

MARI-LIIS KALDOJA

Mild traumatic brain injury in childhood:
pre-injury social-emotional behavior,
social-emotional and cognitive outcome and
implications for attention rehabilitation



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LIST OF ORIGINAL PUBLICATIONS

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Author of the present dissertation contributed to the publications as follows:

- For Studies I and II the author set the aims, collected data, conducted all analyses and wrote the papers as the corresponding author.
- For Study III, the author was responsible for the aims and neuropsychological testing. The author also participated in data collection, statistical data analyses, and in collaborative writing as an equal contributor.
- For Study IV, the author was responsible for formulating the research questions, neuropsychological testing and statistical data analysis. The author also participated in collaborative writing as an equal contributor.

I. GENERAL INTRODUCTION

Traumatic brain injury (TBI), also referred to as closed-head injury or head trauma, is one of the most common causes of death and disability in children (Bruns & Hauser, 2003; Langlois, Rutland-Brown, & Thomas, 2004). In Estonia, childhood TBI incidence rate is as high as 369: 100,000 and younger children from 0–4 years belong to the most vulnerable risk group (Ventsel, et al., 2008). The incidence rate is higher for boys than for girls (405: 100,000 and 330: 100,000) and boys between 0–4 years of age have also the highest rates of TBI related emergency department visits, hospitalizations and deaths (Faul, Xu, Wald, & Coronado, 2010; Ventsel et al., 2008).

More than $\frac{3}{4}$ of children sustaining TBI show a good recovery (Kraus, 1995). However, a good recovery does not always mean a full recovery and many children who have suffered from TBI have to face different transient or permanent neurological, emotional, behavioral and/or cognitive problems (e.g., difficulties in verbal communication, attention, memory, learning and self-regulation etc.) (Anderson, Morse, Catroppa, Haritou, & Rosenfeld, 2004; Catroppa & Anderson, 2004; Catroppa & Anderson, 2005; Ganesalingam, Sanson, Anderson, & Yeates, 2006; Hanten, et al., 2004; Hawley, Ward, Magnay, & Long, 2004; Krawczyk et al., 2010). These impairments may not be notable immediately after the injury, but could start to impact children's lives as they grow older. In literature this delayed onset of defects is referred to as a "sleepers effect", "latent deficit" or child "growing into his or her lesion" (Eslinger, Gratatan, & Damasio, 1992), all referring to the interactions between deficits and failure to develop age-appropriate cognitive, social-emotional, and fine- and gross-motor competences.

Recent work complement this long-held approach by suggesting that after a few years of protracted recovery period, even children with severe TBI gradually stabilize and start showing developmental progress, but many of them still never seem to catch up with their peers (Anderson, Godfrey, Rosenfeld, & Catroppa, 2012).

I.1 Incidence of TBI

According to KIDS database in the US, in any given year approximately 70: 100,000 children between 0 and 17 years are hospitalized because of TBI (Schneier, Shields, Hostetler, Xiang, & Smith, 2006). Incidents are mainly reported following the contacts with the health care system and epidemiological evidence suggests that mild TBI (for more details about the classification of TBI see below) constitutes 80–90% of the total incidence, moderate TBI to 7–8% of the total incidence, and severe TBI to 5–8% of the total incidence (Cassidy et al., 2004; Hawley, Ward, Long, Owen, & Magnay, 2003; Rutland-Brown, Langlois, Thomas, & Xi, 2006). Between the years 2001 and 2004 about 82% of pediatric TBI cases in Estonia were classified as mild (303:

100,000), while moderate or severe TBI was diagnosed in 18% of the cases (Ventsel et al., 2008).

In the US, similarly to other developed countries, infants and toddlers under the age of 4 have the highest incidence rate of TBI with secondary peak in adolescence and yet another peak in the elderly (Rutland-Brown et al., 2006). Schneier et al. (2006) showed that 11.6% of children admitted to hospital because of TBI are infants below the age of 1 year and 17.4% between the ages of 1–4. In Estonia, children aged 0–4 years have more than 1.5 times higher childhood TBI incidence rate (566: 100,000) compared to the overall pediatric population (369: 100,000), and as already stated above, little boys are at a particularly high risk (572: 100,000 for boys and 559: 100,000 for girls) (Ventsel et al., 2008). The accurate incidence rate for childhood TBI may be even higher. Many children with milder injuries never seek medical consult or remain undiagnosed by medical personnel. Furthermore, in some epidemiological studies, emergency department managed TBIs remain uncounted altogether (for more details, see reviews by Bruns & Hauser, 2003; and Cassidy et al., 2004).

1.2 Risk factors for childhood TBI

Many demographic, as well as child and parent related risk factors, including but not limited to male gender, child temperament and behavioral difficulties, single-family household, family's low socioeconomic status, parental psychiatric or alcohol/drug problem, low levels of parental supervision, have been identified for childhood accidental injuries (Bijur, Kurzon, Overpeck, & Scheidt, 1992; Khambalia et al., 2006; Kraus, Rock, & Hemyari, 1990; McKinlay et al., 2010; Morrongiello, Corbett, McCourt, & Johnston, 2006; Morrongiello, Ondejko, & Littlejohn, 2004; Schnitzer, Dowd, Kruse, & Morrongiello, 2015).

While studying the birth cohort of 1966 in Northern Finland, Winqvist, Jokelaines, Luukines, and Hillbom (2007) found male gender to be one of the two most powerful predictors (in addition to parental alcohol misuse) for an increased risk of childhood TBI before the age of 14. The male gender as an important risk factor for childhood TBI may not be notably dominant in infancy, but the gap between boys and girls steadily widens throughout the childhood and adolescence (Collins et al., 2013; Ventsel et al., 2008; for a review, see Thurman, 2014). According to a more explanation oriented approach (variety of factors that may elevate injury risk are identified and analyzed) by Morrongiello and Dawber (1999), in early childhood boys and girls are differentially socialized by their parents. This difference in socialization, which encourages autonomy and independence among boys, also promotes greater risk-taking, and thus may lead to a higher occurrence of accidental injuries in boys. Compared to girls, boys also tend to evaluate injury risks as lower (Hillier & Morrongiello, 1998), attribute injuries more often to bad luck and hold more optimistic bias towards potential injuries (Morrongiello & Rennie, 1998).

Other behavioral markers, especially externalizing behavioral problems like oppositional behavior patterns, aggressiveness, hyperactivity, impulsivity and

constant sensation seeking are also associated with the elevated risk for childhood accidental injuries (including accidental TBI) (Byrne, Bawden, Beattie, & DeWolfe, 2003; Morrongiello & Sedore, 2005; Schwebel, Hodgens, & Sterling, 2006). According to Morrongiello, Ondejko, and Littlejohn (2004b), young children who engage in more risk taking or sensation seeking behaviors suffer more often from accidental injuries, suggesting that there might be innate differences in sensation seeking and injury risk. They also concluded that children's general compliance with rules and behavioral guidelines is an important risk factor for home injuries.

Aside from compliance and autonomy, an essential social-emotional skill that affects the occurrence of accidental injuries is self-regulation or inhibitory control (Schwebel & Plumert, 1999). Sinopoli and Dennis (2012) have defined self-regulation/inhibitory control as the ability to ignore distraction, to attend selectively, to prevent an action from being executed, or to stop an action in progress. Children who are very extravert during toddler and pre-school years, and at the same time have difficulties with self-regulation, are prone to suffer more accidental injuries (Schwebel & Plumert, 1999). Other emotional and behavioral difficulties as well as psychiatric disorders already present before the injury are also identified in children with TBI (Bijur, Golding, Haslum, & Kurson, 1988; Brown, Chadwick, Shaffer, Rutter, & Traub, 1981; Byrne et al., 2003; Gerring et al., 1998; Max et al., 1997; for a review, see Max, 2014). More so, maternal alcoholism is positively associated with different types of children's accidental injuries, and children with both parents having a drinking problem are in even greater risk (Bijur et al., 1992). In terms of childhood TBI, parental alcohol misuse is the number one most powerful predictor for the occurrence of TBI in childhood (Winqvist, et al., 2007).

I.3 Main causes of TBI

For infants and toddlers up to 14 years of age, approximately 67% of TBI cases are caused by falls, followed by the second most common cause – being hit with an object (10.1% of cases) (McKinlay et al., 2008). In adolescents and young adults, sports (especially rugby) and motor vehicle accidents are the two main causes for TBI in the U.S (approximately 27.7% and 23.4% of the cases respectively) (McKinlay et al., 2008). Worldwide, sports and leisure activities are reported to be the cause of approximately 20% of pediatric TBI incidence, but geographical location and season (e.g., in winter there are more snowboard and ski accidents, while in summer more cycling and roller-skating injuries) have their impact (Crowe, Babl, Anderson, & Catroppa, 2009; Engberg, & Teasdale, 1998; Research and Training Center in Rehabilitation and Childhood Trauma, 1993). In Estonia, the main cause of childhood TBI in all age groups is falling (63.6% of the cases), and in children up to 4 years of age, falling causes 84.4% of TBI incidence. Among children 4–15 years old, falls are still number one cause of TBI (55.88% of the cases), with the road and traffic accidents (as a

pedestrian, passenger or cyclist) being the second common (30.88% of the cases) (Ventsel et al., 2008).

1.4 Mild, moderate and severe TBI in childhood

TBI is often identified according to the International Classification of Diseases Version 10 (World Health Organization, 1993) and on the basis of injury severity. Already in the early nineties, the American Brain Injury Association recommended a following three-degree severity classification of TBI: mild, moderate, and severe (Mild Traumatic Brain Injury Committee, 1993). Despite these commonly used classifications, a significant amount of individual variability remains within the classification system and within the injury severity groups (Roosenbeek, Maas, & Menon, 2009). Furthermore, the exact criteria to define childhood TBI and to classify the severity of the injury in children are even more imprecise (for systematic review, see Chan, Thurairajah, & Colantonio, 2015). That said, in terms of a patient's prognosis, treatment and possible rehabilitation needs, the classification of TBI severity is medically important. The issue of timely and accurate classification of TBI severity is even more critical for pediatric population, as problem-specific age-appropriate early intervention substantially contributes to an ongoing recovery processes and improves the overall outcome (Chevignard, Toure, Brugel, Poirier, & Laurent-Vannier, 2010; Kirkwood et al., 2008; Ponsford et al., 2001; Wade, Michaud, & Brown, 2006; Wade et al., 2015).

