including activities such as searching in the menu, playing together, using different controllers). Safety instructions (exercise area, strap, balance) were given as well as individual advice tailored to the therapist's or teacher's estimation of the risk on sensory or behavioural loss of control. All participants were encouraged to play the assigned games each for at least 20 minutes per week and to play in total two hours per week (at home, at school or during an individual rehabilitation session in rehab). Playing games other than the three assigned games was permitted. At the second training session, scheduled at about six weeks after the first, the progression was evaluated, and instructions on the use of the three assigned games or additional games were provided. During the 12-week intervention period,

therapists and teachers had weekly contact with the participants by e-mail or telephone. In addition, they sent a text message to the participants' cell phone every week as a reminder to play.

Assessment methods

Assessments were done by the six therapists and teachers delivering the intervention, and two neuropsychologists/psychometrics who performed the neuropsychological tests. Before the start of the study, all professionals took part in a training session on the execution of the various measurements. Assessments were done at baseline (before the first treatment session) and 12 weeks thereafter.

Sociodemographic and disease characteristics

Sociodemographic data were gathered by means of a semi-structured interview. Data on disease history and severity were obtained from medical records. Sociodemographic characteristics included: age (years), sex (male/female), work status (yes/no/not applicable), school type (level/not applicable), special school (yes/no/not applicable), experience with gaming (yes/no; if yes: experience with Wii yes/no).

Disease characteristics comprised: cause of ABI (traumatic or non-traumatic) and time since diagnosis (< 1 year, between 1-2 years, 2-3 years, 3-4 years, > 4 years). In addition, it was recorded whether patients currently received therapy (yes/no) and if they were using an assistive device (yes/no).

Adherence with the intervention

Adherence to the intervention was measured by recording the participants' attendance to the two training sessions.

Physical, recreational and social activity

Outcome measures of physical, recreational and social activity included a single question on physical activity and a multidimensional questionnaire.

Time spent on physical activity: All participants estimated the time spent on physical activities over the past week on a 4 point scale: 1: 0-29 minutes, 2: 30-59 minutes, 3: 60-119 minutes, and 4: 120 minutes or more.

CAPE (Children's Assessment of Participation and Enjoyment), a questionnaire which was developed in Canada, measuring self-reported participation in recreation and leisure activities outside of mandated school activities. The CAPE was found to be reliable and valid.[21] It is translated and validated for the Netherlands.[22] There are three levels of scoring for the CAPE: overall participation scores; scores for two domains (formal and informal activities); and scale scores for five types of activities (recreational, active physical, social, skill-based,

self-improvement). The CAPE provides information on five dimensions of participation: diversity, intensity, experienced pleasure, with whom and where.
Three domains of the CAPE were used for this study, consisting of 55 items, clustered in informal recreation (12 items), physical (13 items) and social activities (10 items). The original CAPE inquires about activities carried out in the past four months. For the purpose of this study, the time frame was adapted to the past week. The completion time is about 20 minutes.

Cognitive/neuropsychological functioning
Cognitive/neuropsychological functioning was measured by means of the Amsterdamse Neuropsychologische Taken (ANT) program.[23] The ANT program evaluates various aspects of cognitive functioning, such as working memory, attention, information processing, executive functioning and visuospatial perception. The ANT was found to be suitable to detect neuropsychological dysfunctions in patients with leukaemia after chemotherapy[24] and psychiatric conditions commonly associated with attention deficit disorders.[25-27]
For this study the following 4 neuropsychological tests from the ANT were administered: Baseline Speed (BS) (test of attention), Feature Identification (FI) (test of memory), Shifting Attentional Set-Visual (SSV) (test of response inhibition and flexibility) and Tracking (TR) (test of visual motor coordination)'.

1. Baseline Speed (BS), a test of attention (alertness) involving minimal cognitive effort. The participant is required to press a mouse-key as quickly as possible when a fixation cross in the centre of the computer screen changes into a white square (n = 32 trials for left and right hand each). Main outcome parameters are the mean reaction time (in milliseconds) of the dominant hand and the within-subject standard deviation of the reaction time (i.e. response speed stability).
2. Feature Identification (FI), a test of memory, measures the ability to discriminate complex visuospatial patterns. This task requires manipulation and monitoring of working memory content. The participant must decide whether a specific visuospatial pattern (a 3x3 matrix of six white and three red squares) is present in a display signal of 4 patterns (n = 80 trials). The difference recognition time (in milliseconds) and accuracy (number of errors) between the similar and dissimilar condition were measured.
3. Shifting Attentional Set - Visual. (SSV), a test of attentional flexibility, an important aspect of executive functioning. A coloured square moves randomly to the right or to the left on a horizontal bar that is permanently present on the computer screen. The task consists of three parts. Depending on the colour of the square, compatible responses (part 1), or incompatible responses (part 2) are required, by pressing the mouse-key on the same side as the direction of movement of the square (part 1), or on the side opposite to the direction of movement of the square (part 2). In these parts, the stimulus-response (SR) compatibility is fixed (either spatially compatible or incompatible). The incompatible condition requires

inhibition of pre-potent responses. During part 3, the colour of the moving square varies randomly, requiring attentional flexibility by continuously having to adjust response type (compatible/incompatible). Discrepancy time (in m sec) and accuracy (number of errors) of the fixed task conditions (averaged across part 1 and 2) and of discrepancy time and accuracy (number of errors), averaged across part 1 and 3, were the outcome parameters.

4. Tracking psychomotor task, which measures quality of movement along a planned trajectory. This task requires the child to trace the mouse cursor in between an outer circle and an inner circle presented on the computer screen (two parts: in clockwise direction with the right hand and in counter-clockwise direction with the left hand). The speed (in sec) and mean deviation (accuracy of movement) were used as outcome parameters.

Achievement of individual treatment goals

With respect to the treatment goals and their achievement, participants were asked to rate their performance regarding a body function or activity related to the treatment goal on a numeric rating scale ranging from 1 "very poor" to 10 "very good" at baseline and after the intervention. A higher score after treatment as compared to the baseline score was considered to be an improvement.

Quality of life

Quality of life was measured with the PedsQL (Paediatric Quality of Life Inventory),[29] consisting of 23 items, divided over subscales: Physical Functioning, Emotional Functioning, Social Functioning, and School Functioning. To compute scale scores, the mean was computed as the sum of the items divided by the number of items within that scale. In addition, to create a Total Scale Score the mean was computed as the sum of all the items over the number of items answered on all the Scales.

The PedsQL has a separate youth and parent version for 4 age groups: 5-7, 8-12, 13-18 and 19-25 years old'. In this study both were used. The reliability and validity are well demonstrated.[26] The time for filling in each version is approximately 5 minutes, with individual differences depending on work speed.

