Executive outcome in pediatric mild TBI as measured by parent rating of daily functioning

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Master's Thesis in Psychology

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Subject: Psychology	
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Abstract: The existing literature on neurobehavioral outcomes after a pediatric mild traumatic brain injury (mTBI) is conflicting, despite of its common occurrence. The present study examined parent-rated executive functioning (EF) of children with mTBI at 1–3 months after injury compared to peers with an orthopedic injury (OI). The study sample consisted of 51 children, 37 with mTBI and 14 with OI, aged 7–16 years at the time of the injury. Parent version of Behavior Rating Inventory of Executive Function (BRIEF) questionnaire (Gioia, Isquith, Guy & Kenworthy, 2000) was used to measure the EF of the children. Additionally, a Full-Scale Intelligence Quotient (FSIQ) score was calculated for all children. Three different summative scores were retrieved from the BRIEF questionnaire and set as dependant variables in the following analysis. A multivariate analysis of covariance was conducted to analyse the effects of injury type (TBI, orthopedic) on parent-rated EF skills when controlled for FSIQ. The results showed no significant group differences on EF skills. A subsequent case-by-case analysis showed that despite of the lack of a group difference, a higher percentage of the children in mTBI group compared to the OI group had clinically significant BRIEF scores (T score ≥ 65) on all three of the composite scores. The results from this study do not support the hypothesis that children with mTBI as a group would show more EF problems in their everyday life at 1–3 months after injury compared to their peers with orthopedic injury. Nevertheless, a percentage-wise larger sub-group of children with mTBI than with OI showed clinically elevated BRIEF scores, suggesting that some children with mTBI develop executive problems. This highlights the need for careful individual assessment, as a small percentage of the mTBI children could be in need for support.	
Keywords: Mild traumatic brain injury, mTBI, pediatric, BRIEF, executive function, parent rating	
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ÅBO AKADEMI – FAKULTETEN FÖR HUMANIORA, PSYKOLOGI OCH TEOLOGI

Ämne: Psykologi	
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Titel: Lindrig traumatisk hjärnskada och föräldraskattade exekutiva funktioner hos barn och unga	
Handledare: Mari Saarinen och Mira Karrasch	
Abstrakt: Forskningsresultaten på de kognitiva följderna av barns lindriga traumatiska hjärnskador (THS) är motstridiga, trots att traumatiska hjärnskador hör till de mest förekommande pediatriska skadorna. Denna studie granskade exekutiva funktioner (EF) hos barn med lindrig hjärnskada, jämfört med barn med ortopedisk skada (OS). Studiens sampel bestod av sammanlagt 51 barn i åldern 7–16, varav 37 barn hade en lindrig THS och 14 en OS. Föräldraskattade EF mättes med hjälp av föräldraformuläret the Behavior Rating Inventory of Executive Function (BRIEF). Information om barnets allmänna kognitiva förmåga erhölls med hjälp av Wechsler Intelligence scale for children (WISC IV; Wechsler, 2010). En multivariat kovariansanalys gjordes för att mäta effekterna av skada (lindrig traumatisk hjärnskada, ortopedisk skada) på tre olika summapoäng från BRIEF, medan effekterna av intelligensnivån kontrollerades för. Resultaten visade inga signifikanta gruppskillnader mellan barn med lindrig THS och OI på EF. Efter dessa icke-signifikanta resultat utfördes en mera deskriptiv jämförelse på de barn som överskred poänggränsen för klinisk signifikans på de tre BRIEF skalorna ($T \geq 65$). Denna jämförelse visade att en procentuellt större andel barn visade kliniskt signifikanta poäng i THS gruppen jämfört med OS gruppen. Resultaten ur denna studie stöder inte hypotesen att barn med en lindrig traumatisk hjärnskada skulle visa mera problem med EF jämfört med barn som fått en ortopedisk skada. Däremot kan en andel av barnen som fått en lindrig traumatisk hjärnskada utveckla problem med EF. Dessa fynd betonar behovet av en noggrann individuell bedömning för att identifiera de barn som kan vara i behov av fortsatt stöd efter en lindrig THS.	
Nyckelord: lindrig traumatisk hjärnskada, pediatrisk, exekutiva funktioner, BRIEF, föräldraskattning	
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INTRODUCTION

Traumatic brain injury (TBI) accounts for a significant portion of injury-related disability and death worldwide in children and adolescents (Anderson & Catroppa, 2006; Sariaslan, Sharp, D'Onofrio, Larsson & Fazel, 2016; Sesma et al., 2008). As a large portion (70-90%) of all treated brain injuries are mild, mild traumatic brain injuries (mTBI) are amongst the most frequently occurring pediatric injuries overall (Cassidy et al., 2004, Maas et al., 2017; McKinlay, 2009).

Neurobehavioral outcomes after TBI in children are not yet fully understood, and several controversies still exist. When looking at all levels of severity of pediatric TBI studies have found reduced performance in different domains including language, memory, psychosocial functioning and motor, perceptual and spatial skills (Babikian & Asarnow, 2009; Levin & Hanten, 2005). This wide variety of symptoms is characteristic of TBI, reflecting the existing heterogeneity of the injuries (Babikian & Asarnow, 2009). The outcome following TBI is moderated by the different pathophysiological changes in the brain following the injury, and still, when changes in the brain are detected, the cognitive impairments following these changes are not consistent or manifested (McInnes, Friesen, MacKenzie, Westwood & Boe, 2017). Many of these moderating factors are problematic not only for pediatric patients but for patients of all ages, but in pediatric TBI the fact that the brain is still developing makes age a particularly important moderating factor.

The real impact of a TBI may sometimes become noticeable later in the development process when expectations increase and it becomes more difficult for the child to meet environmental, behavioral, academic, emotional, and social demands (Gioia & Isquith, 2004; Slomine et al., 2002). A child can appear to have no symptoms after the injury but later on suffer from significant impairments (Hudspeth & Pribram, 1990; Yeates & Taylor, 2005). Different cognitive skills develop throughout childhood and since the child's nervous systems is still under development, a TBI in childhood can disrupt or delay functions that are still not established (Nadebaum, Anderson & Catroppa, 2007). The findings from a study by Hessen et al. (2007) indicate that children with mild TBI may be more sensitive to development of prolonged mild neuropsychological dysfunction compared to adults with similar head injuries.

Studies have also struggled with measuring the extent of the impairments. A majority of symptoms disappear within the first weeks after the injury and it is not always clear whether the deficits will be permanent; therefore, the timepoint of the assessment plays a significant role (Babikian & Asarnow, 2009). These factors inevitably lead to the wide range of cognitive and behavioral symptoms reported in different studies.

It has been established that the majority of children with moderate to severe TBI experience some cognitive and/or behavioral impairments, albeit perhaps temporarily. However, knowledge on the cognitive symptoms following mTBI is more limited, despite its common occurrence (Anderson & Catroppa, 2006). The existing literature shows little evidence for long-term group-level impairments in mTBI detected with standardized cognitive testing (Kirkwood et al., 2008). On the other hand, when comparing subjective symptom reports from children with mTBI to peers with other types of injuries, children with mTBI report more frequent and severe problems (Yeates & Taylor, 2005). The complications are more often noticed at the individual level, when some of the children with an injury initially classified as mild might develop long-term problems requiring support by health professionals (Cassidy et al., 2004; Hessen, Nestvold & Anderson, 2007; Taylor et al., 2010). This is what more recent studies have been trying to further explore, and findings indicate that 5–20 % of children with mTBI do experience prolonged or persistent symptoms (McInnes, Friesen, MacKenzie, Westwood & Boe, 2017). These estimates have since been criticised by Iverson, Karr, Gardner, Silverberg and Terry (2019) for being based on flawed methodology.