Most often, classification of TBI severity is based on injury characteristics, level of consciousness, or the severity of computer tomography (CT) and/or magnetic resonance imaging (MRI) appearances. The level of consciousness is usually measured with the Glasgow Coma Scale (GCS) at the time of injury (Teasdale & Jennet, 1974). The GCS consists of three separately assessed components: eye opening (1–4), best verbal response (1–5) and best motor response (1–6), providing a total score from 3 (worst) to 15 (normal).

TBI is severe if the GCS score is below 8 with a loss of consciousness and/or there is posttraumatic amnesia lasting more than 24 hours, and/or if the patient is in a coma for more than 6 hours (Bishop, 2006; Chung et al., 2006). Most of these patients with severe TBI need immediate and intensive medical treatment. About one half of severely injured children have a poor outcome (Reid, Roesler, Gaichas, & Tsai, 2001). Severe TBI may result in serious physical and neurological deficits and many children with severe TBI have to face short- and/or long-term cognitive and behavioral disabilities (Babikian & Asarnow, 2009; Chapman et al., 2004; Crowe et al., 2012).

TBI is classified as moderate if initial GCS score is between 9 to 12 with a loss of consciousness between 30 minutes and 24 hours, and/or a period of posttraumatic amnesia from 24 hours to 7 days (APA, 2013). Regardless of the mental state, if there is a focal CT lesion, the TBI is classified at least moderate if not severe. In cases of moderate TBI, secondary symptoms such as hemato-

mas and brain swelling that require surgery may also be present. In children with moderate TBI, most common physical and psychological symptoms are tiredness, headaches, dizziness, word-finding problems, difficulties in thinking, attention, memory, planning, organizing, concentration, and irritability. Patients with moderate TBI are a very heterogeneous group with significant variability in terms of trauma severity, hospital course, and recovery. In addition, the subjective, cognitive, emotional, and functional deficits following moderate TBI can be quite extensive and prolonged (Vitaz, Jenks, Raque, & Shields, 2003).

The most common and least severe form of TBI is mild TBI. More so, mild TBI is one of the most common neurological conditions occurring during childhood (McCarthy & Kosofsky, 2015). Misleadingly, over the years various terms such as mild head injury and concussion have been used synonymously with mild TBI. The diagnosis of mild TBI is challenging as it is mainly based on injury characteristics. According to Rosman, Herskowitz, Carter, and O'Connor (1979), mild TBI is diagnosed if the GCS score is 13 or higher during an acute period of injury; there may be other clinical symptoms like disorientation, altered mental status, and headache or vomiting with no focal neurological signs, no intracranial mass lesion, and no requirements for intracranial surgery. The Mild Traumatic Brain Injury Committee (1993), however, suggests that TBI is mild if a person who has had a head injury manifested at least one of the following: any period of loss of consciousness (LOC) of up to 30 minutes; any loss of memory for events immediately before or after the accident (i.e., post-traumatic amnesia, PTA) not longer than 24 hours; any alterations in mental state at the time of the accident (feeling dazed, disoriented, or confused); or focal neurological deficits that may or may not be transient. Similar criteria have also been adopted by DSM-5, where the neuropsychiatric sequelae of TBI are approached in the framework of neurocognitive disorders (APA, 2013). Diagnosing a mild TBI in a clinical setting is a complicated task (for a review, see Levin & Diaz-Arrastia, 2015). Compared to moderate and severe childhood TBI, mild childhood TBI diagnosis is more of a vague concept. That said, there is however, a tendency to restrict mild pediatric TBI diagnosis to those injuries not exceeding LOC of 15 minutes, PTA of less than 1 hour and the GCS scores 13 and higher (De Kruijk, Twijnstra, & Leffers, 2001). Pediatric mild TBI is often thought to be a benign condition with an apparently good short- and long-term outcome. In light of the large pediatric mild TBI incidence rate, it is indeed reassuring to know that most of these children recover well. However, some children suffering from mild TBI do experience post-injury disturbances, like subtle memory problems and concentration difficulties, tiredness, fatigue, dizziness, mood disorders (e.g., symptoms of anxiety and/or depression, irritability), behavioral disturbances, suggesting chronic brain damage (Crowe et al., 2012; Hessen, Nestvold, & Anderson, 2007; for a review, see Babikian & Asarnow, 2009 and McCarthy & Kosofsky, 2015). That said, the lack of consensus on definition of mild TBI (see also Cassidy et al., 2004) is probably one of the major causes of the contradicting conclusions regarding the outcome of mild pediatric TBI in research literature.

1.5 The mechanisms of TBI

The processes happening in the brain during TBI are best described in sequences and are typically referred to as primary and secondary injuries or primary and secondary processes (Mendelow, Teasdale, & Jennet, 1990).

According to Veenith, Goon, and Burnstein (2009), primary brain injury is the direct injury to the brain cells incurred at the time of impact. Mansfield (2007) claims that primary injury includes the physical deformation of the skull, brain, and/or blood vessels, and is the result from external objects striking or penetrating the head, sudden acceleration, deceleration or torsion. He further concludes that acceleration and deceleration are common in motor vehicle accidents, whereas rotational forces are exerted by violent shaking, where laceration, contusion and bleeding are caused by the impact of the brain smashed against the interior of the cranium; contra-coup injuries as well as diffuse axonal injuries may also occur (for more details, see a review by Mansfield, 2007).

Primary brain injuries, comprising a single area of the brain, are referred to as the focal brain injuries, while injuries involving at least two, but frequently more areas of the brain, are referred to as diffuse injuries. Types of focal brain injuries include but are not limited to contusions (bruising that occurs focally in the brain), epidural and subdural hematomas, and skull fractures.

Literature suggests that after childhood TBI, up to 20% of children may develop a skull fracture (Harwood-Nash, Hendrick, & Hudson, 1971). It is also common that in newborns and infants, a skull fracture is concealed by a hematoma, which may result in significant blood loss (Mann, Chan, & Yue, 1986; Raimondi & Hirschauer, 1984). Further, according to Stalhammer (1990), up to 40% of the epidural hematomas in children occur without a skull fracture.

Focal brain injuries like contusions and hematomas after TBI are more common in older adolescents and adults, whereas infants and younger children who have greater brain-water content and disproportionately large head compared to the rest of their body, along with weak cervical ligaments and muscles, tend to suffer from diffuse brain injuries (Mazzola & Adelson, 2002). These diffuse injuries may occur in forms of concussion, diffuse axonal injury and traumatic subarachnoid hemorrhage.

Different classifications of diffuse brain injury exist (e.g., four subgroup categorizations based on the results of CT scans proposed by Marshall et al., 1991). Concussion is the most common form of diffuse brain injury. It is defined as traumatically induced physiological disruption of brain function with a short period of altered or loss of consciousness (Mild Traumatic Brain Injury Committee, 1993). The second most common form of diffuse injury after concussion, the diffuse axonal injury or white matter shearing injury occurs when acceleration and/or deceleration forces lead to the disruption of an axonal degeneration (Adams et al., 1989; Ganarelli et al., 1982).

In cases of mild TBI, the changes in white matter may primarily be caused by axonal damage, but when the injury is more severe both axonal damage and myelin damage are typically present (Kraus et al., 2007).

Focal or diffuse trauma with physical deformation of skull, brain and blood vessels can result in a series of biochemical processes that often lead to the secondary brain injury (Veenith et al., 2009). Secondary brain injury develops and evolves minutes, hours, days or even weeks after the initial impact to the brain. Neuropathologically, secondary injury is caused by a dynamic interplay between the changes in cerebral blood flow (hypo- and hyperperfusion), impairment of cerebrovascular autoregulation, cerebral metabolic dysfunction and inadequate cerebral oxygenation (for more details, see a review by Werner & Engelhard, 2007).

Secondary brain injury may also occur if the child develops post-traumatic seizures following the initial TBI. According to Formisano et al. (2007), post-traumatic seizures increase intra-cranial pressure and propose extra metabolic demands on the brain. Post-traumatic seizures are more common after severe brain injury and up to 9–15 % of children may develop new-onset epilepsy after severe TBI (Appleton & Dammellweek, 2002; Park & Chugani, 2015).

1.6 Brain injury and developing brain

There is plenty of empirical as well as clinical evidence to conclude that due to the overall plasticity, young brain may recover surprisingly well from focal injuries (Kolb & Tomie, 1988; Kolk, Ennok, Laugesaar, Kaldoja, & Talvik, 2011; Trauner, Chase, Walker, & Wulfeck, 1993; Ilves et al., 2014; Villablanca & Hovda, 1999). However, the diffuse injuries during the time of rapid growth and development of the brain could result in far worse outcomes (Stiles, 2000). After an extensive literature review on the outcomes of childhood TBI Levin (1992) concluded, that children who were injured during infancy had poorer outcomes than children who had sustained their injuries later in life. Animal studies by Bitigau and colleagues (1999) yielded somewhat similar findings, adding to the existing literature that the worst outcomes of very early brain injuries are evident when the injury occurs during a critical stage of brain development.

2. COGNITIVE AND SOCIAL-EMOTIONAL DEVELOPMENT IN CHILDHOOD

As stated above, TBI may affect cognitive, social, behavioral and emotional functioning. More so, after childhood TBI, difficulties with executive functioning and social cognition may become especially notable (Bornhofen & McDonald, 2008; Chevignard, Catroppa, Galvin, & Anderson, 2010; Dennis, Guger, Roncadin, Barnes, & Schachar, 2001; Nadebaum, Anderson, & Catroppa, 2007; Shmidt, Hanten, Li, Orsten, & Levin, 2010; Snodgrass & Knott, 2006; Turkstra, McDonald, & DePompei, 2001) and these difficulties often result in poor short- and long-term social and behavioral outcomes (Januzs, Kirkwood, Yeates, & Taylor, 2002; Yeates et al., 2004). While childhood TBI often causes diffuse brain injury, the frontal and temporal areas of the brain are still most vulnerable to the effects of TBI. Important basic cognitive skills like attention and working memory, however, rely on the proper functioning of these frontal and temporal brain areas (D'Esposito et al., 1995; Kane & Engle, 2002; Osaka et al., 2003). Many authors believe that executive dysfunction and social-emotional as well as behavioral problems children exhibit after TBI are at least partially mediated by this frontal overlap (Levin & Hanten, 2009; Lipton et al., 2009; Muscara, Catroppa, & Anderson, 2008). Thus, in enhancing better cognitive, social-emotional and behavioral outcomes and quality of life after childhood TBI, the remediation of different aspects of attention is increasingly important.