Statistical analysis

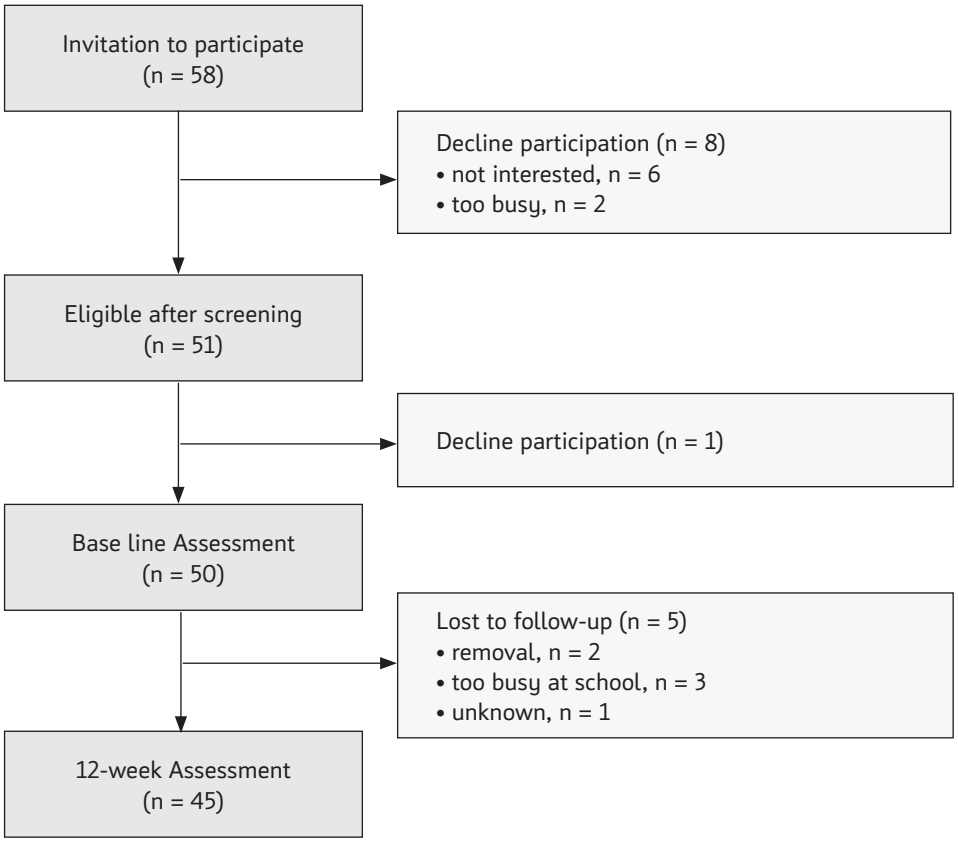
All continuous variables were, according to their distribution, expressed as mean with standard deviation (SD) or median with the interquartile range (IQR). For continuous variables, differences in results at 0 and 12 weeks are presented as the mean change scores from baseline with the 95% confidence interval, and compared using paired t-tests or Wilcoxon signed rank tests, where appropriate. For all analyses, a p-value less than 0.05 was adopted as the criterion for statistical significance. All data were analysed using SPSS version 17.0 software (SPSS, Chicago, IL).

RESULTS

Adherence with the intervention

Forty-five of the 50 included patients (90%) completed the study (see Figure 1). All 50 patients completed the 2 training sessions, but after that 5 were lost to follow up due to lack of time caused by school (3), removal (2) and lack of motivation (1).

Figure 1 Flowchart of patients with acquired brain injury participating in an observational study on the effectiveness of the Nintendo Wii



The baseline characteristics of the included patients and the patients who completed the study are shown in Table 1.

Table 1 Characteristics of 50 patients with acquired brain damage participating in an observational study on the effectiveness of the Nintendo Wii

	All patients n=50	Completers n=45	Non-completers n=5
Age, years			
8-12 (child)	5	4	1
13-18 (adolescent)	30	27	3
19-30 (young adult)	15	14	1
Male sex	31	26	5
Cause of brain damage			
Traumatic	27	22	5
Non-traumatic	23	23	0
Lesion			
Left hemisphere	16	14	2
Right hemisphere	8	6	2
Diffuse	23	22	1
Unknown	3	3	0
Time since diagnosis, years			
0-2 years	9	5	4
> 2 years	39	38	1
Unknown	2	1	1
Current rehabilitation treatment	29	25	4
Current use of assistive device(s)	11	10	1
Main problem[#]			
Gross motor functions	35	33	2
Fine motor functions	27	26	1
Information processing	47	42	5
Language, communication	21	20	1
Solitude, isolation	19	17	2
Self confidence	24	23	1
Physical activity	27	24	3
Experience with gaming (> 3 months)	46	42	4

[#] all patients were asked to list 3 main problems regarding their functioning

Physical, recreational and social activity

Table 2 shows a significant decrease in diversity and an increase in intensity of the reported amount of time spent on physical activity between 0 and 12 weeks. Regarding the CAPE, significant differences over time were seen in diversity of recreational activities and intensity of physical activities. No significant changes were found on the CAPE dimensions related to context (i.e., with whom and where they participate in activities) and enjoyment of activities.

Table 2 Baseline, follow up and change scores of measures of physical, recreational and social activity in patients with acquired brain injury using the Nintendo Wii

	Baseline	Follow-up	Mean Change (95% CI)#	p-value*
	Median (interquartile range)	Median (interquartile range)		
Amount of physical activity	(n=50)	(n=45)		
Physical activity score (1-4)	2.00 (2.00)	3.00 (2.00)	-0.48 (-0.82-0.13)	**.01**
CAPE	(n=43)	(n=43)		
Diversity				
Recreational activities	6.00 (3.00)	5.00 (3.00)	0.60 (0.12-1.08)	**.02**
Social activities	5.74 (3.00)	5.00 (3.00)	0.12 (-0.53-0.76)	.87
Physical activities	3.00 (2.00)	3.00 (3.00)	-0.37 (-0.95-0.20)	.11
Total	14.69 (5.00)	14.08 (5.00)	0.47 (-0.82-1.76)	.49
Intensity				
Recreational activities	2.64 (1.42)	2.48 (1.50)	0.16 (-0.05-0.37)	.14
Social activities	2.90 (1.20)	2.88 (1.80)	-0.02 (-0.31-0.26)	.89
Physical activities	1.32 (1.00)	1.49 (0.77)	-0.19 (-0.40-0.02)	**.04**
Total	2.23 (0.51)	2.17 (0.83)	-0.05 (-0.23-0.13)	.64
Who				
Recreational activities	2.13 (1.17)	2.00 (0.93)	0.12 (-0.10-0.34)	.20
Social activities	2.67 (1.04)	2.75 (1.20)	-0.13 (-0.36-0.11)	.25
Physical activities	2.75 (1.67)	3.00 (1.60)	-0.13 (-0.40-0.13)	.13

CAPE= Children's Assessment of Participation and Enjoyment
#mean change may differ from the difference as computed from the presented median baseline and follow-up values as it concerns the difference obtained by paired comparisons
*p-value of Wilcoxon Signed Rank test

Cognitive/neuropsychological functioning

Table 3 shows the results of the ANT. Due to technical problems we were not able to score the results of five patients. Seven patients failed to complete all four subtests of the ANT, due to a combination of motor problems (n=7), limitations in memory for the instruction (n=3), impulsivity (n=2) or other reasons (n=3). In the patients who completed both ANT tests, there was a significant improvement of the speed of information processing: in reaction time, figure identification, shifting attention, visual motor coordination and in response inhibition. No significant changes were found regarding accuracy.

Achievement of treatment goals

The top-ranked treatment goals and number of patients reporting an improvement are shown in Table 4. Gross motor functioning and Information processing were the two most frequently mentioned goals. At follow-up, two-thirds of the patients reported an improvement, whereas

it appeared that more of them reported an improvement with gross motor function goals than with Information processing goals.

Table 3 Baseline, follow up and change scores of the Amsterdamse Neuropsychologische Taken (ANT) in patients with acquired brain injury using the Nintendo Wii

	Baseline		Follow-up		Mean Change (95% CI)#	p-value*
	n	Median (interquartile range)	n	Median (interquartile range)		
Baseline Speed Reaction time dominant hand	33	303.00 (84.50)	33	287.00 (51.50)	25.27 (4.87-45.68)	**.01**
Baseline Speed Standard deviation	33	74.00 (55.00)	33	63.00 (26.50)	18.97 (-6.60-44.54)	.20
Feature Identification Difference recognition time similar and dissimilar condition	37	867.50 (361.00)	37	675.50 (278.25)	116.64 (32.23-201.05)	**.01**
Feature Identification Number of errors	37	15.00 (15.00)	36	15.00 (16.88)	-0.24 (-5.43-4.95)	.88
Shifting Attentional Set Visual Time difference condition 1 and 2	40	287.00 (302.75)	39	192.00 (283.00)	72.08 (23.25-120.91)	**.005**
Shifting Attentional Set Visual Discrepancy errors condition 1 and 2	40	2.00 (4.00)	39	2.00 (3.00)	-0.19 (-2.29-1.90)	.67
Shifting Attentional Set Visual Discrepancy time of time difference condition 1 en 3	38	422.00 (308.00)	38	381.00 (365.00)	14.97 (-45.94-75.88)	.48
Shifting Attentional Set Visual Discrepancy errors condition 1 en 3	39	3.00 (5.00)	38	3.00 (5.25)	1.24 (-0.77-3.24)	.56
Tracking Speed	40	1.36 (1.36)	38	1.65 (1.11)	0.32 (-0.74-1.38)	**.047**
Tracking Accuracy	40	97.40 (9.52)	38	95.84 (10.69)	-0.44 (-4.69-3.81)	.20

Mean change may differ from the difference as computed from the presented median baseline and follow-up values as it concerns the difference obtained by paired comparisons. *p-value of Wilcoxon Signed Rank test.