There is a lack of established recommendations for postacute rehabilitation and long-term interventions, for children suffering TBI, as most of the standards applied in the pediatric field are still borrowed from approaches used in the adult field (Anderson & Catroppa, 2006). Scandinavian guidelines were produced by Astrand, Rosenlund and Undén (2016) in an attempt to find more evidence-based ways of treating pediatric populations after a mild or moderate head trauma. They emphasize that new research is needed due to rapid development within the field of pediatric neurotrauma, and state that the poor quality of evidence gathered thus far is a limitation to their study. This motivates further research on mTBI symptomatologies with pediatric samples. It is well established that the age at injury plays a role in the recovery from TBI, emphasizing the need for more age-sensitive studies and clinical guidelines (Sariaslan, Sharp, D'Onofrio, Larsson & Fazel, 2016).

Defining Mild Traumatic Brain Injury

A traumatic brain injury is defined as a disruption of brain structure or function, or other evidence of pathology in brain, caused by an external force (Menon, Schwab, Wright & Maas, 2010). There is, however, no consensus on the definition of mild TBI: the diagnostic criteria may vary across studies and there are several terms used synonymously, complicating the comparisons between different studies. This shortcoming is not only limited to the pediatric field, but a problem with mTBI research in general. The term concussion has sometimes confusingly been used in the literature synonymously with mTBI (Karr, Areshenkoff & Garcia-Barrera, 2014), yet some argue that a concussions should be considered only as a subtype of mTBI, and that the terms should therefore not be used interchangeably (Hamilton & Keller, 2010).

Pertab, James and Bigler (2009) addressed the opposing conclusions in the literature of mTBI by re-analysis of existing meta-analyses, including studies with samples of all ages. Since the diagnostic criterion for mTBI varied across different studies, they tried to explore diagnostic criteria as a moderating variable for mTBI outcome. However, they found too much heterogeneity across the studies to make a detailed exploration of the effects and could therefore not draw any conclusions on this issue. Of the 25 studies included, three studies failed to define the criteria they had used, several studies had vague criteria, and some had atypically low inclusion criteria for mTBI (two studies defined mTBI as a blow to the head that caused the person to stop what they are doing). Seven studies met the American Congress criteria and one study used the American Academy of Neurology criteria. This highlights the need for more consistency in defining mTBI and is another explaining factor to the conflicting results of the research on mTBI (McKinlay, 2009; Cassidy et al., 2004).

The criteria for mild TBI in adults in Finland include a Glasgow Coma Scale (GCS) of 13-15 points (½ hour after injury and after that for the whole follow-up period). Furthermore, one of the following needs to be present: not more than 30 minutes of loss of consciousness (LOC), not more than 24 hours of post-traumatic amnesia (PTA), minor intracranial findings in head CT or MRI (such as a small amount of blood in subarachnoid space or a small subarachnoid haematoma; Brain Injuries: Current Care Guidelines, 2017). These were the guidelines used when defining mTBI in this study.

Assessment of Executive Functions

Disruption of executive functions (EF) is one of the most pervasive consequences of TBI (Nadebaum, Anderson & Catroppa, 2007). EF include a variety of related abilities that are collected under the same construct, although they can also be seen as distinct functions. EFs are involved in all purposeful activity or supervisory functions and are fundamental for directing, coordinating and regulation of cognitive and behavioral action (Gioia, Isquith, Kenworthy & Barton, 2002; Gioia, Kenworthy, Isquith, 2010) Impairments in EF can lead to difficulties with sustained attention, inhibition, problem solving, self-regulation, shifting, strategic planning, initiation and organization (Jacobson, Williford & Pianta, 2011; Slomine et al., 2002). These problems may occur in the absence of other cognitive deficits (Gioia & Isquith, 2004).

Broadly speaking, EF skills can be measured with different types of approaches: either by measuring performance in cognitive tests or by using rating scales. Standardized cognitive measures or performance-based tests focus on more controlled performance and distinct skills, conducted in distraction-free environments. Rating scales provide information on symptoms in relation to everyday functioning. Ratings can be conducted by the person affected or a person close to the affected (a so-called proxy-rating). It has been argued that ratings provide more ecologically valid information (Gioia & Isquith, 2004).

One problem is that the results from these two measurement types do not always correlate, leading to a gap between standardized cognitive testing and experienced/observed symptoms (Gioia & Isquith, 2004; Gioia, Kenworthy, Isquith, 2010, McKinley, 2009; Yeates & Taylor, 2005). EF deficits can be difficult to identify using single tests and standardized neuropsychological measures, as the problems they cause are often complex and depend on environmental factors (Slomine et al., 2002). When the testing situation is a standardized environment, with little distractions and very clear instructions, it is more likely that the person can perform better and cope with possible deficits (Silver, 2000; Slomine et al., 2002). Both of these measures and approaches are needed, since different deficits can be detected with neuropsychological assessments and others with monitoring the person in real life settings, still both contribute to understanding the deficits.

The Behavior Rating Inventory of Executive Function (BRIEF) questionnaire aims to capture behavioral expressions of executive dysfunction as they are presented in everyday functioning (Gioia & Isquith, 2004). The scores are measured across eight subscales further comprised into two composites: The Behavioral Regulation Index (BRI) and the Metacognition Index (MI). These two composites are further summarized to a General Executive Composite Score (GEC) that incorporates all of the scales. The BRIEF questionnaire allows teachers or parents to assess the child's EF during daily activities, and includes aspects of the child’s metacognitive, behavioral, and emotional abilities. BRIEF has been validated as a tool for assessing executive functions in typically developing and children and in different clinical groups, including TBI (Gioia & Isquith, 2004). The majority of studies using BRIEF have been conducted with moderate-to-severe TBI, and its implementation for mTBI cases needs therefore to be examined further (Maillard-Wermelinger et al., 2009).

Previous studies

To the best of the author’s knowledge there are only three studies examining EF in pediatric mTBI and controls using a parent completed BRIEF. In a study by Maillard-Wermelinger et al. (2009) test performance on Cambridge Neuropsychological Testing Automated Battery (CANTAB) and parent completed BRIEF in 8–15 year old children with mTBI (n = 186) was compared to that of children with mild orthopedic injuries (n = 99). The parents completed the BRIEF at 3- and 12-months post-injury follow-up assessments. The results indicated that there were no significant executive dysfunction problems in mTBI patients one year after injury as measured with CANTAB and BRIEF. However, there was a significant difference on one of the subscales in BRIEF, indicating that the mTBI children had more problems with organizing of materials compared to their peers in the orthopedic injuries group.

In the second study by Sesma et al. (2008) caregivers of 330 children aged from 5–15 with mild-to-severe traumatic brain injury, 185 of which had an injury classified as mild, were asked to participate in a study measuring EF with BRIEF. The study design also included a control group of children with orthopedic fractures (n = 103). Caregivers had to complete BRIEF questionnaires within 3 weeks of hospitalization (baseline), 3 and 12 months after injury. The results showed that all severities of TBI (mild, moderate, and severe) differed on all three of the BRIEF composite scores (GEC, BRI and MI), indicating more executive dysfunction at the 12 months post injury measurement in the TBI group when compared to the fracture control group. There was also a significant difference between GEC scores at 3 months after injury between the mTBI and the fracture group.

In the third study Nadebaum, Anderson and Catroppa (2007) they only included children aged 7 or younger at the time of injury. The results of this study are not therefore directly comparable to the two previous BREIF studies. In this study performances on different EF measures were compared between children with a TBI (mild, moderate and severe) and an uninjured comparison group. No significant differences in BRIEF scores were found between mild and moderate TBI patients when compared to controls, and the EF performance overall on different measures was considered to be within normal expectations for these patient groups.

The conflicting findings of these three studies highlight the unclarity surrounding the neuropsychological sequelae of pediatric mTBI, regarding the perceived EF difficulties measured with BRIEF. In sum, two of the previously presented studies did not find any significant group differences between children with mTBI and OI, on any of the three BRIEF composite scores. One study did find results indicating more EF dysfunction in the pediatric mTBI group compared to the orthopedic fracture group, when measuring both 3 and 12 months after injury.