2.1 Attention

In his classic work, William James, one of the most influential psychologists of the 19th century states that "Everyone knows what attention is," and continues to explain that "It is the taking possession by the mind, in a clear and vivid form, of one out of what seems several simultaneously possible objects or trains of thought. Focalization, concentration, of consciousness are of its essence. It implies withdrawal from some things in order to deal effectively with others, and is a condition which has a real opposite in the confused, dazed, scatterbrained state" (James, 2004).

Since then, different definitions and different models of attention have been proposed (e.g., Posner and Boies' neuroanatomical model, 1971; Sohlberg and Mateer's treatment model, 1987, 1989; Mirsky's neural model of attention, 1991, 1999). In most of these models, attention is seen as a set of different processes that directly affect new learning, memory, communication, problem solving, perception and most of the other dimensions of cognition. Sohlberg and Mateer's (1987, 1989) treatment model, Attention Process Training (APT), which is based on the rehabilitation work done with brain injured patients, consists of five interrelated components (focusing, sustaining, alternating, dividing and selective attention). In this model, focusing and sustaining attention are considered lower level processes, whereas selective attention,

alternating and dividing attention are more complex processes that at least partially rely on the proper working of lower level processes.

According to Park, Allen, Barnery, Ringdahl, and Mayfield (2009), another influential clinical model of attention, that is most suitable for describing the nature of attention impairment in patients with TBI, is Mirsky and colleagues' Neural Model of Attention (Mirsky, Anthony, Duncan, Ahearn, & Kellam, 1991; Mirsky, Pascualvaca, & Duncan, 1999). Based on the phenomenological taxonomy of attention and the results of neuropsychological testing of brain injured adults and children, this heuristic neural model claims that attention processes are functions of major and distinct cerebral systems and are neuro-anatomically linked to certain cerebral systems (Mirsky et al., 1991). Early neural model of attention (Mirsky, 1987; Mirsky et al., 1991) consisted of four separate components: focus or execute (capacity to concentrate attentional resources on a specific task), shift (ability to shift focus from one aspect of a stimulus to another), sustain (ability to stay in task in a vigilant manner), and encode (mnemonic aspects of attention). After further research, stability (capacity to maintain a regular, predictive response rhythm to task stimuli over time) as a fifth component was included in the model (Mirsky & Duncan, 2001).

2.2 Memory

Memory is a construct or a term used to describe the structure and processes involved in encoding, storage and subsequent retrieval of information (Melton, 1963). These processes are crucial for human survival.

“The renaissance man in the study of human cognition” – Alan Baddeley – has shown that individuals are capable of storing huge amounts of information in long-term memory, thus making rapid and accurate retrieval process a major priority (Baddeley, 1999). He explains that the retrieval process depends on the encoding process at the time of learning. Thorough encoding is an important part of the effective and rich storage and retrieval processes. This process of storing information is what most people think of as memory.

Historically, memory includes concepts of sensory register and short- and long-term memory (Atkinson & Shiffrin, 1968). Short-term memory allows to temporarily store a limited amount of information, whereas long-term memory enables more stable and permanent storage. Baddeley and Hitch (1974) have proposed a concept of working memory (process of holding information briefly while working with it) – a gateway between short- and long-term memory. Working memory is also temporal and limited in its capacity, but at the same time is a complex system that can direct attention, apply strategies and control retrieval. Working memory is comprised of four separable, interacting components: central executive (involved in attention control and range of regulatory functions), phonological loop (speech-based storage and rehearsal foundation for verbal information), visual-spatial sketchpad (short-term storage of visual and spatial information), and episodic buffer (binds information across informa-

tional domains and memory subsystems into integrated chunks) (Baddeley, 1986, 1992, 2000, 2003).

Working memory is a key component in higher cortical processes such as reading, mathematics and behavioral self-regulation (Bayliss, Jarrold, Gunn, & Baddeley 2003; Daneman & Carpenter, 1980). However, the exact underlying nature of the processes, resources and demands on working memory during different higher order cognitive process is still a debate (Bayliss, Jarrold, Gunn, & Baddeley, 2003; Cocchini et al., 2002; Daneman & Carpenter, 1980; Friedman & Miyake, 2000; Gathercole & Pickering, 2000; Jarvis & Gathercole, 2003; Shah & Miyake, 1996).

2.3 Executive functions

Executive functions refers to a construct or an umbrella term that is used to describe a range of higher order cognitive skills (e.g., inhibition, working memory, cognitive flexibility, planning) required to engage in purposeful goal-directed behavior and anticipate the consequences of action. Executive functions or executive skills can be described through three separable, integrated processes: attentional control (comprised of self-regulation, inhibition, interference), cognitive flexibility (comprised of working memory, attentional shifting, divided attention, feedback utilization), goal setting (comprised of initiating, planning, problem solving, reasoning and strategic behavior) (Stuss, 1992). While these processes are the basis for executive behaviors, the overall outcome is greatly mediated by the individual time required to process information. In light of the above, theoretical framework for the developmental model of executive functions was proposed by V. Anderson and colleagues (2001), and P. Anderson (2002), who also expanded the current view by adding the information processing (comprised of fluency, efficiency and speed of processing) as the fourth process. These four processes are basic processes in Beauchamp and V. Anderson's (2010) Attention-Executive component in the *SOCIAL* model that is also the theoretical underpinning for the present dissertation.

2.4 Development of cognitive functions

Childhood is a time of vivid development. Similarly to physiological maturation, children's cognitive functions (attention, memory, visual-spatial abilities, executive functions etc.) undergo a rapid change. Cognitive functions show a prolonged developmental trajectory through childhood. To accurately identify the deviation from the expected developmental trajectory, it is important to understand the typical/normal development of these skills and the concept of mature cognition.

Davidson, Amson, Anderson, and Diamond (2006) defined mature cognition as the ability of holding information in mind (including complicated representa-

tional structures, mentally manipulating that information, and acting based on it), acting based on choice rather than impulse (exercising self-control or self-regulation) by resisting inappropriate behaviors and responding appropriately, and quickly and flexibly adapt behavior to changing situations.

The maturation of cognitive functions is dependent on the maturation of underlying neural processes. For example, Anderson (1998) has argued that the development of executive functions is strongly mediated by the prolonged neurodevelopment of the prefrontal cortex. Functionally the most complex brain area, prefrontal cortex, has the longest period of maturation (Schubert, Martens, & Kolk, 2014). The myelination of prefrontal white matter continues even in early adulthood (Klingberg, Vaidya, Gabrieli, Moseley, & Hedehus, 1999). Analogically, executive functions start to develop already during infancy (Diamond & Goldman-Rakic, 1989) and display several growth spurts through childhood, with some of the most notable changes occurring between the ages of 0–2 years, 7–9 years, in adolescence and in the late twenties (De Luca et al., 2003; Levin et al., 1991; for a review, see Anderson, 2001). Klimkeit, Mattingley, Sheppard, Farrow, and Bradshaw (2004) have shown that the largest improvements in the development of attention and executive functions occur between 8–10 years of age, and that attention and executive functions may develop in parallel. Rebok et al. (1977) have also stressed the importance of the years from 8–10 in the development of attention and suggested that more gradual changes occur between the ages of 10–13.

Still, different components of attention and executive functions may display slightly different developmental trajectories (Welsh, Pennington, & Groissner, 1991). The development of basic inhibitory functions precedes the development of more complex functions of selective attention (Klenberg, Korkman, & Lahti-Nuuttila, 2001; Davidson et al., 2006). Attentional control skills like inhibition and self-regulation develop remarkably between the ages of 0–6 years (Diamond & Goldman-Rackis, 1989; Diamond & Taylor, 1996). Sustained attention, which is the first attention component to mature, shows rapid development in infancy and pre-school years, and may be fully mature by the age of 7 (McKay, Halperin, Schwartz, & Sharma, 1994; Rebok et al., 1997). Selective attention is thought to undergo rapid changes between the ages of 5–8 and less notable changes between 9–12 years of age (Korkman et al., 2001). Yet, others have shown that selective attention can mature even as early as around the age of 7–10 (McKay, Halperin, Shwartz, & Sharma, 1994; Plude, Enns, & Brodeur, 1994; Tipner et al., 1989).

For processing speed, which also starts to develop very early in life, the first growth spurts are seen between 3–5 years of age (Espy, 1997; Welsh, Pennington, & Groisser, 1991) and with the second wave somewhere between 9–12 years of age (Kail, 1986).

Similarly to executive functions and attention, memory performance also evolves throughout the childhood. Conte et al. (1995) used the recalling of spatial position and a jigsaw puzzle tasks to study visual-spatial working memory and showed that most visual-spatial working memory capacities develop with

age: they found that the visual-spatial working memory increased significantly between the ages of 7–11 years.

Neuropsychological studies involving children with specific visual-spatial deficits have been very enlightening in understanding the development of visual-spatial working memory and visual-spatial abilities (e.g., Bearden et al., 2001; Lehnung et al., 2001; Lehnung et al., 2003; Schwartz, Kramer, Ablin, & Matthay, 2000; Swanson et al., 1991). Unfortunately, different assessment methods as well as different definitions of visual-spatial abilities make it difficult to compare these studies. One possibility to overcome such methodological issues in future research is by utilizing well recognized, standardized, widely used and developmentally appropriate assessment methods. Research suggests that one of these methods could be Rey-Osterrieth Complex Figure Test (ROCFT) or Rey Complex Figure Test and Recognition Trial (RCFT) (Anderson, Anderson, & Garth, 2001; Ashton, Donders, & Hoffman, 2005; Gallagher & Burke, 2007; Kirkwood, Weiler, Bernstein, Forbes, & Waber, 2001; Kushner, Bodner, & Mineshew, 2009; Loring, Martin, Meador, & Lee, 1990; Lu, Boone, Cozolino, & Mitchell, 2003; Meyers & Meyers, 2003; Meyers & Meyers, 1995; Ogino et al., 2009; Sami, Carte, Hinshaw, & Zupan, 2004; Seidman et al., 1995; Shin, Park, Park, Seol, & Kwon, 2004; Sowell, Delis, Stiles, & Jernigan, 2001; Waber & Holmes, 1985; Waber & Holmes, 1986; Watanabe et al., 2005).