Table 4 Treatment goals ranked 1 and their achievement in patients with acquired brain injury (ABI). Results are expressed as numbers of patients

	Treatment goal ranked 1	Improvement at follow-up
Gross motor functions	19	15
Fine motor functions	1	1
Information processing	18	8
Language, communication	3	3
Solitude, isolation	0	0
Self confidence	2	1
Physical activity	1	1
Unknown	1	-
Total	44	29 (66%)

Quality of life

Table 5 shows the results of the PedsQL. Concerning the PedsQL questionnaires completed by the patients, no significant changes over time were seen for any of its domains. For the parent-completed PedsQL questionnaires, a statistically significant improvement was seen in the domain school functioning. Overall, the improvements seen with the parent-completed PedsQL were larger than with the child version.

Table 5 Baseline, follow up and change scores of PedsQL in patients with acquired brain injury using the Nintendo Wii. Values are expressed as median and interquartile range, unless stated otherwise

	Baseline		Follow-up		Mean Change (95% CI)#	p-value*
Patient Administered PedsQL	n	Median (interquartile range)	n	Median (interquartile range)		
Physical Functioning	47	81.25 (25.00)	45	78.13 (23.44)	0.57 (-3.71-4.85)	.71
Emotional Functioning	47	75.00 (25.00)	45	75.00 (20.00)	0.61 (-3.62-4.85)	.63
Social Functioning	47	80.00 (25.00)	45	80.00 (30.00)	3.17 (-1.26-7.60)	.17
School Functioning	46	62.50 (20.00)	45	65.00 (25.00)	-2.02 (-5.95-1.90)	.36
Total Functioning	47	76.09 (20.45)	45	73.91 (18.94)	0.63 (-2.21-3.47)	.66
Parent Administered PedsQL						
Physical Functioning	40	67.19 (37.61)	30	76.56 (36.72)	-3.77 (-12.11-4.56)	.22
Emotional Functioning	40	65.00 (28.75)	30	70.00 (26.25)	-3.26 (-8.13-1.61)	.18
Social Functioning	40	62.50 (30.00)	30	75.00 (37.50)	-3.53 (-11.36-4.31)	.17
School Functioning	39	55.00 (25.00)	29	70.00 (32.50)	-11.39 (-19.3- -3.48)	.009
Total Functioning	40	62.77 (22.42)	30	70.55 (31.79)	-5.10 (-10.98-0.79)	.06

Mean change may differ from the difference as computed from the presented median baseline and follow-up values as it concerns the difference obtained by paired comparisons.
*p-value of Wilcoxon Signed Rank test.

DISCUSSION

In this proof-of-concept observational study it was found that the targeted assignment of Nintendo Wii games increased physical activity, the speed of information processing, attention, response inhibition, and parent-perceived Quality of life (QoL) in children and youth with ABI. In addition, the majority of participants indicated an improvement of their major treatment goal. No changes were seen regarding the context of activities as measured with the CAPE, accuracy and patient-perceived quality of life.

In general the results of the present study are in line with those of other studies employing the Wii in patients with ABI,[17-20] all demonstrating positive effects on motor functioning. In contrast with the previous studies, our study included outcome measures regarding overall physical activity, neuropsychological functioning, societal participation and quality of life. In our study we failed to demonstrate an effect of the intervention on societal participation (diversity, i.e. with whom and where) and enjoyment of activities as measured with the CAPE. So far, the CAPE has only sparsely been employed in longitudinal studies in patients with cerebral palsy. In these cases it was not used with the aim to detect changes over time. In research with patients with ABI the CAPE was not used before. Additional research is needed to examine the validity and responsiveness of this measure in this patient group.

In addition, with the exception of school functioning (scored by parents), no changes of quality of life, as measured with the PedsQl were seen. It remains to be established to what extent gaming has an impact on QoL and to what extent the PedsQl is able to detect clinical changes in patients with ABI. In addition, whereas some of the previous studies included measures of posture and balance[19,20] at all our study did not specifically aim to examine the effect of the Wii on these measures. As problems with balance are likely to be common in the patient group with ABI, future research should include a measure of balance.

The variety of dimensions of health status and outcome measures used in the available studies underlines the need for consensus on a core set of outcome to be used in studies on virtual reality and interactive video gaming in patients with ABI . Such a core set would have to cover all elements of health status, including body structures and functions, activities, societal participation, and personal and environmental factors, supported by imaging techniques such as functional Magnetic Resonance Imaging (fMRI). With the choice of outcome measures, the age range of the patient group must be taken into account, as many instruments have only been validated in patients of specific age groups.

Another issue that needs attention is an adequate description of the intervention with the Nintendo Wii. In some of the aforementioned studies with the Nintendo Wii a limited number of games was employed. In our study, despite using a fixed protocol, the potential range of games that could be matched to specific treatment aims was relatively large, so that a standardized description of the intervention is difficult to make. If however the choice had

been more limited, the preselected games may not have matched the patients' individual preferences and situation, which could have had a negative impact on adherence with the intervention. Currently, initiatives are being taken to develop a standardized classification of VR and gaming, to support clinical decision making as well as research.[14]

Regarding compliance, all participants took part in both training sessions. We did not register the actual time spent on gaming, as adherence with filling out detailed diaries in this did not appear feasible in this patient group. Therefore, in future research, adding a 'timer' to the game, to record the length of time spent gaming) is needed. This is in part reflected by the response to the questionnaires, which ranged between 90 and 99% at both time points. In addition, the proportion of patients who completed the ANT was also limited, a software problem caused loss of data of 5 participants during data analysis. These observations stress the need to carefully select outcome measures that are feasible in this patient group and the inclusion of sufficient numbers of patients, as attrition rates can be substantial.

This study has a number of limitations. Its most important weakness is the absence of a comparison group, so that no firm conclusions about the effectiveness of the intervention can be drawn. In addition, the employment of a large set of outcome measures may have enhanced the chance of finding statistically significant differences. However, the favourable findings warrant the need for larger clinical trial, comparing the effectiveness of an intervention with the Nintendo Wii with other interventions that proved to be beneficial in patients with ABI.

CONCLUSIONS

This study substantiates the potential benefits of gaming in patients with ABI. A larger, controlled study is required to prove the effect of gaming on motor, communicative, neurocognitive and social emotional functions and activities in this patient group.

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Declaration of Interest statement

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8

Chapter 8
Summary and general discussion

SUMMARY

Aims of the thesis

Paediatric acquired brain injury (ABI) is a major public health issue[1] and often results in pervasive, lifelong consequences for the child and his or her family. The literature suggests that the long-term consequences of paediatric ABI, in particular with respect to participation, are underestimated, poorly understood and managed.[2] Given this lack of knowledge, this thesis aimed

- To determine the occurrence and causes of ABI in children and youth in the Netherlands (chapters 2 and 3).
- To systematically review the literature on factors associated with participation in children and youth with ABI (chapter 4).
- To translate, adapt and validate an instrument to measure participation after paediatric ABI into the Dutch language (chapter 5).
- To evaluate the family impact in a cohort of children and youth with ABI and their family (chapter 6).
- To explore the potential effect of virtual reality (gaming) on physical, cognitive and social functioning of children and youth with ABI (chapter 7).

Main findings

Chapter 2 concerned a retrospective, multi-centre cohort study on the occurrence and causes of acquired brain injury (ABI), including traumatic brain injury (TBI) and non-traumatic brain injury (NTBI), among Dutch children and youth.