Aim of the Study

The aim of the present study was to evaluate the neuropsychological functioning of children and adolescents with mTBI at 1 to 3 months after injury, and to determine whether their executive functioning as measured with the parent-completed BRIEF questionnaire differs from that of a control group consisting of children and adolescents with orthopedic injury. Since the evidence of experienced symptoms after a mTBI is leaning to a direction that the deficits are not detected at group level with cognitive testing (Babikian & Asarnow, 2009; Kirkwood et al., 2008), the present study focused on parent evaluations of perceived problems. Based on previous research, parents to children with mTBI report more preserved problems than parents of control children (Yeates & Taylor, 2005), motivating the investigation of the effects of mTBI on EF in less controlled situations. The hypothesis was that children with mTBI show more executive problems in everyday life when compared to peers with orthopedic injury, and when controlling for the overall intellectual performance level.

METHOD

The data for the present study was collected and retrieved as a part of a larger pediatric research project initiated in 2018 (Cognitive and psychosocial recovery in pediatric mild traumatic brain injury, Saarinen et al.). The aim of the research project is to retrospectively study children and adolescents with mTBI in terms of neuropsychological sequelae 1 to 3 months after injury and determine whether their neurocognitive functioning differs from their peers. Additionally, long-term consequences of the injury will be studied in terms of neuropsychological outcome, health-related quality of life, and family functioning. The present study used parts of this projects data to have measures on gender, age, overall intellectual performance level (FSIQ) and EFs as measured by parent ratings.

Participants

During years 2010–2016 there were 694 patients treated at the Turku University Central Hospital with a first hospital treated head trauma and linked CT and/or MRI examination, who had sufficient information in the patient records about the initial management, and were under 16 years of age at the time of injury. Of these cases, 178 patients (27 %) had undergone a neuropsychological evaluation between 1–3 months after the injury, according to the hospital's pediatric TBI protocol. Children whose TBI was classified as mild were included in the study group. Eligibility criteria for mTBI included the Glasgow Coma Score (GCS) of no less than 13/15, loss of consciousness (LOC) of less than 30 minutes, and post traumatic amnesia (PTA) for no more than 24 hours. In cases where the GCS score was not entered in the patient database, it was estimated retrospectively based on the documented clinical information. Only patients aged 7–16 years at the time of injury (n = 120) were included in this study, in order to make the study group more homogenous and the neuropsychological results more comparable within the study population. The inclusion and exclusion process is presented in *Figure 1*.

The control group consisted of children aged 7–16 treated in the Turku University Hospital due to an orthopedic injury (OI). The data gathering process was put on hold due to the outbreak of the coronavirus pandemic, before the aimed sample size of 30 children was reached. The final control group sample only included 14 children with OI who were successfully recruited and tested before the outbreak of the pandemic in Spring 2020. The total sample consisted of 51 children, of whom 45.1 % were girls and 54.9 % boys. The demographics and background characteristics of the sample is shown in Table 1.

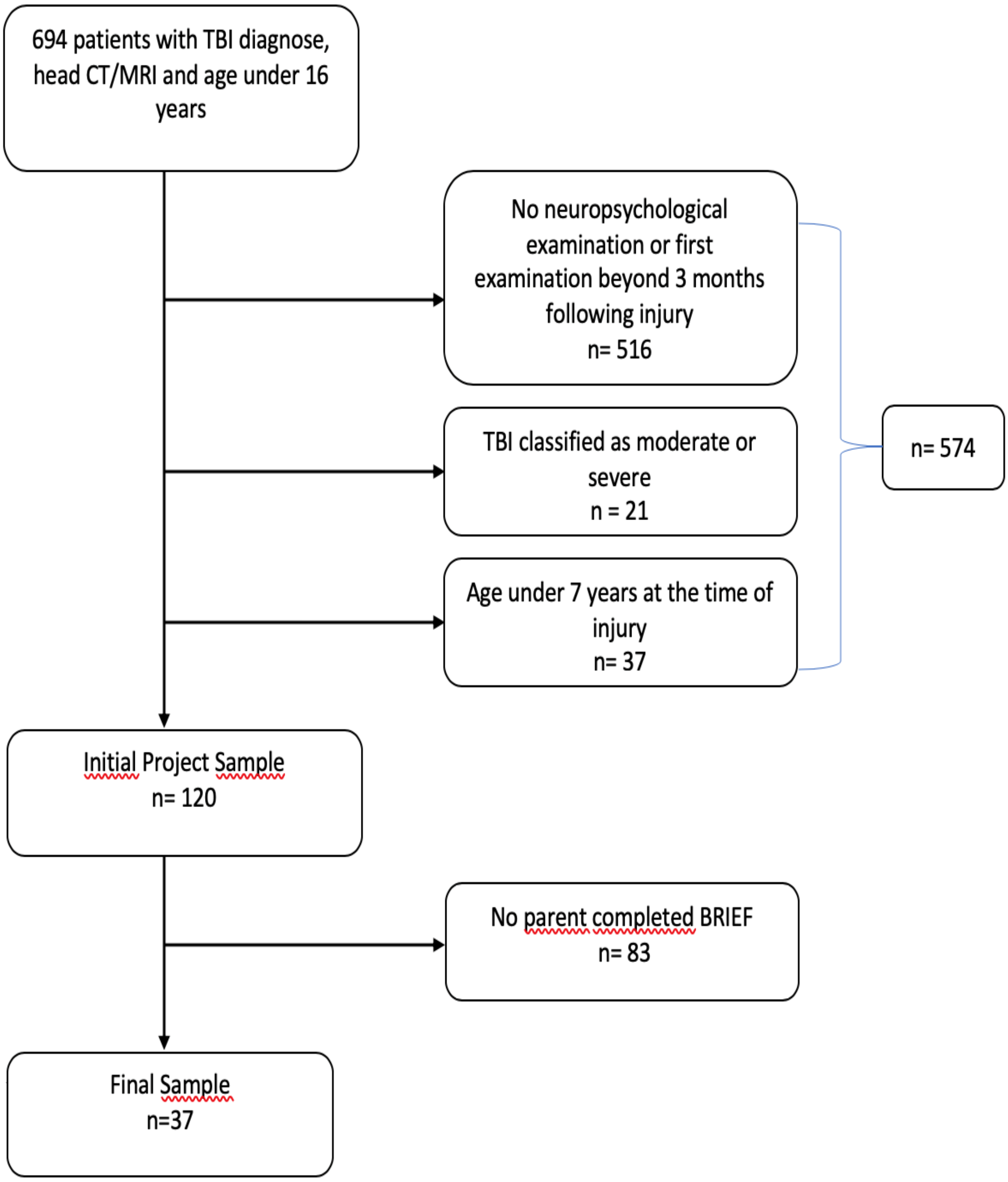

Figure 1. Flow Chart of the Inclusion and Exclusion Process of mTBI Patient

Table 1. *Demographics and Background Characteristics of the Sample (N=51)*

		Total (%)	MTBI (n=37)	OI (n=14)
Gender	*Girls*	23 (45.1)	16	7
	Boys	28 (54.9)	21	7
Age	*Mean (SD)*	12.1 (2.4)	12.0 (2.5)	12.2 (2.5)
	Min	7.3	7.3	7.4
	Max	15.5	15.2	15.5
FSIQ	*Mean (SD)*	99.5 (16.7)	96.2 (17.2)	108.4 (11.4)
	Min	62.0	62.0	89.0
	Max	139.0	139.0	129.0

Procedure

The data collection took place in two stages. The pediatric mTBI cases were consecutive patients treated at the Turku University Hospital during 2010–2016. Clinical and demographic data, as well as data from neuropsychological assessments and MRI scans, were retrospectively collected from the patient records. As the data collection was retrospective, the specific tests and questionnaires conducted to the patients in the clinical setting varied. For the present study only cases having the following information were included: TBI classified as mild, age between 7–16 at the time of the injury, and a neuropsychological evaluation at 1–3 months after the injury including a parent completed BRIEF questionnaire.

The second phase of the data collection concerned the controls who were children treated at the Turku University Hospital pediatric surgery unit due to an orthopedic injury. The OI group was chosen as a control group because they shared the experience of a physical injury and the potential effects of a hospital stay. Patients aged 7–16 years at the time of injury were invited to participate. A neuropsychological test battery, consisting of tests similar to the ones conducted with the mTBI cases, was scheduled and conducted 1–3 months after the orthopedic injury. Prior to participation informed parental and child consent were obtained. At the assessment, clinical and demographic data were collected with a clinical interview conducted to the child and parent. After this interview the child completed neuropsychological testing while the parent completed BRIEF questionnaire. Access to medical records was requested to rule out prior head injuries treated at the hospital. Approval for the study was granted by the Ethics Committee of The Hospital District of Southwest Finland and The Turku University Hospital.