ROCFT is a neuropsychological test developed by Rey (1941) more than 50 years ago to evaluate visual memory (Rey, 1941; Corwin & Bylsma, 1993, for a translation). Few years after its first launch, Osterrieth standardized and normed the test for both children and adults (Osterrieth, 1944). He was also the first to show the suitability of the ROCFT to evaluate visual-spatial planning and organizational skills (Osterrieth, 1944, 1993). While ROCFT is generally described as a test of planning and organization skills, other lower-order skills like visual perception, visual-motor skills, fine motor skills and visual memory are also important to successful overall performance (Anderson, 2001). ROCFT, now widely used in pediatric neuropsychological testing, is applicable to children as young as 6 years of age, and allows better understanding of normal developmental change in visual-spatial abilities (Akshoomoff & Stiles, 1995a, 1995b; Anderson et al., 2001). Its suitability for differentiating children with brain-injury from non-injured peers has also been proven (Garth, Anderson, & Wrennall, 1997).

2.5 Development of social-emotional competences

Brain areas known to regulate cognitive functions overlap substantially with the areas responsible for the regulation of social-emotional functioning. Orbital ventromedial prefrontal cortex is associated with social-affective functions (Adolphs, 2001; Grady & Keightley, 2002). Emotion processing relies on the limbic system, frontal cortex, and somatosensory cortex (Bornhofen & McDonald, 2008; Radice-Neumann, Zupan, Babbage, & Willer, 2007). Developmental trajectories of social-emotional and cognitive functions are parallel, and when these two competences do not co-develop, children often have difficulties with many aspects of their environment (Carlson, Mandell, & Williams, 2004).

The notion of social-emotional and cognitive functioning linkage is not a new one. Already in 1978, Vygotsky claimed that social interaction plays a fundamental role in the cognitive development. Through interaction within the sociocultural environment, elementary mental functions – referring to attention, sensation, perception and memory, develop into higher mental functions (i.e., to sophisticated and more complex mental processes) (Vygotsky, 1978). Social interaction, a form of communication with underlying emotional components (Halberstadt, Denham, & Dunsmore, 2001), and social experiences are intimately connected to emotional competence. Only in very rare occasions is social competence present without appropriate emotional functioning (Semrud-Clickeman, 2009).

Yeates and colleagues (2007) have proposed a social cognitions' model: Social Heuristic Model, where interactions and effects between social outcome, cognitive abilities and other mediating factors are well described. This approach stems from the ideas of social cognitive neuroscience and the studies of social competence in developmental psychology. Relationships among social information processing, social interaction and social adjustment are of interest, and bidirectional relations among those different levels of social competence (e.g., how self-perception of adjustment may affect social interaction and vice versa) are targeted (for more details, see Yeates et al., 2007).

Basic skills that are crucial for social-emotional functioning and social competence emerge and mature at various stages of development and rely on previously learned skills and abilities. The developmental aspects of social-emotional behavior and the emergence and interplay of social and cognitive competence throughout childhood are even better addressed by Beauchamp and Anderson (2010).

“We have often made a big distinction between cognitive development and social development, but the two interact: if you don't have the skills to inhibit inappropriate behaviors or to communicate adequately, then that will have an impact on the way you socialize,” claims Beauchamp, when describing their integrative approach (Krakow, 2011). This approach consists of internal and external factors, brain development and integrity, and cognitive capacities (attention-executive, communications and socio-emotional skill) (Beauchamp & Anderson, 2010). Their *Socio-Cognitive Integration of Abilities Model (SO-*

CIAL) explains how cognitive, socio-emotional, communicative, biological and environmental dimensions interact to predict social functioning within a developmental framework (see Figure 1).

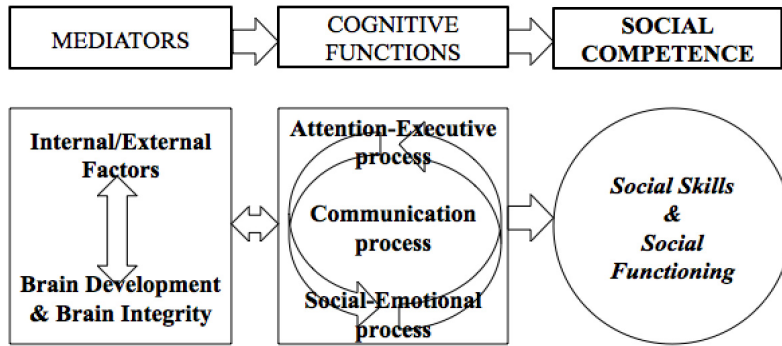


Figure 1. Socio-Cognitive Integration of Abilities Model (SOCIAL). *Adapted from* Beauchamp and Anderson’s (2010), “SOCIAL: An Integrative Framework for Development of Social Skills” by M. Beauchamp and V. Anderson, *Psychological Bulletin*, 136, 1, p. 48.

According to this approach, social skills and their emergence depend on the normal maturation of the brain, cognition and behavior within a supportive environmental context. Furthermore, the underlying social brain networks that are vulnerable to environmental influences mediate the implementation of social skills. Combination of these factors and individual social skills determines how a child interacts with his/her social environment (i.e., their social competence) (Beauchamp & Anderson, 2010).

While Beauchamp and Anderson (2010) emphasize the importance of normal brain development, they also conclude that *SOCIAL* model is particularly suitable for understanding the nature of disrupted brain development in the cases of TBI.

More so, both models of social cognition introduced here emphasize the importance of external factors like family environment and SES (parental education, family income) in more accurately predicting the short- and long-term outcome in social functioning after childhood brain injury.

3. COGNITION AND SOCIAL-EMOTIONAL BEHAVIOR AFTER CHILDHOOD TBI

As stated above, TBI in childhood is a serious health concern because of several short- and long-term behavioral and cognitive problems (e.g., Anderson et al., 2004; Anderson et al., 2006; Beauchamp et al., 2011; Catroppa & Anderson, 2005). These problems are especially apparent after severe TBI (Anderson et al., 2004; Catroppa & Anderson, 2005; Chapman et al., 2004). However, there is plenty of evidence to believe that mild TBI can also cause various neurological and cognitive difficulties (Hawley et al., 2004; Hessen et al., 2007; McKinelay, Dalrymple-Alford, Horwood, & Fergusson, 2003). Some children who have suffered from brain injury may do surprisingly well on neuropsychological assessments, but exhibit impairments in everyday life: when learning and acquiring new skills, interacting socially with others (Anderson, Damasio, Tranel, & Damasio, 2000). Even if it may seem that a child has fully recovered after the injury, years later this child may still exhibit various cognitive, socio-emotional and behavioral disturbances (Anderson et al., 1997; Anderson et al., 2000; Ewing-Cobbs, Fletcher, & Levin, 1985).

3.1 Cognitive outcome after childhood TBI – focus on attention, speed of processing, visual-spatial planning and visual memory

After TBI, various aspects of cognition may be affected: impairments in attention are seen in a short- as well as in a long-term (Catroppa, Anderson, Morse, Haritou, & Rosenfeld, 2007; Levin et al., 2007; Max et al., 2004; Yeates et al., 2005).

Anderson et al. (2012) have shown that shifting, divided attention, and attentional control (complex attention skills) may be more vulnerable to the negative impact of TBI, and recover slower than attentional capacity, selective attention, and sustained attention (simple attention skills). Park et al. (2009) argued that impairments in shifting and focusing attention are the most common attention problems after TBI, and that these impairments in focusing attention are relatively common even after mild TBI with otherwise preserved abilities in other cognitive areas.

Immediately after the injury, impairments are also evident in processing speed and in sustained and divided attention, but in terms of recovery, within a three month span processing speed and divided attention improve, while sustained attention typically remains impaired (Kwok, Lee, Leung, & Poon, 2008).

Children with severe TBI need more time to process information (Anderson, Catroppa, Morse, Haritou, & Rosenfeld, 2005; Anderson & Pentland, 1998; Brookshire, Levin, Song, & Zhang, 2004; Catroppa et al., 1999; Catroppa & Anderson, 2005; Catroppa et al., 2007). Donders and Janke (2008) studied chil-

dren with complicated mild to severe TBI and showed that information processing speed is associated with injury severity – more severely injured children were notably slower. Anderson and Pentland (1998) studied adolescents who had sustained moderate to severe TBI during childhood, and showed that attention problems and information processing deficits persist even years post-injury, suggesting that although there is a global attention deficit, processing speed is still most impaired.

Specific memory aspects often affected by childhood TBI are learning, recall/retrieval and recognition (Farmer, Haut, Williams, Kapila, & Johnstone, 1999; Roman et al., 1998). Impairments in immediate and delayed recall for verbal memory have received relatively much attention (Catroppa & Anderson, 2002; Donders, 1993; Levin et al., 1993; Morris et al., 2010; Roman et al., 1998), and impairments in immediate recall for non-verbal visual-spatial information have also been confirmed (Catroppa & Anderson, 2002; Donders, 1993; Lowther & Mayfield, 2004).

In a study by Lowther and Mayfield (2004), children with moderate and severe TBI demonstrated impairments on both immediate recall of visual and verbal information and on delayed recall of verbal information (impairment was observed in free recall task as well as in a task measuring the remembering of information presented sequentially or associated with something). Compared to children with milder injuries, children with severe TBI are thought to perform more poorly in visual recall (Donders, 1993). In visual-spatial recognition memory and visual learning, severely injured children are facing significantly more difficulties than mildly injured children (Ewing-Cobbs, Levin, Fletcher, Miner, & Eisenberg, 1990; Levin, Eisenberg, Wigg, & Kobayashi, 1982; Levin et al., 1988). Still, Farmer et al. (1999) and Gerrard-Morris et al. (2010) have shown persistent weaknesses in visual memory in children with mild TBI.

Anderson, Catroppa, Morse, and Haritou (1999) have further claimed that when children's memory is tested in the early stages post-injury, the impact of injury severity to memory performance might not be evident, but if these children are re-tested at least one year after the brain injury, the dose-response relationship is notable (the more severe the injury, the greater the memory deficit).

In executive functioning, difficulties after childhood TBI are reported in problem solving and planning. The associations between severe head injury and deficits in planning skills after the injury have been replicated in many studies (e.g., Brookshire et al., 2004; Pentland & Anderson, 1998).

Besides the severity of injury, the other important factor thought to contribute to the overall cognitive outcome after childhood TBI is the age at the time of injury. In line with the “double hazard model”, young children who sustain a severe TBI in the early childhood, or a moderate or severe TBI in infancy, may be particularly vulnerable to residual cognitive impairments (Anderson & Catroppa, 2005).

3.2 Social-emotional behavior after childhood TBI

Socio-emotional difficulties in childhood can partially be explained in terms of impaired executive functions (Anderson et al., 1999; Ylvisaker & Feeney, 2002).