For this purpose patients, aged 1 month-24 years and diagnosed with ABI in 2008 or 2009, were identified from the registries of three hospitals. 1892 patients were included: 1476 with TBI and 416 with NTBI. With respect to severity, the large majority of cases were mild: 82.4% and 81.4% in TBI and NTBI groups, respectively.

Based on these figures, the estimated total relative incidence rates of TBI and NTBI per 100 000 per age groups were 271.2-15.4-2.3 (0-14 years) and 261.6-27.0-7.9 (15-24 years) for mild-moderate-severe TBI and 95.7-11.8-1.3 (0-14 years) and 73.8-6.1-1.6 (15-24 years), for mild-moderate-severe NTBI, respectively.

In patients with TBI aged 0-4 years, accidents in or about the family home were the most common, whereas in patients aged 5-14 and 15-24 years, traffic accidents were the most frequent cause. With respect to the causes of NTBI meningitis and encephalitis were relatively frequent in the 0-4 year old group, whereas brain tumours showed a peak in the 5-14 year old group. Stroke occurred with a relatively similar frequency in the three age groups.

Based on the same retrospective cohort study, *Chapter 3* described clinical characteristics and medical treatment in patients, aged 1 month-24 years, who presented with a traumatic

brain injury at one hospital in the Netherlands in 2007 and 2008. 472 patients met the inclusion criteria; severity of the injury was classified as mild in 342 (72.5%) patients, moderate in 50 (10.6%) patients and severe in 80 (16.9%) patients.
Of all included patients, 343 (72.7%) were admitted to the hospital. The medium length of stay was 7 days, 3 days and 1 day in patients with severe, moderate and mild TBI, respectively. In patients with severe TBI a significantly larger number of complications occurred during the clinical course than in patients with mild or moderate TBI. Twenty-four (5.1%) patients died, of whom 22 had a severe TBI.
In 398 patients (84.3%) a brain CT (computer tomography) scan or MRI (magnetic resonance imaging) scan was performed, with 78 of them (19.6%) having a normal brain CT scan. The latter contributed to the decision to discharge them to their home. 107 (22.7%) patients with TBI received no hospital follow-up care after discharge. Patients with severe TBI significantly more frequently received outpatient treatment after discharge, in particular rehabilitation, as compared to patients with mild or moderate TBI. 24 (16.7%) of the patients with mild TBI patient had follow-up and were reporting long-term cognitive impairments, whereas 60 (42.0%) of these patients had no abnormalities on brain CT scan at admission. This latter finding supports the need for routine follow up of children and youth with mild TBI.

Chapter 4 concerned a systematic review on the determinants of participation of children and youth with ABI. Employing the usage of a recommended, explicit participation outcome measure as one of the inclusion criteria for this review, five clinical studies were selected. The measures of participation included in these studies concerned the Child and Adolescent Scale of Participation (CASP) and the Children's Assessment of Participation and Enjoyment (CAPE). Potential determinants of participation were categorized according to the International Classification of Functioning, Disability and Health (ICF). The factors which were found to be most consistently associated with one or more dimensions of participation (defined as a similar (positive or negative) relation found in more than 1 study and not disputed in another study) were: severity of ABI; sensory functioning (Health Condition); movement functions, cognitive and behavioural functioning (Body Functions and Structures); accessibility and design of the physical environment, acceptance and support from other people, socioeconomic status and availability of special services and programmes (Environmental Factors).

Chapter 5 described the process of translation and adaptation of the questionnaire for parents of the Child and Family Follow-up Survey (CFFS), developed to monitor the long-term outcomes of children and youth with ABI. The CFFS consists of 3 subscales, the Child and Adolescent Scale of Participation (CASP), the Child and Adolescent Factors Inventory

(CAFI), and the Child and Adolescent Scale of Environment (CASE). After translation and adaptation, the psychometric qualities of the CFFS-Dutch Language Version (DLV) were determined among 147 patients with ABI, from 2 up to 3 years after onset of injury. Most of these patients were participants of the cohort study described in chapters 2 and 3.

This study showed that all three subscales of the CFFS-DLV proved to be reliable and valid instruments to measure long-term outcomes of children and youth with ABI. The internal consistency of the 3 subscales was high, with Cronbach's alpha being 0.95 for the CASP-DLV, 0.89 for the CAFI-DLV and 0.83 for the CASE-DLV. Moreover, there were significant mutual correlations among the CASP-DLV, CAFI-DLV and CASE-DLV, underlining the value of the CFFS-DLV in determining and understanding associations between extent of participation (CASP), extent of impairment (CAFI) and environmental barriers (CASE).

In *Chapter 6* the impact of ABI on the family of the child as well as its determinants were studied in connection with the cohort study described in chapters 2 and 3. Two to 3 years after onset of ABI, family impact was measured by means of the Paediatric Quality of Life Inventory Family Impact Module (PedsQL™FIM) in 108 children. Their age ranged between 5 and 22 with a median age of 13 years old, 81 (75%) had TBI and 27 (25%) NTBI. The condition was classified as mild, with the patient experiencing no or few consequences, in 62 (77%) of the patients with TBI and in 22 (81%) of the patients with NTBI. Overall, the impact on the family after the paediatric ABI was considerable. Multivariable analysis showed that the severity (moderate/severe>mild) and type (NTBI>TBI) of ABI and the presence of health problems before the injury occurred were associated with a higher family impact (Total Score on the PedsQL™FIM). The PedsQL Family Impact Module seems to be a useful instrument in this patient group.

Chapter 7 explored the effects of usage of the Nintendo™Wii on physical, cognitive and social functioning in youth and adolescents with ABI. In this proof-of-concept, observational study 45 patients aged 8 up to 30 years old were included, with 35 (78%) of them longer than 2 years after onset of their condition and 22 (49%) having TBI.
The 12-week intervention consisted of the assignment of three computer games to every patient, matching the individual and self-chosen treatment goals and taking into account the individual's motor and cognitive limitations and interest. After 2 instruction sessions, patients were encouraged to play games for at least 20 minutes per day and/or 2 hours per week. Trained therapists/teachers had weekly contact with the participants by e-mail or telephone. Assessments were done at baseline and after 12 weeks. It was found that physical activity, the speed of information processing, attention, response inhibition, and parent-perceived Quality of life (QoL) were improved directly after the intervention. Two-thirds of the patients

reported an improvement of their individualized treatment goal. No differences over time were seen for patient-perceived QoL and participation in leisure activities.

GENERAL DISCUSSION

ABI in children and youth in the Netherlands: occurrence, terminology and hospital policy

The results of the studies included in this thesis suggest that the incidence of ABI in children and youth is considerable. Moreover, it was found that relatively many have long-term health problems, including limitations in psychosocial functioning, participation and QoL and that the impact on their families is substantial. These findings underscore the need for an increasing awareness for the impact of paediatric ABI. According to the 'Good Practice Recommendations' of the International Paediatric Brain Injury Society[3] "there must be an increased awareness and recognition that ABI can affect young people throughout the course of their development up into adulthood, provoking changing and emerging needs". Moreover, these recommendations stated that "there must be further education of medical practitioners and teachers, especially regarding cognitive and behavioural consequences which can be overlooked in comparison to those affecting motor function".[3] Ralph[4] systematically reviewed literature on knowledge, (mis)conceptions and attitudes towards survivors of ABI. She concluded that, despite the observation that public knowledge increased over the last 25 years, there are a number of common misconceptions (such as a complete recovery can be achieved by all survivors and (speed of) recovery is dependent on patients' effort), that may result in decreased acceptance and support by professionals as well as family and friends.

ABI is defined as 'any post-neonatal damage to the brain, due to an external cause (traumatic brain injury, TBI) or internal cause (non-traumatic brain injury, NTBI)'. However, there is confusion about the terminology: a) ABI is used for a wide variety of diagnoses and as an umbrella concept for an even larger variety of possible consequences.[5] It has therefore been been suggested to use "ABI" for the overall diagnosis and reaching consensus about a more specific definition of TBI[6] and NTBI[7], using the International Classification of Diseases (version 10) codes[8]. In addition, consequences of ABI should probably not be called ABI but should be defined more specifically, according to the International Classification of Functioning, Disability and Health for Children and Youth (ICF-CY). For example: a 17 year old adolescent who had a subarachnoid hemorrhage (ICD 60.3) at the age of 12 years old, may have visual field loss (ICF b2101), impaired quality of vision (b2102), problems with reading (d166) and failed to pass an entry assessment in higher professional education (d8250).