Measures

Demographic data and injury characteristics were retrieved from the medical records. Injury symptoms at 1–3 months following mTBI were retrospectively gathered from the patient records and were based on the clinical interview carried out as a part of the neuropsychological evaluation. Requesting this information from the child or the parents is a part of the pediatric TBI protocol of the hospital. The Full-Scale Intelligence Quotient score (FSIQ) of the Wechsler Intelligence scale for children (WISC IV), was used to define children's overall neurocognitive ability at 1–3 months following mTBI. For the OI group demographic data were retrieved from medical records and from a clinical interview, also including questions about injury symptoms 1–3 months following injury and done in the same manner during the neuropsychological evaluation as with the mTBI patients. During the neuropsychological evaluation five subtests (Similarities, Vocabulary, Block Design, Digit Span, and Coding) from the Wechsler Intelligence scale for children were administered to be able to calculate The Full-Scale Intelligence Quotient score. Additional neuropsychological tests conducted to the OI group are not further described here, since measures used in this present study are only limited to age-adjusted versions of Wechsler Intelligence Scales and Behavior Rating Inventory of Executive Functioning (Gioia, Isquith, Guy & Kenworthy, 2000).

BRIEF is a standardized 86-item parental and teacher rating scale developed to assess discrete behaviors that reflect executive function problems in everyday surroundings (Gioia, Isquith, Guy & Kenworthy, 2000). The child’s EF difficulties are measured across eight subscales (Inhibit, Shift, Emotional Control, Initiate, Working Memory, Plan/Organize, Organization of Materials and Monitor). The overall executive functioning is summed to a General Executive Composite Score (GEC) and can further be divided into two composites. These two composites are the Behavioral Regulation Index (BRI), which measures how the child regulates his or her behavior, and the Metacognition Index (MI), that measures the child's problem solving, planning and organizational skills. All scores are expressed in *T* scores (M = 50, SD = 10), with higher scores indicating more deficits. *T* scores at or above 65 (1.5 SD over the mean) can be considered as having a clinical significance (Gioia, Isquith, Guy & Kenworthy, 2000). The parent version of the BRIEF, which is used in this study, has good reliability. Test-retest correlations are range between .76 and .85, and internal consistencies from .80 to .97, in the normative sample of Gioia et al. (2000). The Official Finnish translation of the BRIEF was used in this study.

Data Analysis

The statistical analyses were performed using IBM SPSS Statistics 25.0 for Macintosh (IBM Corp., 2017). Before determining the covariates bivariate correlations (Pearson) were conducted separately for age, gender and FSIQ on all three dependent variables (BRIEF-GEC, BRIEF-BRI, and BRIEF-MI). Furthermore, two tests were performed to explore if the groups would differ on age or gender, and if this would need to be considered when interpreting the results. An independent samples t-test was performed to determine if the groups differed on age and a contingency table analysis (Chi-Square test) of gender and injury type (TBI, orthopedic) was performed to determine if the groups differed on the distribution of gender.

For the main analysis, a multivariate analysis of covariance (MANCOVA) was conducted to explore the possible differences between the groups (mTBI vs. OI) on three dependent variables. The dependent variables were the three measures retrieved from BRIEF: GEC, BRI, and MI. FSIQ was entered as a covariate, after ensuring that it did not correlate with the independent variable.

RESULTS

Regarding the analyses of the three possible covariates age, gender, and FSIQ bivariate correlations (Pearson) were conducted. No statistically significant correlations were found between age and BRIEF scores (BRIEF-GEC, $r(49) = .11$, $p = .424$; BRIEF-BRI, $r(49) = .06$ $p = .677$; BRIEF-MI, $r(49) = .12$, $p = .411$). All bivariate correlations between gender and BRIEF scores were also non-significant (BRIEF-GEC, $r(49) = .17$, $p = .249$; BRIEF-BRI, $r(49) = .23$, $p = .107$; BRIEF-MI, $r(49) = .14$, $p = .342$). Since adding weak covariates is not recommended, age and gender were left out from the analyses. The results showed, however, that FSIQ was associated with performances on 2 out of 3 BRIEF test scores (BRIEF-GEC, $r(49) = -.30$, $p = .035$; BRIEF-BRI, $r(49) = -.18$, $p = .218$; BRIEF-MI, $r(49) = -.32$, $p =.021$). FSIQ was thus entered as the only covariate.

Analyses done to explore the impact of background factors on the results in the main analysis revealed non-significant results. No difference in age between the mTBI and OI group was observed $t(1,49) = .250$, $p = .619$. The results from the contingency table analysis (Chi-Square test) also revealed non-significant results $\chi^2\,(1) = .187$, $p = .665$, indicating that age and gender were equally distributed between the mTBI and OI group. There was therefore no indication that differences on these background factors would have impacted the results.

Prior to running the multivariate analysis of covariance (MANCOVA) the assumptions for this analysis were analysed. Firstly, the distributions of normality and outliers for all three of the dependant variables and the covariate were analysed. Normality was tested with normality tests, Q-Q plots, and normality histograms. The analyses showed that the covariate (FSIQ) was normally distributed ($p = .200$), when for all three dependent variables Kolmogorov-Smirnov and Shapiro-Wilk were significant ($p < .05$). A visual interpretation of the histograms showed that they were slightly positively skewed, indicating non-normal distributions for the dependent variables. When SPSS do not acquire a robust test for MANCOVA (Field, 2013), the results must be interpreted in the light of the violation of this assumption.

The analysis of outliers showed two outliers in the mTBI group and one in the OI group. The decision was made not to exclude any of these, since BRIEF as a variable provide both a floor and ceiling value, and the outliers are therefore likely to reflect the studied phenomenon, and its wide spread of outcomes. Furthermore, linearity between the dependant variables and the covariate were analysed with a matrix scatter and showed that the sample meets this assumption. Lastly, the conditions of both homogeneity of variance and homogeneity of regression slopes were analysed. When the results on these tests showed non-significant values for each dependent variable and for the interaction of the independent variable and FSIQ ($p > .05$), the assumption of these conditions were met and hence FSIQ could be added as a covariate.

For the main analysis a multivariate analysis of covariance was conducted with all three composites from BRIEF as dependent variables and FSIQ as covariate. The analysis revealed no statistically significant main effect of injury (mTBI, OI) on BRIEF scores $F(3,46) = .792$, $p = .505$, *partial* $\eta^2 = .049$. Mean scores of the two groups on the BRIEF variables are shown in *Figure 2.*