In children with TBI, the injury to fronto-temporal and limbic regions may affect cognitive and emotional aspects of social behavior (Levin & Hanten, 2005).

Injuries in temporal cortices, amygdala, anterior cingulate, basal forebrain and prefrontal cortex may result in an impaired emotion regulation and Theory of Mind deficits (e.g., understanding the emotional expressions and mental states of others) (Bornhofen & McDonald, 2008; Schmidt, Hanten, Li, Orsten, & Levin, 2010; Snodgrass & Knott, 2006; Turkstra, McDonald, & DePompei, 2001; Yeates et al., 2007).

Therefore, after TBI, many children cannot control their behaviors when frustrated and are less able to respond appropriately in overwhelming situations (Hooper et al., 2004; Savage, De Pompei, Tyler, & Lash, 2005). They tend to show poorly regulated negative affect, exhibit mood swings, flat affect and socially improper emotional expressions, as well as react more impulsively (Ganesalingam et al., 2006; Ganesalingam, Sanson, Anderson, & Yeates, 2007). They may have low self-esteem, higher levels of loneliness, poor adaptive behaviors and are likely to exhibit more maladaptive and aggressive/antisocial behaviors (Andrews, Rose, & Johnson, 1998).

The devastating effects of TBI on social and emotional behavior have also been shown by William and Mateer (1999). Their childhood TBI patients not only demonstrated behavioral regression following their injuries (tantrum behavior, increased dependency), but also showed abnormal development of social skills and compromised behavioral/emotional restraints, as they grew older.

A study by Tonks, Williams, Frampton, Yates, and Slater (2007) confirmed that childhood brain injury has a negative effect on emotion-recognition skills as injured children performed relatively poorly in all emotion-recognition tasks involved. They further stressed that even when the cognitive abilities are intact, the emotion processing may still be severely impaired. Social cognition impairments accompanied with lower self-regulation and executive functions may explain the findings of Prigatano and Gupta (2006), who showed that children with TBI have fewer friends than their non-injured peers.

Difficulties in social cognition and social-emotional behavior tend to be relatively stable. The prevailing problems of social maladjustment and poor quality of life are present even several years post injury and are more notable in patients with more severe childhood TBI (Cattelani, Lombardi, Brianto, & Mazzucchi, 1998). Worse long-term outcomes for children with severe TBI in social problem solving and overall social competence have been shown in many studies (Janusz et al., 2002; Yeates et al., 2004). Still, Ganesalingam et al. (2006) who studied self-regulation and social and behavioral functioning in 6–11 year children with moderate and severe TBI, did not find any significant differences in overall social functioning between moderate and severe TBI groups, but when compared to their uninjured peers, children with moderate and

severe TBI demonstrated poorer social and behavioral functioning. According to their parents' and teachers' reports, children with TBI had more externalizing behavioral problems (e.g., defiance, tantrums, destructiveness, restlessness) and they had difficulties in initiating friendships with peers, giving compliments, requesting help, and helping family members and peers. More so, children with moderate and severe TBI were more impulsive, easily distracted and displayed less emotional awareness, empathy and situationally appropriate affect (Ganesalingam et al., 2006).

That said, short- and long-term social-emotional and cognitive outcomes after childhood mild TBI are still not sufficiently understood.

The individual publications of this dissertation aim to broaden the overall understanding of the short- and long-term social-emotional (Studies I and II) and cognitive outcomes (Studies III and IV) of childhood mild TBI.

3.3 Improving the outcome of children with TBI – focus on attention rehabilitation

Attention difficulties that are fairly common after childhood TBI, have negative impact on children's academic as well as social lives. Therefore, the remediation of affected attention functions is crucial in terms of improving the injured child's overall quality of life and well-being.

Remediation of attentional difficulties is traditionally addressed by constantly using exercises designed for specific components of attention (e.g., focused attention, divided attention) (Cicerone et al., 2000). In the late seventies Ben-Yishay', Rattok, and Diller (1979) introduced different cognitive exercises to train alertness, selective, divided and sustained attention. These exercises were similar to tasks used in clinical diagnostic assessments and originated from the claim that if patients constantly perform different attention exercises, they become more proficient and their attention difficulties will decline over time (see also Zocolotti et al., 2011). This drill and practice approach has been dominant in cognitive rehabilitation with adults and has also been applied to pediatric cognitive remediation.

Furthermore, many of currently applicable cognitive training techniques in pediatric cognitive remediation are actually modifications of methods originally designed for adults (Warschusky, Kewman, & Kay, 1999). This modification approach has proven its efficacy. For example, 14 children with ADHD who were trained with an adapted version of the Attention Process Training ("Pay Attention") showed improved attention, better academic achievement and were reported to be less inattentive-impulsive by their teachers (Kerns, Eso, & Thomson, 1999).

Positive effects of attention impairment remediation in children have also been gained by therapist guided interventions with Amsterdam Memory and Attention Training for Children (Amat-c) (Catroppa et al., 2015; Catroppa, Stone, Rosema, Soo, & Anderson, 2014; Sjö, Spellerberg, Weidner, &

Kihlgren, 2010; van't Hooft et al., 2005; van't Hooft et al., 2007; van't Hooft & Norberg, 2010). The Amat-c was the first known method specially designed for children and originally consisted of 20-week cognitive training program focusing on attention, memory, metacognitive strategies and repetition (Hendriks & Broek, 1996). Since then, the Amat-c program has further been improved (Catroppa et al., 2014; van't Hooft et al., 2005). It still consists of three phases that increase in complexity as they progress; each phase typically lasts 6 weeks, including 30 minutes of daily exercises. Exercises are done under the supervision of a teacher or a parent either at home or at school. A weekly outpatient therapeutic intervention beyond the specific training tasks is provided. During these sessions participants can share their cognitive, emotional and behavioral experiences. Therapeutic behavior modification techniques that focus on learning strategies and in the accomplishment of school tasks are also part of the program. Slightly different versions of Amat-c for specific age groups have been developed – one version is applicable for the 8–12 year-old children and the other for children over the age of 13 (van't Hooft et al., 2005; van't Hooft et al., 2007, see also Catroppa et al., 2014).

In a study by van't Hooft et al. (2005) children with acquired brain injuries showed improvement in selective attention, sustained attention, and memory performance after trainings with Amat-c. More so, as these beneficial effects generalized to school, van't Hooft et al. (2005) claimed that combination of hierarchical practice, the adoption of learning skills and strategy acquisition, as well as the weekly contacts with a trained professional and the active involvement of the parents and teachers, all contributed to the positive intervention effect.

Galbiati et al. (2009) also utilized therapist offered training to remediate attention in children with TBI. Their intervention program comprised of different tabletop and computerized tasks (e.g., Rehacom program). Galbiati et al. (2009) targeted selective attention, focused attention, sustained attention, divided attention, inhibition, and shifting. For each construct, a reflection on how the various components of attention influence tasks was followed by a demonstration of strategies, which are crucial to manage and control cognitive functions. Thus this rehabilitation program targeted meta-attention, using material that stimulated greater self-awareness of cognitive functioning. Authors justify their approach by claiming that such awareness rising at an early age enables to achieve greater cognitive and behavioral control. Further proof for the efficacy of this mixed approach (a combination of a process-specific approach and metacognitive strategies) comes from their data, which clearly showed that this intense 6 months long therapist offered attention specific neuropsychological training significantly improved concentration and reduced impulsiveness and distractibility in 6–18 year old children with TBI (Galbiati et al., 2009).

The pioneer of neuropsychological rehabilitation, Cicerone, has also recommended computer-based interventions with active therapist involvement. He claims that “therapist can help to promote insight into cognitive strengths and

weaknesses of the patient, develop compensatory strategies, and contribute to the transfer of skills into real-life situations” (Cicerone et al., 2000).

However, because typical development comprises of ongoing changes in abilities throughout childhood, the assessment of pediatric cognitive rehabilitation impact is very difficult.

Therefore, there is a need for more accurate and systematically controlled research in the field of evidence-based rehabilitation of attention functions in children with TBI. Thus, in Study IV, one modern child-friendly computer-based attention rehabilitation method with precise procedural protocol is introduced. Quite importantly, the findings from the Study IV aim to further guide the emerging field of neuropsychological rehabilitation of attention functions in children with brain injuries in Estonia.

4. AIMS AND HYPOTHESES

The main aim of the present dissertation was to broaden the overall understanding of social-emotional and cognitive aspects of childhood mild TBI.

To fulfill this aim, individual studies of the present dissertation focus more thoroughly on different social-emotional risk factors for mild TBI, social-emotional and cognitive outcome after mild TBI and an applicable computer-based intervention method to remediate attention after childhood brain injury.

The specific objectives were formulated as follows:

1. To identify pre-injury social-emotional behavioral risk signs in different age groups of very young children with mild TBI (Study I).
2. To identify any possible gender-specific social-emotional behavioral risk signs for mild TBI in infants and toddlers (Study II).
3. To examine the social-emotional outcome after early childhood mild TBI (Study I).
4. To examine gender specific social-emotional outcome in young boys and girls after mild TBI in early childhood (Study II).
5. To examine important aspects of cognitive functioning (information processing speed, visual-spatial planning and visual memory) in an acute period of TBI and during follow-up two years after the injury (Study III).
6. To specify the nature of attention difficulties in children with mild TBI (Study IV and unpublished data).
7. To test a computer-based rehabilitation method to remediate attention difficulties in children with brain injuries (Study IV).

In the Study I, it was hypothesized that compared to their non-injured peers, the children with mild TBI would show more pre-injury social-emotional problems and after the injury these problems would tend to get worse. It was also hypothesized that, at least in toddler-years, self-regulation difficulties could be an alarming sign for mild TBI.

In the Study II, the possible gender-specific social-emotional risk signs for mild TBI were addressed and the hypothesis of gender as a distinct contributor in predicting social-emotional outcome after early childhood TBI was tested.

In the Study III, which focused on cognitive outcome after TBI, it was hypothesized that compared to the mildly injured children, the children with more severe TBI would have more serious problems with visual-spatial planning, processing speed and visual memory. Hypothesis that two years after injury, the children with moderate/severe injuries would struggle with visual memory and information processing speed whilst the children with mild TBI would perform within an age appropriate normative ranges, was investigated.

In the first part of the Study IV, the nature of specific attentional impairments in children with mild TBI and epilepsy was investigated and in the second part, results of the pilot study of computer-based attention remediation program were introduced.