Regarding the classification of severity of paediatric ABI, different systems are used for TBI and NTBI. Severity of paediatric TBI is usually determined by the GCS score, but the literature on its predictive properties for the outcome is conflicting[9]. Classification of the

severity of paediatric NTBI is usually done by the mRS, although this measure has not been validated for all potential causes of NTBI.[10]

The differences in the classification systems for severity within and among TBI and NTBI suggest that conclusions on the relationship between severity and long-term outcomes should be interpreted with caution, which applies to the results presented in this thesis as well. It remains to be established to what extent a combination of an appropriate set of neuroimaging (MRI) and age-specific clinical and neuropsychological assessments may improve the early classification of severity of children and youth with ABI. Neuropsychological testing in the initial post-injury phase appears to have additional predictive value with respect to the short and long-term outcome, enabling prompt treatment, follow-up or referral if needed, thereby compounding long-term disabilities and reducing health care costs.[11] A risk index including the health status of the child and family before ABI has also been suggested as a means to structure an efficient triage and follow-up, especially for the mild TBI group.[12]

Concerning the *registration* of the diagnosis ABI and its severity, our study with medical records of patients with a hospital based diagnosis of ABI found that registration was often incomplete (e.g. registration of Glasgow Coma Score, modified Rankin Scale, suspicion physical abuse). This observation underlines the need for consistent implementation of guidelines, e.g. 'Care of patients with mild traumatic head/brain injury'.[10]
Furthermore, variation in the clinical management (admission or not, length of stay, usage of CT or MRI, and the scheduling of follow-up) of patients with TBI presenting at one hospital was found in our study as well. A larger, prospective study is however required to draw more valid conclusions on potential variability in hospital policies after TBI.

Prevention is probably the best intervention for ABI. We found that the causes of TBI differ strikingly among age categories, a finding that can be used when considering preventive measures, like appealing and age-specific education for children, youth, parents and caregivers, health care providers and teachers. This education could e.g. include signs and symptoms of abusive head injury or the risk of TBI as a direct (drugs affecting brain functions) or indirect (causing accidents and abuse) result of alcohol and drug abuse. Regarding TBI, the relatively high percentage of accidents in and around the house in the 0-4 years group and the relatively high percentage of (suspicion of) physical abuse in the age group 15-24 years, as seen in the study presented in Chapter 2 and 3, was notable. Raising awareness in children and youth, parents and caretakers of risk factors for TBI is warranted, such as adequate fixation in a car seat, chair or stroller or helmets for children in traffic. Vulnerability of the developing brain should be addressed in primary and secondary education. Tailor-made education and support could also be an effective intervention to decrease the burden of NTBI.[14]

Participation of children and youth with ABI and families

Children and youth with ABI are at risk for participation problems, both in the stages of recovery as well as later on. A 'double hazard' effect has been reported, where social disadvantage with severe injury leads to poorest long-term outcome.[15] Participation is the most relevant outcome of recovery and main goal of rehabilitation. However, a better general understanding and improvements of assessment and treatment are required to decrease the impact of paediatric ABI on participation of youth and their families.

Recommendations based on this thesis are: a) implement the ICF-model to improve comprehension of participation (problems) after paediatric ABI; b) measure and monitor participation after paediatric TBI and NTBI and c) develop and evaluate trajectories optimising participation.

a) The ICF-CY model[16] is a suitable model to demonstrate the complex, interrelated and dynamic nature of participation of children and youth in relation to the specific nature and impact of paediatric ABI. Figure 1 shows a proposal for a 'participation model', based on the results of the systematic review on determinants of participation in ABI (Chapter 4).

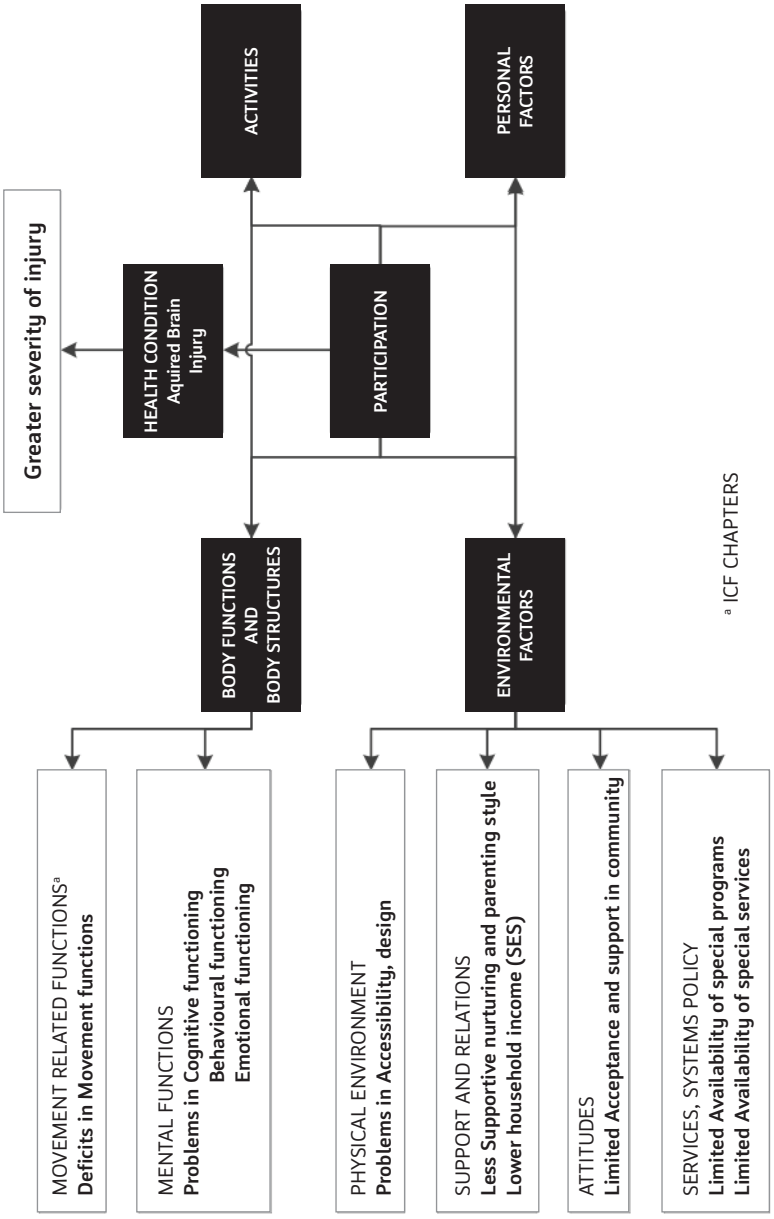
The proposed model could probably be discussed and refined in focus groups with patients with ABI, parents and professional experts. This should preferably be done separately for TBI and NTBI, in order to improve understanding of participation in these two different forms of ABI.

b) Improvement of the assessment and monitoring of participation (in patients) and of QoL (in patients and parents) in paediatric TBI and NTBI is needed. This may on the one hand increase the understanding of (factors associated with) participation outcomes in paediatric ABI, and on the other hand enable the evaluation of interventions such as rehabilitation programmes. The CASP-DLV and CASE-DLV are promising instruments in this respect, which could probably be combined with the PedsQL HR QL (Chapter 5), in particular since all three are recommended as outcome measure in ABI.[17]

Ideally, participation is monitored at different time points and on the long-term (Chapter 4). Families with a child with ABI should be monitored regarding the impact of the condition as well, for which aim the PedsQL Family Impact Measure (FIM) seems a suitable instrument (chapter 6). The assessment of the health-related quality of life of parents, included in the FIM, is indicative for their healthcare needs. Implementation of these instruments in Dutch outpatient clinics for rehabilitation care should be considered using the results of follow-up studies to determine which groups 'at risk' for a worse outcome should be monitored on a structural basis.