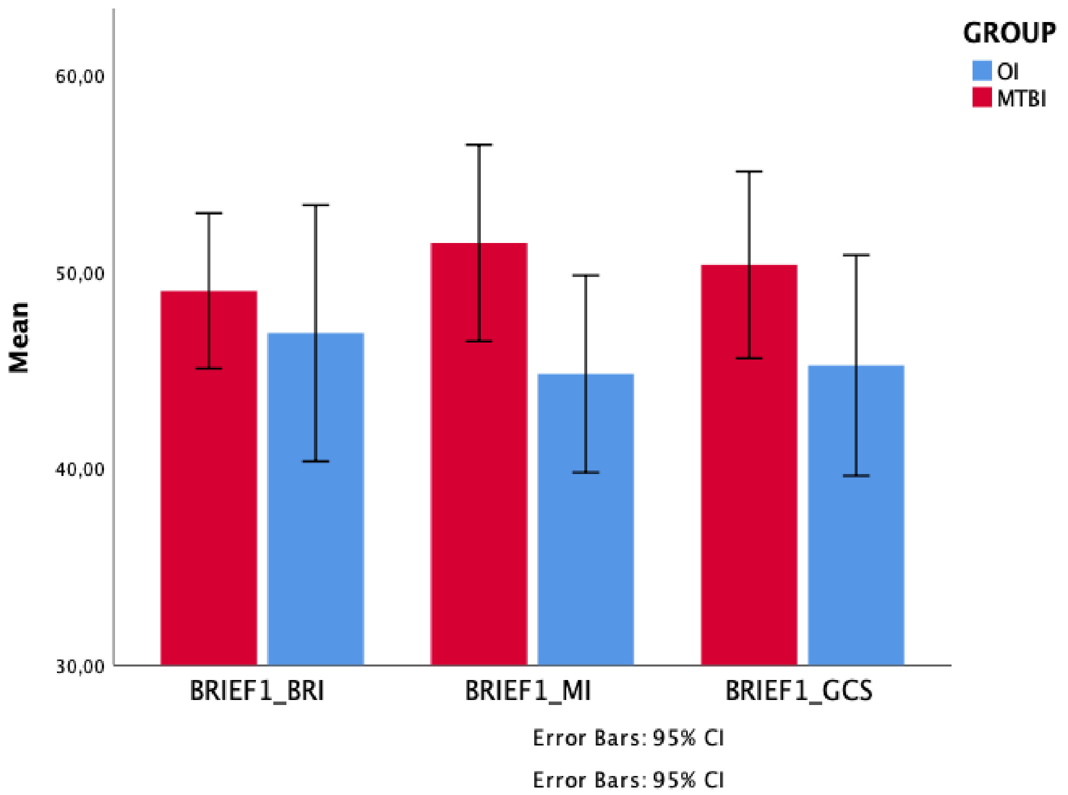

Figure 2. Clustered Bar Diagram of the BRIEF Mean T Scores

Follow-up analyses

Correlative analyses. After the non-significant findings, a correlation analysis was conducted to explore possible differences in rating styles between the mTBI and the OI group. When using proxy-ratings it is of interest to examine if there are differences in rating styles or standards between groups. A hypothesis for this follow-up analysis was that if the assumed association between lower FSIQ and higher BRIEF scores (i.e. that lower overall intellectual functioning would be associated with more executive problems) would differ between groups, this could explain some of the unexpected results. Bivariate correlations (Pearson) were conducted between FSIQ and the General Executive Composite Score (GEC), separately for both of the groups (mTBI and OI). For the mTBI group there was a trend-level negative correlation between FSIQ and BRIEF (lower FSIQ associated with higher BRIEF scores, and higher BRIEF scores indicating more executive problems) $r(35)=-.30$, $p = .069$. For the OI group a corresponding negative correlation was not found $r(12)=.028$, $p = .924$. This difference indicates that the parents of the children in the two groups may indeed have used somewhat different rating styles.

Case-by-case analyses. Since the literature suggest that recovery after a mTBI seems to be good at group level, and the complications are more often noticed at the individual level, the non-significant results further motivated to a more case-by-case way of analysing the data. When looking at the cut of scores for the three BRIEF composites and comparing the clinically significant cases (T score ≥ 65) for both groups, differences were detected between the groups. For the BRIEF General Executive Composite Score there were 19 % (7/37) in the mTBI group and 7 % (1/14) in the OI group exceeding the line of clinical significance. For the Behavioral Regulation Index, the percentages were 11 % (4/37) for mTBI and 7 % (1/14) for OI. For the Metacognition Index, the percentages were 16 % (6/37) for mTBI and 0 % for OI. This is graphically presented as a dot plot of BRIEF scores by group (mTBI, OI) separately for the three different BRIEF scores in *Figure 3, 4* and *5.* A statistical analysis (two-sided Fisher's exact test) was conducted to explore differences between children showing clinical scores on any of the BRIEF scales between the mTBI group (21.6 %) and the OI group (7.14 %). Results from this test showed a difference that was non-significant ($p = .414$).

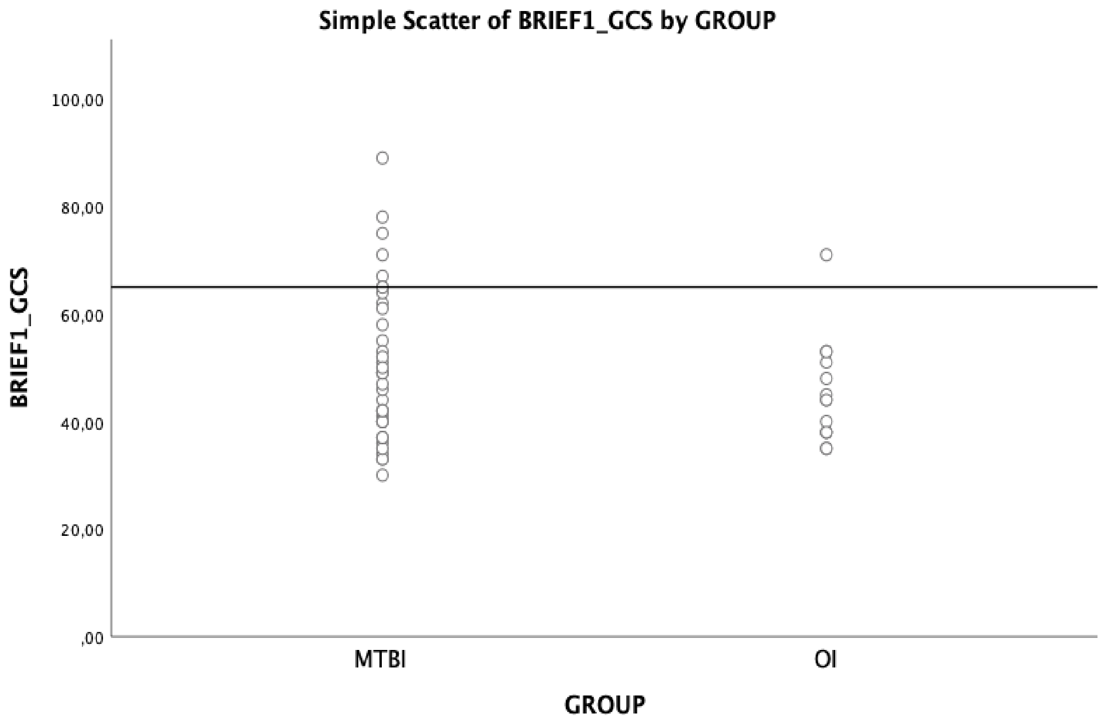

Figure 3. BRIEF General Executive Composite Score T-scores for mTBI (n = 37) and OI (n = 14)

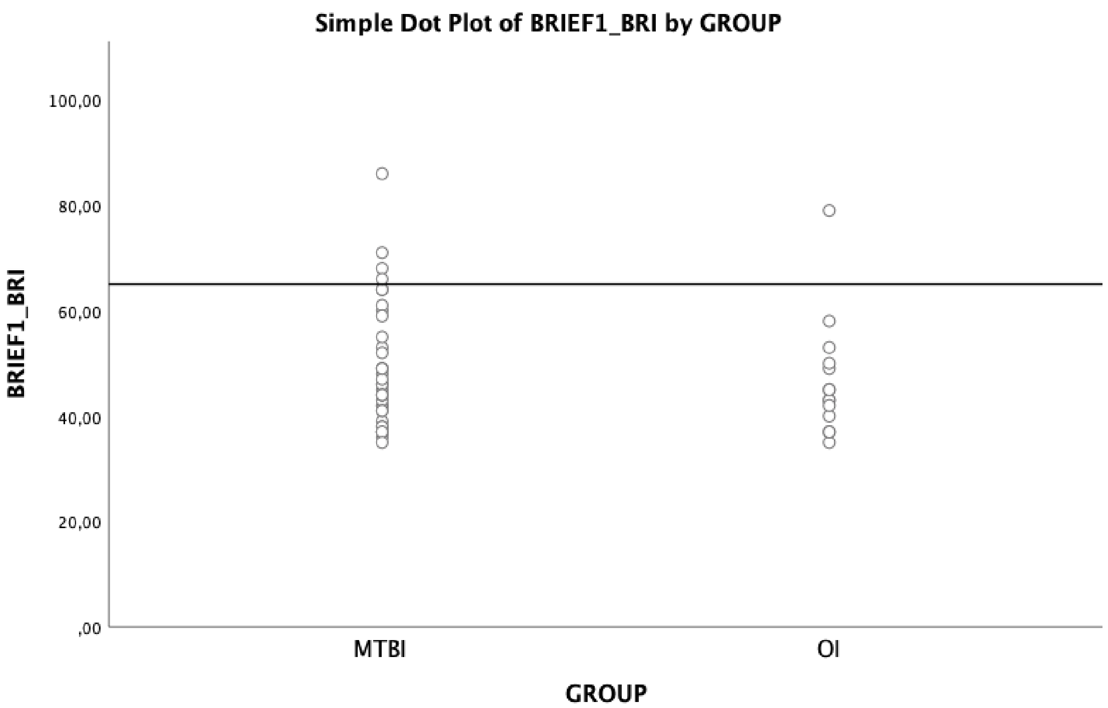

Figure 4. BRIEF Behavioral Regulation Index T-scores for mTBI (n = 37) and OI (n = 14)