5. PATIENTS AND METHOD

Studies I and II

The studies I and II were carried out from December 2005 to May 2009 at Tartu University Hospital's Children's Clinic in the Department of Neurology and Neurorehabilitation, utilizing the same dataset of parental ratings of 35 children with mild TBI (mean age: $M = 34.09$ months, $SD = 19.92$ months) and 70 matched controls (mean age: $M = 33.99$ months, $SD = 19.80$ months). These prospective case-controlled studies used a parental assessment to ascertain pre-injury and post-injury social-emotional behavior in infants and toddlers with mild TBI.

Patients' inclusion criteria included documented mild TBI, age between 3 and 65 months, hospitalization in Tartu University Hospital's Children's Clinic and parental informed consent to participate in the study.

The control group children were recruited from Tartu and Tartu County Family Physician Centers' and were selected on the basis of their matching characteristics to the mild TBI group in terms of sex, age and parents' education.

The follow-up assessment was conducted 9 months ($SD = 3.41$ months) after the first assessment, and 27 children with mild TBI (mean age: $M = 39.26$ months, $SD = 18.35$ months) and 54 matching controls (mean age: $M = 39.25$ months, $SD = 18.41$ months) participated.

The screening tool *Ages and Stages Questionnaires: Social-Emotional (ASQ: SE)* by Squires et al. (2002) was used to assess social and emotional behavior at the baseline and follow-up.

During the first assessment, the parents of children hospitalized with mild TBI and the parents of controls completed the ASQ: SE age-appropriate questionnaire retrospectively describing their child's behavior within the previous 2 weeks.

At follow-up, the children with mild TBI and the controls were re-assessed with age-appropriate ASQ: SE. During the follow-up assessment, the parents were again advised to assess their child's behavior retrospectively within the past 2 weeks.

Shapiro-Wilk's test was applied to control the distribution of the data and as some subscales and single-item scores exhibited non-normal distribution, nonparametric procedures were used throughout the analysis. Mann-Whitney U test was applied to analyze social-emotional behavior between the two groups. As a measure of the effect size after the Mann-Whitney U test, the r (in Study I) or rg (in Study II) were computed. To analyze the within-group long-term effects, Wilcoxon's matched pairs test was applied, followed by the matched-pairs rank biserial correlation as a measure of the effect size. The overall significance level was set to $\alpha = .05$. Statistical data analysis was performed with the statistical data analysis package SPSS Statistics 21.

Study III

The Study III was carried out in Tartu University Hospital's Children's Clinic at the Department of Neurology and Neurorehabilitation from December 2005 to April 2009. 38 patients (26% females; mean age: $M = 9.45$ years, $SD = 2.52$ years) who were hospitalized in Tartu University Hospital's Children's Clinic due to TBI and who were over the age of 6 participated in the Study III.

Patients were evaluated during the acute period of trauma ($M = 5.3$, $SD = 10.1$ days after injury) and again during the follow-up ($M = 2.23$, $SD = 0.93$ years after the injury).

Rey Complex Figure Test and Recognition Trial (RCFT) (Meyers & Meyers, 1996, 2003) was used to assess patients' visual-spatial planning, information processing speed and visual memory. Patients also underwent a neurological evaluation and an interview with parents was conducted.

Participating patients were divided into three groups according to the pediatric brain injury severity categorization proposed by Barker, Scolding, Rowe, and Larner (2004): children with mild, moderate and severe TBI. Due to a small number of children in moderate and severe TBI groups, only two groups were composed for further analyses – the children with mild TBI and children with moderate or severe TBI. Differences in cognitive measures between these two groups in an acute period of injury and during follow-up were analyzed with independent sample *t*-test. Dependent sample *t*-test was used to detect the within-group changes during the two-year period. As a measure of effect size, Cohen's *d* was computed. The overall significance level was set to $\alpha = .05$. Statistical data analysis was performed with the statistical data analysis package SPSS Statistics v22 for Mac.

Study IV

The controlled intervention study was approved by The Research Ethics Committee of the University of Tartu and was conducted between March 2010 and April 2012 in Tartu University Hospital's Children's Clinic. Eight patients between 9 and 12 years of age ($M = 11.14$, $SD = 0.90$ years) with either partial epilepsy ($n = 3$) or mild TBI ($n = 4$) and 18 typically developing children ($M = 10.6$, $SD = 0.66$ years) participated.

The Attention module of FORAMENRehab Cognitive Rehabilitation Software® (FORAMENRehab) was used as a computer-based cognitive intervention tool.

The attention rehabilitation took place during a 6-week period, twice a week, and overall 12 meetings were conducted. Each individual session varied between 30 and 50 minutes. In these sessions, the therapist did not only introduce the tasks, but also motivated and guided the child individually in order to help him/her to cope better with new complicated situations and to generalize learned techniques into everyday context.

The training procedure followed a strict protocol while recognizing the child's current level of abilities. To estimate the effect of intervention, the same

baseline exercises were conducted at the first and the last sessions, and the results of the performance were later compared.

All eight children attended all 12-intervention sessions, thus making the compliance atypically high (100%) for an intervention study.

To determine the long-term effect of the intervention, 7/8 patients were reassessed with baseline exercises 1.63 ($SD = 0.07$) years after the end of the intervention.

The one-time testing of healthy controls composed of a baseline assessment with the FORAMENRehab Attention module and took about 30 minutes.

Statistical data analysis was performed with statistical data analysis package IBM SPSS Statistics v21. Independent sample t -test was used to compare patients' and controls' baseline performance. However, due to a small number of participating patients, Wilcoxon's signed rank test was applied to analyze short- and long-term changes in patients' attention functions. The overall significance level was set to $\alpha = .05$.

6. RESULTS AND DISCUSSION

6.1 Pre-injury difficulties in social-emotional behavior as risk signs for mild TBI

The results of the Study I confirm the viewpoint of pre-existing social-emotional and behavioral problems clearly showing that among children with mild TBI, there are more pre-injury general social-emotional difficulties ($Z = -2.298$; $p = .022$, $rg = 0.28$). The results of the Study I also expand our knowledge of the exact nature of these problems by showing that children with mild TBI tend to have significant pre-injury problems in self-regulation ($Z = -2.825$; $p = .005$; $rg = 0.34$) and in autonomy ($Z = 2.209$; $p = .027$; $rg = 0.21$), and less notable pre-injury difficulties in adaptive functioning compared to typically developing peers ($Z = -1.801$; $p = .072$; $rg = 0.19$) (see Figure 2).

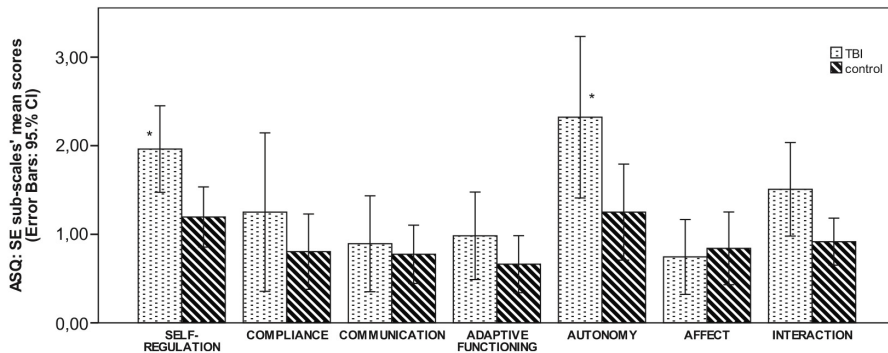


Figure 2. Pre-injury social-emotional behavioral problems – a comparison between mild TBI and control group children (higher scores indicate more problems).

* Statistically significant difference: $p < .05$

Adding to the previous literature, the results of the Study I also indicate that there are different age-specific pre-injury social-emotional risky behaviors. We found that 12-month old babies who, compared to their typically developing peers, demonstrate more overall social-emotional difficulties ($Z = -2.208$, $p = .027$; $rg = 0.81$) with significant problems in affective behaviors ($Z = -2.143$; $p = .032$; $rg = 0.66$), may be especially prone to early childhood mild TBI. 30-month-old toddlers facing more overall social-emotional difficulties ($Z = -2.248$, $p = .025$; $rg = 0.67$) with more salient difficulties in self-regulation ($Z = -2.880$, $p = .004$; $rg = 0.83$) and in communication ($Z = -2.183$, $p = .029$; $rg = 0.54$), and 60-month-olds with specific problems in autonomy ($Z = -2.573$, $p = .011$, $rg = 0.56$) may also be more likely to suffer from mild TBI.

The Study II continued to reveal specific social-emotional risk signs for mild TBI. The findings of the Study II suggest that there indeed are different social-emotional behavioral risk signs for mild TBI in male and female babies and toddlers. Boys who have more self-regulation, interaction and autonomy difficulties, and girls who have worse adaptive functioning, are more likely to incur a mild TBI ($p < .05$) (more detailed information is presented in Table 1).

These findings are at least partially concordant with the work of Morrongiello, et al. (2004), who argued that young boys with compliance issues are at elevated risk for in-home injuries (including falls causing a mild TBI).

While Granic (2010) suggested that gender differences in children's risky behaviors can be detected at least as early as the preschool period, the results of the Study II give reason to presume that some gender-specific risky behaviors are notable even in infants as young as three months.

Among other aspects, the Study II also addressed the issue of gender differences in social-emotional behavior in typically developing children. No significant differences or noteworthy trends in social-emotional behavior between typically developing boys and girls were revealed. Nevertheless, the results of the Study II indicate that among young children with mild TBI, some pre-injury gender differences are present – the boys from mild TBI group have worse pre-injury self-regulation skills than the girls from mild TBI group ($Z = -1.542$, $p = .063$, $r = 0.260$). When acknowledging that social-emotional behavior in typically developing young boys and girls is rather similar, distinctively worse pre-injury self-regulation in young boys from mild TBI group may at least partially explain the highest TBI incidence rate in young boys reported by Ventsel et al. (2008).

In conclusion, according to our data, infants and toddlers with mild TBI display significantly more pre-injury social-emotional difficulties with self-regulation and autonomy than their non-injured peers. Furthermore, important age- and gender specific social-emotional behavioral risk signs for mild TBI can be identified. Pre-injury affective problems in 12-month-olds, self-regulation and communication difficulties in 30-month-olds, and pre-injury autonomy disturbances in 60-month-olds could be seen as risk signs for mild TBI. Therefore, parents and caregivers of little boys who struggle with self-regulation and autonomy issues and parents and caregivers of little girls who have problems with adaptive functioning should also be more attentive and precautionous.