c) Development and evaluation of interventions specifically for paediatric ABI. The literature on participation in ABI suggests that interventions should be: early, targeted and tailor-made[18], connected and well-coordinated[19], highly specialised[2] and with longitudinal follow-up through developmental stages.[20]

Figure 1 Participation model



Based on: World Health Organization, 2007

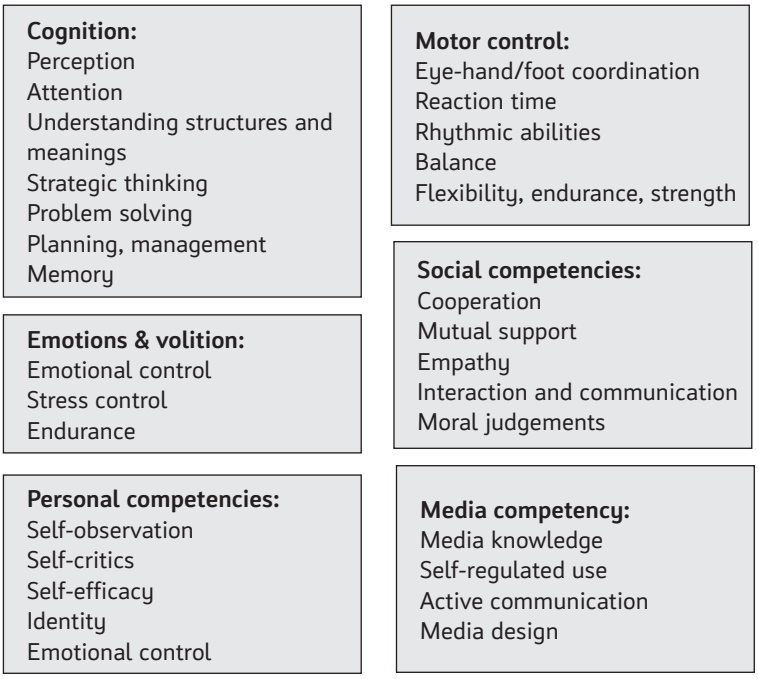
Hospital, rehabilitation and chronic care should be connected, with overlapping programmes and anticipating planning. Currently, parents express dissatisfaction with inadequate service provision, lack of information about ABI and its consequences, waiting times, not knowing where to find appropriate services, and services not adapting to the needs of child and family changing over time.[19] Family factors (functioning, socioeconomic status (SES), family burden) and other aspects of the child's environment (peers, school/work, leisure time) are related to participation and should be addressed in comprehensive rehabilitation programmes. In the recent literature on paediatric ABI and in daily practice there are a number of examples of how the abovementioned recommendations can be put into practice. These examples currently constitute 'practice based evidence' and need to be further evaluated regarding their effectiveness.

1. The Dutch language version of the Brain Stars programme[21] concerned the development of a tailor-made, comprehensive, practical manual for parents and teachers, aiming to educate parents and professionals about pediatric ABI and enhance better understanding and management of its consequences. It includes background information about ABI, related to child and adolescent development, recommended interventions, and worksheets.
2. Hersenletsel en Jeugd (HeJ),[22] a Dutch national project that started in 2011, aims to outline targets for improving paediatric ABI-pathways. HeJ is organized in 6 task forces (acute care-rehabilitation-chronic care-school and work-development - and research), and has resulted in a school protocol for students with ABI, a tool box for family support and enhanced collaboration in research projects.[22] HeJ organises an annual, national symposium for professionals in health care and primary and secondary education to share and disseminate knowledge and special services, programmes and policy.
3. Recently an app, the 'Activiteitenweger' has been developed, to monitor daily activities of people with restrictions in their daily activities as a result of pain and/or fatigue, a common complaint after ABI.[23]
4. An example of evidence based practice is the family-supported rehabilitation of children with TBI in Sarah network of rehabilitation hospitals in Brazil,[24] incorporating the parents, teachers and family into the rehabilitation process.
5. The project 'Friends4Friends' aims to enhance participation of children and adolescents with ABI in recreational time, by means of buddy support by students.[25] Apart form the support of individual patients, it aims to increase awareness and competences of students in professional education. A similar effect is pursued in the project 'Brains4U", embedding managers in a vocational rehabilitation intervention aiming to get paid employment in adolescents and young adults with ABI.[26] 'See potential, not potential problems' is a stimulating slogan in both projects, influencing environmental factors with respect to participation of people with ABI.

The potential of gaming to improve physical, cognitive and social functioning of children and youth with ABI

This thesis evaluated the potential benefits of gaming in patients with ABI (Chapter 7). By providing enhanced environmental stimulation and augmented information to the user, gaming may increase motivation, adherence, and duration or intensity of exercises and the practices of skills. Gaming offers unique opportunities in the rehabilitation of children and youth with ABI as it meets several requirements posed by theories of learning[27] and neurorehabilitation:[28] training is most effective when it is active, intensive, experiential, tailor-made, situated, functional, problem-based and provides immediate feedback. Therefore, it is more and more acknowledged that gaming is a useful addition to or alternative for conventional therapeutic interventions aiming to improve learning and performance of motor skills (e.g. gait, static and dynamic balance, bimanual training, movement and energy expenditure), cognitive skills (e.g. attention, response inhibition, visual-perceptual and speed of processing, communication) and socio-emotional skills (e.g. playfulness, motor confidence, self-control and management) in the rehabilitation of children, youth and adults with ABI.[29,30] Gaming could have an effect competencies as shown in Figure 2.[31]

Figure 2 Competencies potentially enhanced by playing digital games



From: Wiemeyer & Kliem[30]

Game technology rapidly improves, with the international organisation 'Games for Health'[32] aiming to bring healthcare together with the serious gaming industry. The 'off-the shelf' console Nintendo Wii (first release November 2006) enables the performance of whole-body movements and social play. The Microsoft Kinect (first release November 2010, last upgrade in January 2014) enables gaming without the need to physically touch a game controller, it can detect a person's location in 3-D (three-dimensional) space and it can register full-body, head to feet motions more precise. Recent improvements in applications are the development of specific rehabilitation games,[33] the adaptation of consoles in order to adjust to specific motor or cognitive demands, to better focus on quality of movement and influence therapeutically relevant aspects of motion[34] and the design of a personalized virtual environment, e.g. walking at home or biking in a patient's own neighbourhood.[35]
Apart from gaming, the use of other technological applications in rehabilitation increases, examples being telemedicine, the use of computer tablets and smartphones. In this rapidly developing area of practice stakeholders (patients, health care providers, developers, manufacturers, researchers) should probably share their needs and knowledge and collaborate in consortia for the further development, evaluation and implementation of technology in rehabilitation. Collaborations between rehabilitation centres, hospital departments of rehabilitation, (technical) universities and universities of applied sciences and industries is needed to further develop and test gaming and ICT application. The Dutch taskforce 'E-rehabilitation' initiated such a process in Dutch rehabilitation and organized a national symposium in March 2014.

Directions for future research

Registration of data on the incidence and causes of TBI and NTBI in children and youth in a national database is necessary. Only by means of a standardized registry, including all relevant clinical data, based on ICF-categories (Chapter 2,3), and using the electronic registration systems of Dutch hospitals and rehabilitation centres, valid conclusions on the occurrence and outcomes of TBI and NTBI can be made. Further research should preferably be done in patients with mild TBI, by far the largest group of new patients. About 10-20% of youth with mild TBI report significant, ongoing problems impacting adversely participation at home, school or work and in other social relations and interactions. Therefore, research should focus on determinants of outcome and the effectiveness of early interventions in this specific group. Thereby, prediction models for decision making in the (post) acute phase and follow-up can be made, including the appropriate triage to select patient at risk, effecting health status as well as health care and societal costs.
Further research is also suggested with respect to participation of children and youth with ABI, to decrease the current knowledge gap regarding participation outcomes. This will facilitate the evaluation of rehabilitation programmes with respect to participation outcome, including

generalisability in everyday life. A prerequisite for such research is that consensus regarding the definition of participation, the usage of recommended, explicit participation outcome measures and the set of potential determinants to be analysed is attained. Moreover, studies should include large cohorts of children and youth in all age groups and different causes and severity of the injury and should employ a methodologically sound analysis (Chapter 4).