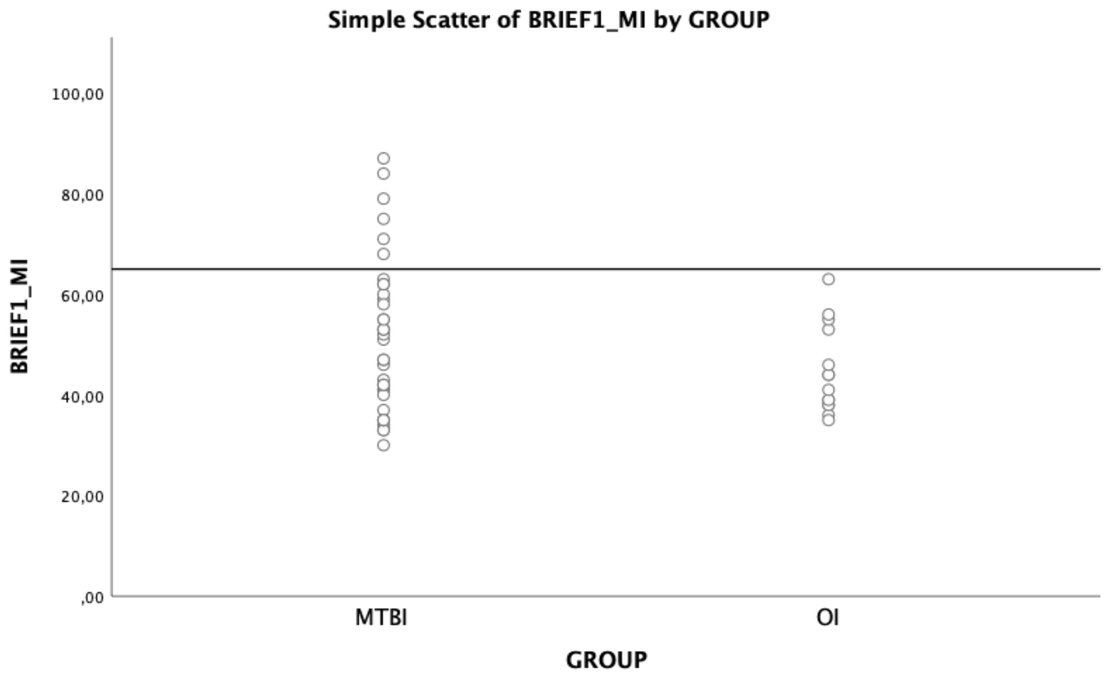

Figure 5. BRIEF Metacognition Index T-scores for mTBI (n = 37) and OI (n = 14)

DISCUSSION

The aim of this study was to explore parent-rated executive functioning in pediatric mTBI. This was important considering the relatively frequent occurrence of pediatric mTBIs and concerning the conflicting research findings on the neurobehavioral outcomes of pediatric mTBI. Since previous research indicates that there is a gap between results from standardized cognitive testing and rating scales, the focus of this study was limited to the less controlled executive functions, presented in real life settings as rated by parents. A hypothesis was that there would be experienced difficulties with EFs, although these might not be detected with standardized cognitive testing. In sum, the aim of the study was to investigate effects of mTBI on parent rated EFs (measured with three different scales from the BRIEF questionnaire), using a OI group as a control group. The hypothesis of this study was that children with mTBI would have higher scores (indicating more problems), on the parent-completed BRIEF questionnaire when compared to peers with orthopedic injury.

Main Findings and Interpretation

The results showed that there were no differences in parent-rated EFs between the mTBI and the OI group, as measured 1–3 moths following injury. In other words, the results did not support the study hypothesis.

When comparing findings from this study to the previous studies having included a control group (Maillard-Wermelinger et al., 2009; Nadebaum et al., 2007; Sesma et al., 2008) it is worth noting that all studies had different inclusion criteria for age at injury. The present study included children over 7 years, the study by by Sesma et al. (2008) that detected differences in EF between groups (mTBI vs. orthopedic fracture) included slightly younger children (5 years and above). In the study by Maillard-Wermelinger et al. (2009) only children aged over 8 years were included, and no significant group differences were found. On the contrary, in the study by Nadebaum et al. (2007), only children aged 7 and under, at the time of injury were included, and this study did not find any significant results. The differing ages of the participants might account for some of the discrepancy, since the age of injury is a moderating factor. It is however not unequivocal when looking at these three studies that age at injury would be the only explaining factor. In addition to age at injury factors known to moderate the outcome are e.g. pre-morbid learning capacity, psychologic functioning, family relationships, as well as organic changes in brain function (Yeats & Taylor, 2005).

Another potential explanation for the results in the present study could be the measurement tool. Parent-version of the BRIEF parent rating questionnaire was used to measure EF. BRIEF is a validated tool for assessing pediatric TBI, although previous research using BRIEF have more often used the tool for detecting EF problems after a moderate-to-severe TBI, and studies on its sensitivity for mTBI is lacking (Maillard-Wermelinger et al., 2009; Nadebaum, Anderson, & Catroppa, 2007). However, studies have found deficits in children with mTBI (Sesma et al., 2008). Thus, the unexpected findings are not likely to reflect limited test validity and any further conclusions on whether or not BRIEF is the right tool for assessing EF functions following a mTBI, cannot be drawn, nor was it an aim of the present study. Since previous studies have found support both for and against detecting differences with BRIEF (Maillard-Wermelinger et al., 2009; Nadebaum, Anderson & Catroppa, 2007; Sesma et al., 2008), more research is needed before determining whether or not BRIEF is the best tool for assessing EFs in mTBI patients.

The correlation analysis conducted as a result of unexpected findings from the main analysis, showed that the OI group differed from the mTBI group in terms of correlation between FSIQ and BRIEF scores. The aim of this additional analysis was to explore the possible differences in the parent rating-trends between the mTBI and the OI group. In the mTBI group the expected negative correlation between general intellectual functioning and executive problems was observed, albeit non-significant, whereas the corresponding correlation in the orthopedic control group was close to zero. This indicated that the parents in the two groups may have been using differing rating styles. Since the correlation analyses were non-significant, the grounds for any further speculations on whether this might have contributed to the non-significant findings are weak.

As the groups (the OI group in particular) were small, a follow-up analysis on the proportion of participants in the respective groups rising above the cut-off for clinically significant impairment was conducted. In fact, a larger percentage of the mTBI group had clinically significant BRIEF scores on all three of the composites, compared to the OI group. The largest difference was found for the Metacognition Index where all of the children in the OI group had scores under the cut-off ($T \geq 65$), compared to the mTBI group where six of the children had scores indicating clinical significance. This could support the previous studies findings that Metacognition Index is the most sensitive of the composites when assessing mild–sever TBI (Gioia, Kenworthy, Isquith, 2010). The findings from this descriptive analysis could support the hypothesis that there are children with mTBI who do experience EF problems, but that these deficits are not detected with studies focusing on group differences. These findings highlight the need for recognizing the child's individual functioning and deficits and the need for careful individual assessment, rather than focusing on EF problems detected at a group level.