Table 1. Pre-injury gender differences in social and emotional behavior – a comparison between mild TBI and control group children

	Boys				Girls			
	Mild TBI group <i>M (SD)</i>	Control group <i>M (SD)</i>	Mann-Whitney <i>U test</i>		Mild TBI group <i>M (SD)</i>	Control group <i>M (SD)</i>	Mann-Whitney <i>U test</i>	
			<i>z</i>	<i>p</i>			<i>z</i>	<i>p</i>
ASQ: SE total*	1.478 (0.949)	0.883 (0.417)	-1.979	.048	1.204 (0.701)	0.995 (0.591)	-0.954	.349
Self-regulation	2.301 (1.232)	1.313 (1.192)	-3.058	.002	1.716 (1.582)	1.357 (1.386)	-0.753	.461
Compliance	1.667 (2.572)	0.694 (1.415)	-1.218	.207	0.500 (1.581)	1.000 (1.884)	-0.884	.587
Communication	0.909 (1.334)	0.568 (1.074)	-1.213	.222	0.769 (1.293)	0.930 (1.230)	-0.419	.697
Adaptive functioning	0.985 (1.132)	0.889 (1.356)	-0.615	.542	1.378 (1.447)	0.593 (1.088)	-2.129	.033
Autonomy	2.778 (2.408)	1.319 (2.025)	-2.293	.222	1.500 (2.108)	1.125 (2.064)	-0.655	.664
Affect	0.663 (1.033)	0.606 (1.002)	-0.272	.787	0.994 (1.268)	1.042 (1.962)	-0.512	.627
Interaction	1.381 (1.378)	0.803 (0.983)	-1.716	.087	1.205 (0.701)	0.995 (0.591)	-1.014	.318

*ASQ: SE total – Ages and Stages Questionnaires: Social-Emotional total score (higher scores indicates more problematic behaviors)

6.2 Social-emotional behavior after childhood mild TBI

Focusing on social-emotional outcome in the Study I, 9 months after the first assessment, the children with mild TBI were reported to exhibit more general social-emotional behavioral difficulties than the control group children ($Z = -2.298, p = .007; rg = 0.31$). These children with mild TBI were struggling with self-regulation ($Z = -2.886, p = .007; rg = 0.34$), autonomy ($Z = -2.582, p = .010; rg = 0.29$) and social interaction ($Z = -3.620, p < .0001; rg = 0.47$) (see also Figure 3).

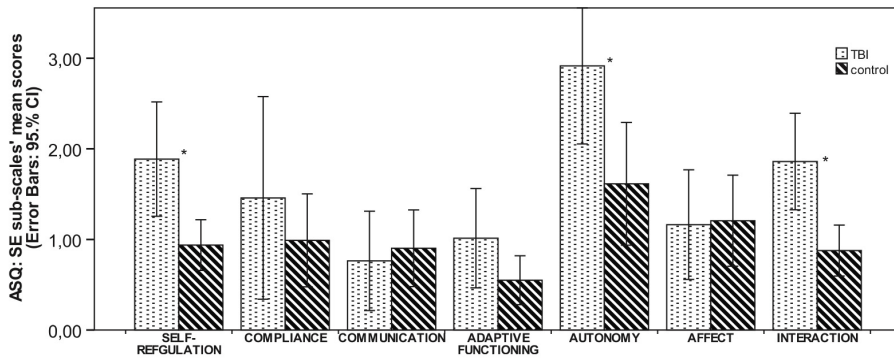


Figure 3. Social-emotional behavioral problems 9 months post-injury – a comparison between mild TBI and control group children (higher scores indicate more problems).

* Statistically significant difference: $p < .05$

More so, the comparison of the results of the baseline assessment and follow-up assessments of mild TBI group children showed that difficulties in social interaction had increased over time ($Z = -2.00, p = .045, rg = 0.33$). A trend towards negative dynamics in behaviors concerning autonomy was also detectable ($Z = -1.94, p = .052; rg = 0.15$).

During the follow-up, we also found that within 9 months, social interaction difficulties in the children with mild TBI had increased, contrary to the control group children who showed notable positive dynamics in social interaction ($Z = -2.064, p = .039, rg = 0.29$). In the development of self-regulation, compliance, communication, adaptive functions, autonomy and affect, no significant differences between mild TBI and control group children were revealed (for details see Figure 4).

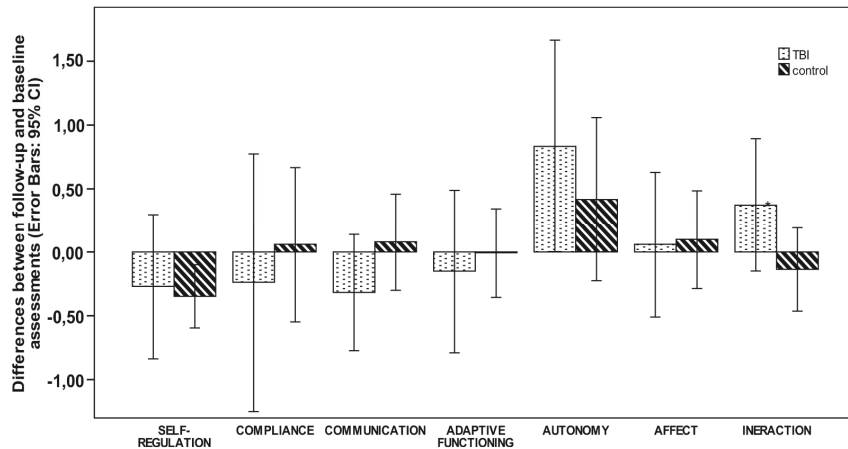


Figure 4. Changes in social-emotional development – a comparison between mild TBI and control group children pre-injury and follow-up assessment. (Score above 0 indicates an increase in social-emotional behavioral problems, while score below 0 indicates a decrease in problems on follow-up assessment).
 * Statistically significant difference: $p < .05$

In the Study II, the results of follow-up assessment of children with mild TBI showed that 9 months post-injury the boys with mild TBI had more difficulties in self-regulation compared to the girls with mild TBI ($Z = -2.043, p < .05, r = 0.403$). A slight trend also suggested more communication difficulties in the boys with mild TBI ($Z = -1.786, p = .096, r = 0.344$).

Compared to the typically developing same gender peers, the boys with mild TBI showed significantly worse results in overall social-emotional behavior ($p < .05$) with salient difficulties in self-regulation and in social interaction ($p < .05$) and the girls with mild TBI showed slight trends towards more social interaction difficulties ($p = .060$; for more details, see Table 2).

The follow-up results of the Study II also showed that after 9 months, both the control group boys and girls were doing remarkably better in self-regulation, while a similar pattern did not describe the mild TBI group. Our results confirm the findings of Rothbart, Sheese, Rosario Rueda, and Posner (2011), who have shown a remarkable improvement in self-regulation skills by the age of 3–4 years in typically developing children. However, when the integrity of the brain development is disrupted, for example due to a diffuse brain injury, the normal development of self-regulation may be affected (Beauchamp & Anderson, 2010; Rothbart et al., 2011).

Table 2. Post-injury gender differences in social and emotional behavior – a comparison between mild TBI and control group children after 9 months

	Boys			Girls			Mann-Whitney			
	Mild TBI group	Control group		Mild TBI group	Control group		U test			
	<i>M (SD)</i>	<i>M (SD)</i>		<i>M (SD)</i>	<i>M (SD)</i>		<i>z</i>	<i>p</i>	<i>r</i>	
ASQ: SE total II*	1.764 (1.248)	0.910 (0.607)	-2.595	1.307 (0.575)	1.166 (0.641)	-0.401	.009	0.383	.699	0.070
Self-regulation II	2.379 (1.588)	1.111 (0.989)	-2.755	1.414 (1.358)	1.035 (1.075)	-0.910	.005	0.406	.374	0.158
Compliance II	1.786 (3.010)	0.962 (1.743)	-0.720	1.000 (2.108)	1.125 (1.898)	-0.397	.511	0.114	.739	0.072
Communication II	1.250 (1.551)	1.000 (1.425)	-0.593	0.303 (0.674)	0.682 (1.423)	-0.455	.586	0.087	.726	0.079
Adaptive functioning II	1.099 (1.417)	0.804 (1.018)	-0.374	0.614 (0.995)	0.386 (0.885)	-0.852	.718	0.055	.422	0.148
Autonomy II	3.393 (2.105)	1.058 (2.141)	-3.335	2.250 (1.845)	2.375 (2.497)	-0.071	.001	0.527	.948	0.013
Affect II	1.068 (1.281)	1.013 (1.722)	-0.568	1.439 (1.494)	1.402 (1.718)	-0.263	.584	0.084	.807	0.045
Interaction II	1.719 (1.280)	0.482 (0.777)	-3.457	2.013 (1.191)	1.273 (0.978)	-1.886	.000	0.510	.060	0.326

*ASQ: SE total – Ages and Stages Questionnaires: Social-Emotional total score (higher scores indicates more problematic behaviors)

In an adult sample, Rassovsky et al. (2006) have shown that after TBI, neurocognitive impairment plays the most prominent role in mediating post-injury adaptive functioning and social outcome. Such poorer social-emotional outcome after childhood mild TBI was also replicated in our Studies I and II, and is an addition to the already existing literature (e.g., Anderson et al., 2012; Andrews, Rose, & Johnson, 1998; Beauchamp et al., 2009; Ewing-Cobbs et al., 2012; Hawley, 2003; Yeates et al., 2004), stating that social interaction difficulties are fairly common after early childhood mild TBI. In accordance with Beauchamp and Anderson's (2010) *SOCIAL* model, impaired social functioning may partially be induced by the prolonged time an injured child needs to process information.

In conclusion, we found that even a mild TBI may have a negative impact on on-going social-emotional development. We also showed that overall social-emotional outcome after mild TBI is somewhat worse for the boys than for girls. More so, our data suggests that 9 months after the injury, the boys continue to do more poorly in self-regulation than the girls. The boys with mild TBI may show worse social interaction and autonomy skills compared to their non-injured same-gender peers, whereas little girls who had suffered mild TBI only show worse social interaction compared to their non-injured same-gender peers.

To sum up, the results of social-emotional behavioral outcome after mild TBI from the Study I and Study II give reason to presume that social interaction skills are most vulnerable to the negative effect of mild TBI. More so, our findings support the previous work of Anderson, et al. (2013), Ganesalingam et al. (2011), and Ryan et al. (2013), who have shown remarkable declines in social competence: especially in social interaction, communication, and the amount and quality of social contact in children after early childhood TBI.