It is further recommended to follow existing guidelines regarding the development of participation measures, pertaining to: a) Definition of the aim of measuring: description (e.g. activities, time, patterns, limitations), discrimination (differences between groups) or evaluation (change over time);[35] c) Employing mixed methods research, combining quantitative and qualitative data;[2] d) Inclusion of environmental factors, differentiation regarding in sub domains with specific aspects of participation (e.g. social interactions at work) and differentiation regarding age (e.g. play of younger children).[36]

Regarding the treatment of patients with ABI, larger, controlled studies on the effect of computer games on motor, cognitive and socio-emotional functions are required. Concerning the measurement of their effectiveness, assessments should preferably include imaging techniques such as functional Magnetic Resonance Imaging (fMRI) and be focused on the transfer of trained tasks to activities in daily life, participation and quality of life.

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9

Chapter 9
Samenvatting
(Summary in Dutch)

Niet-aangeboren hersenletsel (NAH) bij kinderen en jongeren is een belangrijk probleem voor de volksgezondheid[1] door de vaak blijvende gevolgen voor het kind en gezin. De literatuur suggereert dat NAH bij kinderen en jongeren en de lange termijn gevolgen hiervan, in het bijzonder met betrekking tot participatie, voor kind en gezin onderschat en slecht begrepen worden en in onderzoek onderbelicht blijven.[2]
Dit proefschrift heeft daarom als doel om:

a. De incidentie en de oorzaken van NAH bij kinderen en jongeren te bepalen;
b. Een systematisch literatuuronderzoek te verrichten naar factoren die samenhangen met participatie van kinderen en jongeren met NAH;
c. Een doelgroepspecifieke participatievragenlijst te vertalen in de Nederlandse taal en de psychometrische kwaliteiten daarvan te onderzoeken;
d. De impact van NAH bij kinderen en jongeren op het gezin te bepalen;
e. Het mogelijke effect van serious gaming op het fysieke, cognitieve en sociaal functioneren van kinderen en jongeren met NAH te exploreren.

Dit proefschrift bevat een viertal onderzoeken, waarin de bovengenoemde vijf onderzoeksvragen beantwoord worden. De belangrijkste bevindingen (hoofdstukken 2-7) worden hier kort samengevat.
Hoofdstuk 2 van dit proefschrift beschrijft een retrospectief, multicenter cohortonderzoek naar de incidentie en de oorzaken van NAH, zowel met een traumatische (Traumatic Brain Injury, TBI) als met een niet-traumatische oorzaak (Non-Traumatic Brain Injury, NTBI), bij kinderen en jongeren in Nederland.
Hiertoe werden patiënten in de leeftijd van 1 maand-24 jaar, met een diagnose NAH gesteld in 2007, 2008 of 2009, geselecteerd uit de registraties van drie ziekenhuizen in Den Haag en Rotterdam. In totaal werden 1892 patiënten geïncludeerd, 1476 van hen met TBI en 416 met NTBI. De classificatie van ernst van het letsel was bij het merendeel 'licht', namelijk bij 82,4% in de TBI-groep en bij 81,4% in de NTBI-groep. Op basis van deze cijfers en een inschatting van het aantal inwoners in de verzorgingsgebieden van de ziekenhuizen werd de relatieve incidentie van TBI en NTBI per 100 000 inwoners geëxtrapoleerd: voor licht-matig-ernstig TBI was deze respectievelijk 271.2-15.4-2.3 (in de leeftijdsgroep 0-14 jaar) en 261.6-27.0-7.9 (in de leeftijdsgroep 15-24 jaar) en voor licht-matig-ernstig NTBI was deze respectievelijk 95.7-11.8-1.3 (in de leeftijdsgroep 0-14 jaar) en 73.8-6.1-1.6 (in de leeftijdsgroep 15-24 jaar).
TBI was in de leeftijdsgroep van 0-4 jaar vooral het gevolg van ongevallen in of rond het huis, terwijl in de groepen van 5-14 en 15-24 jaar verkeersongevallen de meest voorkomende oorzaak vormden. Meningitis en encefalitis waren relatief vaak de oorzaak van NTBI in de groep van 0-4 jaar, terwijl hersentumoren een belangrijke oorzaak in de 5-14 jaar groep bleken te zijn. Een beroerte kwam in de drie leeftijdsgroepen vergelijkbaar vaak voor.

Gebaseerd op ditzelfde retrospectieve cohortonderzoek, gaat *hoofdstuk 3* dieper in op de klinische kenmerken van het Rotterdamse cohort patiënten, in de leeftijd van 1 maand-24 jaar oud, die met traumatisch hersenletsel (TBI) in 2007 en 2008 in één ziekenhuis werden aangemeld. Ook wordt het gevolgde ziekenhuisbeleid voor deze groep beschreven. 472 patiënten voldeden aan de inclusiecriteria, de ernst van het letsel was licht bij 342 (72,5%), matig bij 50 (10,6%) en ernstig bij 80 (16,9%) van deze patiënten. Van deze groep werden 343 (72,7%) kinderen en jongeren opgenomen in het ziekenhuis. Na ernstig traumatisch hersenletsel was de gemiddelde opnameduur 7 dagen, na matig traumatisch hersenletsel 3 dagen en na licht traumatisch hersenletsel 1 dag. Bij patiënten met ernstige TBI traden aanzienlijk veel complicaties op. Vierentwintig patiënten overleden, 22 van hen na een ernstig TBI. Bij 398 patiënten (84,3%) werd CT-scan of MRI-scan van de hersenen uitgevoerd, bij 78 van hen (60%) werden geen bijzonderheden gevonden en volgde ontslag naar huis. Gegevens over de lange termijn gevolgen waren in het algemeen incompleet geregistreerd in de medische dossiers. Bij 107 (23%) van de patiënten met TBI werd na ontslag geen vervolgafspraak gemaakt. Patiënten met ernstige TBI werden significant vaker doorverwezen naar een poliklinisch behandeltraject, met name naar revalidatie dagbehandeling, dan patienten met matige of lichte TBI. Bijna 17% van de groep met licht traumatisch hersenletsel vertoonde bij follow-up cognitieve beperkingen, terwijl bij 42% van hen geen afwijkingen op de hersenen CT-scan bij opname werden gevonden Deze bevinding ondersteunt de discussie over de noodzaak van een zorgvuldige en efficiënte follow-up van kinderen en jongeren met een traumatisch hersenletsel, ook als dit licht is.

Hoofdstuk 4 presenteert de resultaten van een systematische review naar de determinanten van participatie bij kinderen en jongeren met NAH: er waren 5 studies werden geselecteerd die een expliciete participatie uitkomstmaat rapporteerden en voldeden aan de overige inclusiecriteria. Deze 5 studies toonden aan dat, 12-84 maanden na het ontstaan van het NAH, 25-80% van de kinderen en jongeren werden beperkt in tenminste 1 participatiedomein (thuis, op school of in de samenleving), terwijl de participatieproblemen nauwelijks afnamen in de tijd. Factoren die het meest consistent geassocieerd waren met participatie (gedefinieerd als een vergelijkbaar resultaat in minstens 2 studies en geen tegenstrijdige resultaten tussen studies) waren: een grotere ernst van het letsel, sensorische problemen (ICF component lichaamsfuncties en structuur); problemen in motorische functies, cognitief of gedragsmatig functioneren (component lichaamsfuncties en structuur), aanwezigheid van problemen in de toegankelijkheid en het ontwerp van de fysieke omgeving en het ontbreken van sociale acceptatie en steun. Als consistent positief geassocieerd met participatie scoorden een hogere sociale economische status en de beschikbaarheid van speciale diensten en programma's (component externe factoren).