Limitations of the Study

The results from this study should be interpreted in the context of certain limitations. The small sample size, due to the outbreak of the coronavirus pandemic before the aimed sample size of the OI group was reached, is a limitation that may have impacted the results from this study in different ways. The small sample size leads to the problem that individuals selected to the OI group determines the outcome of the study to a higher degree than with a bigger sample, and the small sample is not necessarily representative of the whole population. Secondly, the small sample size lead to a weak statistical power, which reduces the chance of finding a true effect. Since there is known to be heterogeneity within the population of mTBI patients, big enough samples would be to prefer when intending to find between-group differences. Thirdly, the small sample size lead in this study to a violation of the assumption of normally distributed data for the dependant variables.

There is also a need to consider the impact of the EF rating instrument used in this study. EF was in this study assessed with the parent-rating scale from BRIEF, and a limitation is that these results are not comparable with results from BRIEF teacher-rating forms, self-ratings or standardized cognitive testing. These assessment methods are not equivalent, and the results must always be interpreted with a limitation to the method used. EF comprehend a much larger selection of functions than presented in this study, and this needs to be considered when interpreting the results. When interpreting findings from studies using questionnaires relying on subjective impressions, the different rating styles cannot be controlled for. All parents completing the questionnaire have their own interpretations of the questions, and this can lead to differing standards.

Finally, a limitation of this study is the study design used. When using a retrospective data collection with the mTBI patients and only one timepoint of assessment for the control group, causality cannot be determined. Findings from this study could reflect pre-injury background characteristics that existed between groups, that this study design was not able to control for. In order to make any causal interpretations a longitudinal study design would be necessary.

Conclusions

The findings from this study did not support the hypothesis that there would be any EF deficits following a mTBI, when measured with a parent rating questionnaire. The descriptive information on the scores, however, indicate that larger number of the mTBI children, compared to the OI children, have clinically significant BRIEF scores. This indicates that a part of the mTBI group children experience EF problems in their everyday life according to their parents. These findings only motivate to replicate a similar study with bigger sample sizes, since it was a considerable limitation of this present study. Future studies should continue exploring the consequences of pediatric mTBI, since more research is needed on the consequences of mTBI in order to make future clinical guidelines with access to more evidence-based research findings.

Swedish Summary

Lindrig traumatisk hjärnskada och föräldraskattade exekutiva funktioner hos barn och unga

Traumatiska hjärnskador (THS) står för en stor del av de olyckor som orsakar funktionsnedsättningar och dödsfall (Anderson & Catroppa, 2006; Sariaslan, Sharp, D'Onofrio, Larsson & Fazel, 2016; Sesma et al., 2008). Då en stor del (70–90 %) av alla traumatiska hjärnskador är lindriga, hör lindriga traumatiska hjärnskador till de mest förekommande pediatriska skadorna (Cassidy et al., 2004; Maas et al., 2017; McKinlay, 2009).

Forskningsresultaten på de kognitiva följderna av en THS hos barn och unga är motstridiga. En THS kan leda till att funktioner som bland annat språk, minne, psykosociala funktioner, motorik, perceptuella och spatiala förmågor drabbas som en följd av skadan (Babikian & Asarnow, 2009; Levin & Hanten, 2005). Denna breda variation av möjliga kliniska konsekvenser, även vid skador som klassificerats till samma allvarlighetsgrad, beror på förekomsten av många olika modererande faktorer. Faktorer som konstaterats ha en inverkan på utvecklingen av symtom är bland annat barnets inlärningsförmåga, psykologisk funktionsförmåga, familjerelationer och olika organiska förändringar i hjärnan (Yeats & Taylor, 2005). Då man studerar pediatrisk THS är det även viktigt att ta hänsyn till att barnets hjärna ännu är under utveckling och tidpunkten för skadan kan ha en avgörande betydelse för de kliniska konsekvenserna (Gioia & Isquith, 2004; Slomine et al., 2002). Resultaten ur en studie visar att en barns hjärna kan vara mer sårbar för utvecklandet av neuropsykologiska symtom efter en THS, jämfört med liknande skador till en vuxen persons hjärna (Hessen, Nestvold & Anderson, 2007).

En stor del av de barn som fått en medelsvår eller svår THS upplever någon typ av kognitiva eller beteendemässiga nedsättningar. Det finns dock en viss osäkerhet kring nedsättningarna som följer en lindrig THS (Anderson & Catroppa, 2006). Återhämtningen efter en lindrig skada ser ut att vara tämligen bra på gruppnivå och mätt med standardiserade kognitiva test förekommer få neuropsykologiska nedsättningar (Kirkwood et al., 2008). På individnivå finns det dock barn som efter en lindrig THS rapporterar subjektiva symptom och kan utveckla permanenta problem som kräver vård (Cassidy et al., 2004; Hessen, Nestvold & Anderson, 2007; Taylor et al., 2010).

Det saknas en universellt accepterad definition på lindrig THS, vilket gör att definitionerna varierar mellan olika studier. I Finland definieras lindrig THS för vuxna som poäng mellan 13–15 på Glasgow Coma Scale (mätt en halv timme efter skadan och efter det för hela uppföljningstiden). Vidare ska en av följande vara inkluderade: inte mer än 30 minuter av förlust av medvetande, inte mer än en 24 timmars minneslucka och endast lindriga avvikande fynd vid undersökning av hjärnan får förekomma (Brain Injuries: Current Care Guidelines, 2017). Eftersom det i Finland saknas en definition anpassad för barn och unga, användes definitionen för vuxna i denna studie.

Det finns en bred variation av olika definitioner på exekutiva funktioner (EF). Begreppet innefattar olika funktioner som är samlade under samma paraplybegrepp och gemensamt bidrar till bland annat uppmärksamhetsreglering, kognitiv flexibilitet och informationshantering. Kort kan EF beskrivas som ett slags kontrollcenter som ansvarar för koordinerande och reglerande av meningsfulla aktiviteter (Gioia, Isquith, Kenworthy & Barton, 2002; Gioia, Kenworthy, Isquith, 2010). EF kan mätas antingen med standardiserade kognitiva test eller med hjälp av skattningsskalor. Kognitiva testen utförs i regel i kontrollerade förhållanden med fokus på distinkta funktioner. Med hjälp av skattningsskalor vill man få fram och granska hur EF fungerar i vardagliga miljöer. Skattningsskalorna kan utföras av den drabbade personen själv, eller av någon närstående som har insyn i den drabbades vardagliga funktion. Problematiskt är att resultaten som fås med de standardiserade kognitiva metoderna och med skattningsskalorna inte tenderar att korrelera, vilket leder till en diskrepans mellan dessa två metoder som antas mäta samma sak (Gioia & Isquith, 2004; Gioia, Kenworthy, Isquith, 2010; McKinley, 2009; Yeates & Taylor, 2005).

The Behavior Rating Inventory of Executive Function (BRIEF) är en skattningsskala som används för att mäta EF i vardagen. Föräldern eller läraren bedömer barnets vardagliga beteende på 8 olika delskalor som sedan summeras till två olika sammansatta skalor: The Behavioral Regulation Index (BRI) och Metacognition Index (MI). Vidare summeras dessa två till en summavariabel som innefattar alla inkluderade skalor (General Executive Composite Score; GEC). Tidigare studier som använt BRIEF som skattningsskala för att mäta EF hos barn med lindrig THS har funnit stöd både för och emot förekomsten av exekutiva problem (Maillard-Wermelinger et al.,2009; Nadebaum, Anderson & Catroppa 2007; Sesma et al., 2008).

Eftersom resultaten från tidigare studier tyder på att det finns lite stöd för att man med standardiserade kognitiva test kan upptäcka problem med EF efter en lindrig THS, gjordes valet att endast använda skattningsskalor som mätinstrument i denna studie. Syftet med denna studie var att undersöka gruppskillnader mellan barn med lindrig THS och barn med ortopedisk skada, på föräldraskattade EF medan man kontrollerar för effekterna av intelligensnivå.