Hoofdstuk 5 behandelt het proces van vertaling, aanpassing en validering van de Child and Family Follow-up Survey (CFFS-DLV, ofwel Dutch Language Version, de Nederlandstalige versie), ontwikkeld als vragenlijst voor ouders om de lange termijngevolgen van NAH voor het participeren van kinderen en jongeren te meten en monitoren. De CFFS bestaat uit 3 subschalen: de Child and Adolescent Scale of Participation (CASP-DLV) brengt de actuele participatie van het kind thuis, op school en in de samenleving in kaart. De Child and Adolescent Factors Inventory (CAFI-DLV) inventariseert de kindkenmerken en de Child and Adolescent Scale of Environment (CASE-DLV) de omgevingsfactoren die het participeren beïnvloeden. De psychometrische eigenschappen van de CFFS-DLV werden bepaald bij 147 patiënten met NAH, twee tot drie jaar na het ontstaan van het letsel. Het merendeel van de patienten in dit cohort werd geïncludeerd in het retrospectief cohortonderzoek (hoofdstuk 2 en 3). Alle 3 de subschalen van de CFFS-DLV bleken betrouwbaar en valide instrumenten om de lange termijn gevolgen van NAH op het participeren van kinderen en jongeren te meten. De interne consistentie van de 3 subschalen was hoog, waarbij de Cronbach's alpha 0.95 voor de CASP-DLV, 0.89 voor de CAFI-DLV en 0.83 voor de CASE-DLV was. Bovendien vonden wij significante correlaties tussen de subschalen CASP-DLV, CAFI-DLV en CASE-DLV onderling, waardoor de toegevoegde waarde van de CFFS-DLV in het bepalen en begrijpen van verbanden tussen de mate van participatie (CASP-DLV) en door ouders ervaren beperkingen van het kind (CAFI-DLV) en in de omgeving (CASE-DLV) wordt onderstreept.

In *hoofdstuk 6* wordt de impact van het NAH op het gezin beschreven, ook op basis van het retrospectief cohortonderzoek (hoofdstuk 2 en 3). Daarnaast wordt onderzocht welke factoren de impact op het gezin vooral bepalen. Twee tot drie jaar na het ontstaan van het NAH werd de gezinsimpact gemeten met de Pediatric Quality of Life Inventory Family Impact Module (PedsQL™FIM-DLV). In de gezinnen van 108 kinderen, waarvan een relatief hoog percentage licht TBI had, bleek de gemeten impact op het gezin aanzienlijk. Multivariate analyse toonde aan dat de ernst (matig-ernstig>mild) en de oorzaak (NTBI>TBI) van het letsel geassocieerd waren met een grotere gezinsimpact (totaalscore op de PedsQL™FIM), evenals de aanwezigheid van gezondheidsproblemen voordat het letsel ontstond. De PedsQL Family Impact Module blijkt een adequaat meetinstrument te zijn om gezinsimpact en gezinsfunctioneren na NAH van een kind of jongere te meten.

Hoofdstuk 7 evalueert de mogelijke effecten van gamen met de Nintendo Wii™, een console met vooral motorische games, op fysiek, cognitief en sociaal functioneren van kinderen en jongeren met NAH. Aan deze 'proof-of-concept' observationele studie namen 45 kinderen deel, allen jongeren en jongvolwassenen met NAH, in de leeftijd van 8 tot 30 jaar. Het merendeel van de groep was niet meer in revalidatiebehandeling, bij 35 (78%) van hen ontstond het letsel langer dan 2 jaar voor de interventie. Bij 22 (49%) was er sprake

van traumatisch hersenletsel (TBI). De interventie die 12 weken duurde, bestond uit het spelen van drie games, waarvan de keuze op de patient werd toegesneden, passend bij diens zelfgekozen behandeldoelen en rekening houdend met de individuele motorische en cognitieve beperkingen en belangstelling. Na 2 instructiesessies (door therapeuten en docenten) werden de patienten aangemoedigd om tenminste 20 minuten per dag of 2 uur per week te gamen. Hierbij werden ze ondersteund door therapeuten, die een wekelijks contact per e-mail of telefoon onderhielden. Aan het eind van interventie was er in vergelijking met voor de behandeling een toename van de hoeveelheid fysieke activiteit, verbetering van de snelheid van informatieverwerking, aandachtfuncties, responsinhibitie en (door ouders) waargenomen kwaliteit van leven gezien. Twee derde van de patiënten meldden een verbetering op hun zelfbepaalde doelen. Er werd geen verbetering gezien van de door de patienten zelf ervaren kwaliteit van leven en vrijetijdsbesteding.

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CV

Dankwoord

Curriculum vitae

Arend de Kloet werd geboren op 7 juni 1955 te Den Haag. Na het behalen van het HAVO-diploma (Groen van Prinsterercollege) en het afronden van de opleiding aan de Pedagogische Academie (de Visser Smits) in Den Haag, startte hij als leerkracht aan de 'de Schakel', een school voor voortgezet speciaal onderwijs aan kinderen met leer- en opvoedingsproblemen (LOM) te Rijswijk. Na het behalen van het doctoraal examen pedagogiek, met als specialisatie orthopedagogiek, aan de RU Leiden in 1985, volgde de overstap naar Sophia Revalidatie. Hier behandelde hij kinderen en jongeren met verschillende revalidatiediagnoses, begeleidde gezinnen en leerkrachten, evenals kinderen van volwassen revalidanten en behaalde de registraties behandeling Nederlandse vereniging van pedagogen en onderwijskundigen (NVO (1994), gezondheidszorg-psycholoog (1998), Eye Movement Desensitization and Reprocessing (EMDR)-therapeut (2006), supervisor behandeling (1999), algemene beroepsbekwaamheid (2001) en orthopedagoog generalist (2001).

Vanaf 1995 werd klinisch werk verweven met participatie in regionale en landelijke werkgroepen op het gebied van onderwijs, jeugdzorg en gezondheidszorg, zoals de stuurgroep Developmental Coordination Disorder (DCD), de werkgroep Ontwikkeling en Onderzoek van Hersenletsel en Jeugd (HeJ) en de regionale werkgroep NAH Haaglanden.

Per 1 september 2008 werd hij benoemd tot bijzonder lector Revalidatie aan De Haagse Hogeschool, met 'Participatie: meedoen met beperkingen' als kennisdomein.

In september 2011 startte hij met het promotietraject, met als basis het onderzoek 'NAH bij kinderen en jongeren: een onderbelicht probleem', dat startte in oktober 2009 en werd gefinancierd door het Revalidatiefonds (Grant 2010/0029), het Johanna Kinderfonds en de Stichting Rotterdams Kinderrevalidatie Fonds Adriaanstichting (Grant 2009/0075-1403).

Arend is getrouwd met Caroline van den Berg, samen genieten zij van Liselotte (1987), Jurgen (1990) en Laurens (1993) als hun kinderen.

Portfolio

Publicaties in peer reviewed internationale tijdschriften

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Onderzoek

2012-2014 Friens4Friends (HBO Steunfonds, grantnr, 20120426), ontwikkelingsgericht en implementatie onderzoek naar 'buddy ondersteuning' voor kinderen en jongeren met NAH; i.s.m. I. Verhoeven, M. Langendonk.

2011-2014 Spelenderwijs (Nuts Ohra, grantnr. 1202-006 en Revalidatiefonds, grantnr. 2011184), onderzoek naar het effect van cognitieve games bij volwassenen met cognitieve problemen na CVA; i.s.m. M. Wentink, M. Berger, I. Verhoeven, M. Jacobs, K. van Haastrecht, J. Meesters, T. Vliet Vlieland.

2011-2012 TherapWii (Zon Mw, grantnr. 335020020), ontwikkelingsgericht en implementatie onderzoek naar een digitaal instructieprogramma 'gamen met de Wii' voor professionals; i.s.m. K. van Stein Callenfels, M. Berger, I. Verhoeven, J.Jansen, K. van Haastrecht.

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