Metod

Denna studie gjordes i ett samarbete med ett större pediatriskt forskningsprojekt initierat 2018 (Cognitive and psychosocial recovery in pediatric mild traumatic brain injury, Saarinen et al.). Projektet i fråga strävar efter att retrospektivt undersöka pediatriska THS och kommer även följa upp de långsiktiga konsekvenserna skadan kan ha orsakat. Denna studie använde delar av projektets data för att få mått på deltagarnas kön, ålder, allmänna intelligensnivå och föräldraskattade EF. Studien beviljades etiskt tillstånd av etiska kommittén inom Egentliga Finlands sjukvårdsdistrikt.

Det fanns 694 barn som vårdats på Åbo universitetscentralsjukhus mellan åren 2010–2016 för en traumatisk hjärnskada, som dessutom hade en genomgått en DT och/eller MRI, hade information om en inledande examination och var under 16 år vid tillfället av skadan. Inkluderings- och exkluderingsprocessen för de 37 barn som inkluderades i denna studie presenteras i *figur 1*. Barn i åldern mellan 7–16 som vårdats på Åbo universitetscentralsjukhus för ortopediska skador (OS) rekryterades till en kontrollgrupp. Alla föräldrar och barn undertecknade informerat samtycke innan deltagandet. Rekryteringsprocessen blev tvungen att avbrytas på grund av utbrottet av coronaviruspandemin under våren 2020, innan målsättningen på 30 rekryterade barn uppnåddes. Den slutliga kontrollgruppen bestod således endast av de 14 barn som rekryterades och testades innan pandemin bröt ut. Hela samplet bestod därmed av 51 barn, varav 45,1 % var flickor och 54,9 % var pojkar.

Information om EF erhölls med hjälp av tre olika skalor (GEC, BRI och MI) från frågeformuläret The Behavior Rating Inventory of Executive Function (Gioia, Isquith, Guy & Kenworthy, 2000). BRIEF rapporterar alla poäng som standardiserade *T* poäng, med ett medeltal på 50 poäng och en standardavvikelse på 10 poäng. Högre poäng indikerade mera problem, medan poäng vid eller över 65 (1,5 SD över medeltalet) kan anses ha ett kliniskt värde (Gioia, Isquith, Guy & Kenworthy, 2000). Information om barnets allmänna kognitiva förmåga erhölls med hjälp av Wechsler

Intelligence scale for children (WISC IV; Wechsler, 2010). Fem deltest ur testbatteriet användes för att räkna ut intelligenskvoten (likheter, ordförråd, blockmönster, sifferrepetition och kodning). De statistiska analyserna genomfördes med programmet IBM SPSS Statistics 24.0 för Macintosh (IBM Corp., 2017).

Resultat

Deskriptiva resultat i form av medeltal och standardavvikelser för båda grupperna (lindrig THS och OS) är grafiskt presenterade i *figur 2.* Huvudanalysen, en multivariat analys av varians och kovarians (MANCOVA), genomfördes för att undersöka effekter av skada (lindrig THS och OS) på EF mätt med tre olika skalor från BRIEF (GEC, BRI, MI). Intelligenskvot användes som kovariat. Samtliga antaganden för kovariansanalys kontrollerades innan huvudanalysen gjordes.

Resultaten ur huvudanalysen visade inga statistiskt signifikanta skillnader på BRIEF poäng mellan grupperna ($F(3,46) = .792$, $p = .505$, *partial* $\eta 2 = .049$). Genomförandet av en mer deskriptiv analys på individnivå blev motiverat efter de icke-signifikanta gruppskillnaderna. Denna analys visade att en procentuellt större undergrupp av barn med lindrig THS än med OS hade kliniskt signifikanta BRIEF poäng ($T \geq 65$), på alla tre skalor. Detta presenteras grafiskt i *figurerna 3, 4* och *5*. En statistisk analys (two-sided Fisher’s exact test) gjordes på de barn som visade kliniskt signifikanta poäng på någon av de tre skalorna mellan barnen i lindriga THS gruppen (21,6 %) och i OI gruppen (7,14 %). Resultaten visade att skillnaden mellan grupperna var icke-signifikant ($p = 0{,}414$).

Diskussion

Denna studie ämnade att utforska eventuella problem i exekutiva funktioner efter en pediatrisk lindrig traumatisk hjärnskada med hjälp av föräldraskattning. Resultatet ur denna studie antyder att det inte fanns gruppskillnader i exekutiva funktioner mellan barn som fått en lindrig hjärnskada och barn som fått en ortopedisk skada. Detta överensstämmer med tidigare studier som inte funnit skillnader i EF på gruppnivå (Maillard-Wermelinger et al., 2009; Nadebaum et al., 2007). Värt att notera är att studien som funnit gruppskillnader inkluderade aningen yngre barn i sitt sampel, vilket kan ha påverkat resultaten då ålder är en modererande faktor för utvecklandet av symtom efter en traumatisk hjärnskada (Sesma et al., 2008)

En annan faktor som påverkat resultaten i denna studie är valet av mätinstrument på exekutiva funktioner. Tidigare studier som utforskat följderna av traumatiska hjärnskador och som använt föräldraskattningen BRIEF som mätinstrument har främst inkluderat barn med medelsvåra till svåra skador i sina studier. Bevisen är ännu bristande för hur bra denna skattningsskala är på att upptäcka symtom efter lindriga skador (Nadebaum, Anderson, & Catroppa, 2007; Maillard-Wermelinger et al., 2009).

Eftersom sampelstorleken i denna studie var begränsad, speciellt beträffande kontrollgruppen, gjordes en analys på den procentuella andelen barn med BRIEF poäng över gränsvärdet för klinisk signifikans. Denna analys visade att en större procentuell andel barn hade kliniska värden i den lindriga THS gruppen jämfört med OS gruppen. Detta är i linje med tidigare studier som tyder på att en andel av barn med lindrig THS kan utveckla problem med exekutiva funktioner, även om tillfrisknandet på gruppnivå är bra (Cassidy et al., 2004; Hessen, Nestvold & Anderson, 2007; Taylor et al., 2010). Dessa fynd betonar behovet av en noggrann individuell utredning i den initiala vården för att identifiera de barn som kan vara i behov av fortsatt stöd.

I denna studie bör vissa briser tas i beaktande vid tolkningen av resultaten. En liten sampelstorlek, på grund av utbrottet av coronaviruspandemin, ledde till att den statistiska styrkan i analyserna var bristande. Kausala samband och tolkningar kan inte göras på grund av forskningsupplägget i denna studie. Framtida studier bör använda longitudinella upplägg och mera omfattande kartläggningar för att möjliggöra vidare tolkningar.

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PRESSMEDDELANDE

Barn och unga förefaller klara sig bra på gruppnivå efter en lindriga traumatisk hjärnskada

Pro gradu-avhandling i psykologi
Fakulteten för humanoria, psykologi och teologi, Åbo Akademi

Resultaten från en pro-gradu avhandling i psykologi vid Åbo Akademi tyder på att barn och unga inte uppvisar problem med exekutiva funktioner efter en lindrig traumatiska hjärnskada. Dock tycks en procentuellt större andel barn med lindriga traumatiska hjärnskador överskrida gränsen för kliniskt betydande problem, jämfört med barn som fått en ortopedisk skada. Avhandlingen undersökte exekutiva funktionerna med hjälp av föräldraskattningar över fungerande i vardagen. Tidigare studier inom detta ämne visar motstridiga resultat på hur exekutiva funktioner påverkas som följd av en lindrig traumatisk hjärnskada hos barn och unga.

I datat för denna avhandling inkluderades barn i ålder 7–16. Sammanlagt bestod samplet av 51 barn, 37 med lindrig traumatisk hjärnskada och 14 med ortopedisk skada. Datat var en del av ett större forskningsprojekt initierat 2018 (Cognitive and psychosocial recovery in pediatric mild traumatic brain injury, Saarinen et al.) med målsättningen att utreda neuropsykologiska följder av lindriga traumatiska hjärnskador hos barn och unga.

Avhandlingen utfördes av Janina Söderling under handledning av Mari Saarinen, PsL (VET) och akademilektor Mira Karrasch.

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