6.3 Short- and long-term cognitive outcome after childhood TBI – focus on attention, processing speed, visual-spatial planning and visual-spatial memory

Early childhood TBI affects not only social and emotional outcomes, but has a negative impact on various aspects of cognition. The findings from the Study III showed that soon after TBI, more than 1/3 of injured children were performing below the age expectations in terms of information processing speed, and as many struggle with visual-spatial planning. To be more precise, in the Study III, mild impairment in visual-spatial planning was evident in 10.5%, moderate impairment in 5.3% and severe impairment in visual-spatial planning in 17.4% of the children with TBI.

When difficulties in visual-spatial planning and information processing speed were more thoroughly addressed, our data suggested that the children with mild TBI were showing visual-spatial planning impairments and slowness

in information processing speed similar to the children with more severe injuries (moderate/severe TBI group).

The results of the Study IV also replicated the viewpoint of slowed information processing speed after childhood TBI. The results of the Study IV showed that compared to the typically developing children, the patients (5/8 with mild TBI) tended to need more time to successfully complete tasks that require focusing attention to visual ($t = 1.749$, $p = .093$, $d = 0.676$) or auditory ($t = 4.432$, $p < .001$, $d = 1.538$) stimuli. The trend also suggested that the patients had more difficulties with tasks requiring complex attention – they tended to give more false responses ($t = 0.413$, $p = .069$, $d = 0.28$), make fewer correct picks ($t = -2.187$, $p = .056$, $d = -1.439$) and miss stimuli more often ($t = 2.187$, $p = .056$, $d = 1.439$) than their typically developing peers. In terms of the tracking and sustained attention, no significant differences between the patients and typically developing age-matched peers were revealed (see Figure 5).

More detailed analyses of this data suggested that the children with mild TBI were the worst in focusing attention to auditory stimuli compared to the children with epilepsy and controls ($\chi^2 = 10.749$; $df = 2$; $p < .05$) (our unpublished data).

As already stated previously, the children with TBI are a heterogeneous group and may exhibit various cognitive complaints after injury (memory dysfunctions included). That said, in an acute period of TBI, more than half (52.6%) of the children with TBI participating in the Study III showed pathological memory profiles. Difficulties with information retrieval were among common complaints in 39.5% of the children with TBI, but for some children, the storage (7.9%) or encoding of visual-spatial information (5.3%) was the most challenging.

Further analyses of these memory difficulties showed that mild to moderate or even severe impairments in immediate recall of visual-spatial material were present in 23.7% of the children with TBI and in delayed visual-spatial recall in 26.3% of the children with TBI. Impairments in recognition of visual-spatial material were less common and were documented only in 5.3% children with TBI.

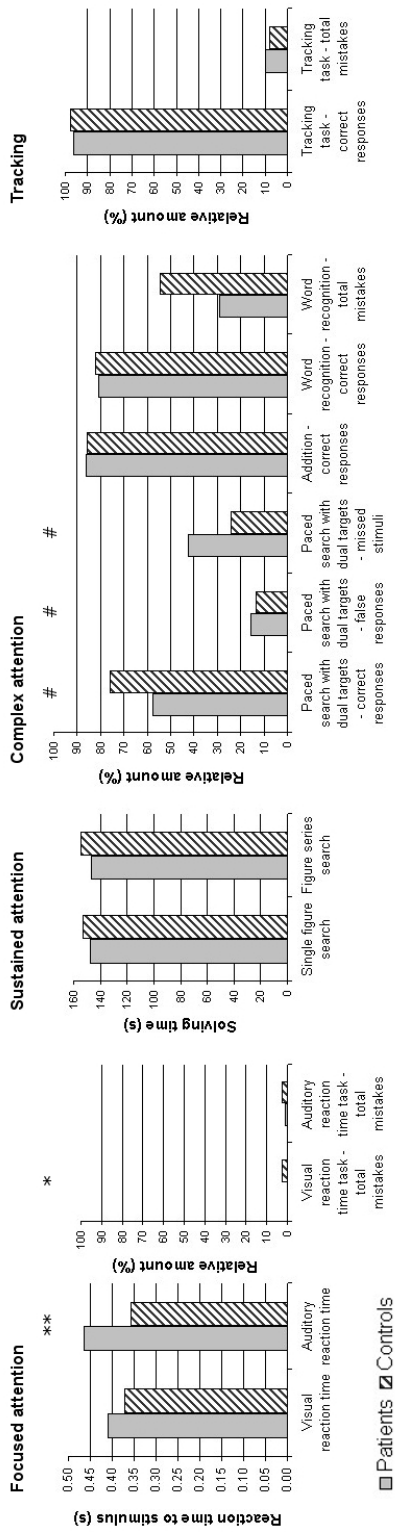


Figure 5. Differences in attention functions – a comparison of baseline performances of attention tasks in patients and controls. Differences between groups are shown as follows (** $p < .001$; * $p < .05$; # $p < .08$).

In the Study III, we also examined memory profile patterns of children with mild and moderate/severe injuries separately. The results showed that in our sample memory profile was pathological in 61.5% of the children with mild TBI and in 33.3% of the children with moderate/severe TBI. Furthermore, in an acute period of injury the children with mild TBI did not do significantly better in immediate and delayed visual-spatial recall tasks than the children with moderate/severe injuries, and a slight trend even suggested better delayed recall in the children with moderate/severe injuries compared to the mildly injured children $t(36) = -1.885$; $p = .068$; $d = -0.675$ (for more details, see Table 3).

Table 3. Differences in visual-spatial memory between children with mild and moderate/severe TBI in an acute period of TBI and during a follow-up

	Rey Complex Figure Test and Recognition Trial memory test results				
	Children with mild TBI <i>M1 (SD1)</i>	Children with moderate/severe TBI <i>M2 (SD2)</i>	<i>t</i>	<i>p</i>	<i>df</i>
<i>Acute Period of TBI</i>					
Immediate recall	44.50 (13.70)	48.75 (10.98)	-0.942	.353	36
Delayed recall	42.08 (12.67)	50.08 (10.96)	-1.885	.068	36
Recognition total correct	49.00 (9.96)	53.25 (8.56)	-1.273	.211	36
<i>Follow-up period after TBI</i>					
Immediate recall	47.27 (10.62)	48.00 (15.86)	-0.168	.868	36
Delayed recall	44.92 (10.68)	48.08 (15.81)	-0.726	.473	36
Recognition total correct	55.65 (8.30)	54.58 (11.88)	0.322	.750	36

Whether these results are only descriptive of our somehow biased sample and/or cause of other unexpected methodological shortcomings of the study, or represent a more accurate estimate of the nature of visual memory problems in an acute period of childhood TBI, will be more thoroughly addressed in our future research. Nevertheless, one possible interpretation of slightly better visual memory in the children with moderate/severe injuries in an acute period of TBI could be due to pre-injury differences in memory performance. While most of the milder brain injuries in childhood are caused by falls and traffic accidents (as a pedestrian or as a cyclist) and thus can at least partially be associated with child's own characteristics (inattention, impulsivity, noncompliance etc.), more severe injuries tend to result from motor vehicle accidents where children under 16 years of age are inactive passengers.

The results of the Study III also showed that two years post injury all children with TBI showed no significant improvements in visual immediate and delayed recall, but an improvement in visual-spatial recognition was clearly

noticeable $t(37) = -2.653, p = .012, d = 0.52$. More thorough examination however revealed that, this improvement in visual recognition was evident in the mild TBI group $t(25) = 2.950, p = .007, d = 0.579$, but not in the moderate/severe TBI group $t(11) = -0.409, p = .690, d = 0.118$ (see Table 4).

Table 4. Visual-spatial memory in children with TBI: a comparison between acute period of TBI and during a follow-up

	Rey Complex Figure Test and Recognition				
	Trial memory test results				
	Acute period of TBI <i>M1 (SD1)</i>	Follow-up period <i>M2 (SD2)</i>	<i>t</i>	<i>df</i>	<i>d</i>
<i>Children with mild TBI</i>					
Immediate recall	44.50 (13.70)	47.27 (10.62)	1.081	25	0.212
Delayed recall	42.08 (12.67)	44.92 (10.68)	1.236	25	0.242
Recognition total correct	49.00 (9.96)	55.65 (8.30)	2.950*	25	0.579
<i>Children with moderate/severe TBI</i>					
Immediate recall	48.75 (10.98)	48.00 (15.86)	0.190	11	0.055
Delayed recall	50.08 (10.96)	48.08 (15.81)	0.610	11	0.176
Recognition total correct	53.25 (8.56)	54.58 (11.88)	-0.409	11	0.118

* $p < .05$

These findings regarding the improvement of visual recognition are in line with the earlier work of Anderson et al. (1999), who claimed that even when there are no significant differences in memory performance between mildly and more severely injured children during an acute period of injury, the dose-response relationship in favor of children with mild TBI will develop over time, and by the beginning of the second year after the injury, more severely injured children should exhibit more dominant memory difficulties compared to children with milder injuries.

However, in terms of information processing speed recovery, the results of the Study III are more promising than suggested by Anderson and Pentland (1998). In the Study III, the two years post brain injury, information processing speed of all children with TBI had improved significantly $t(37) = 2.485; p = .018, d = 0.547$, but in visual-spatial planning skills, no significant change – improvement or decline – was evident. More so, the children with mild TBI did not perform significantly better or worse in visual-spatial planning or visual information processing compared to children with moderate/severe injuries.

When parents and teachers acknowledge attention, information processing speed and specific visual-spatial memory impairments at the time children return to school after the injury, they can help them better cope with the aftermath of the injury and challenges in specific cognitive skills.

In conclusion, our results suggest that soon after injury, half of the children with TBI face visual-spatial memory dysfunction, while one-third struggle because of slowed processing speed and/or impaired visual-spatial planning. These cognitive deficits, especially the impairments in information processing speed, may be accompanied by difficulties in focusing attention to visual and/or auditory stimuli.

For a number of children, these cognitive difficulties are persistent – two years after the injury, over one-third of children with TBI still struggle with visual-spatial planning and even more face specific visual-spatial memory problems. Specific attention and in some cases even extensive intervention/remediation is needed for children who continue to demonstrate cognitive dysfunctions after an acute period of injury.

6.4 Improving attention after childhood mild TBI

In the Study IV, FORAMENRehab Attention module as a suitable method of attention remediation for children with mild TBI and partial epilepsy was tested.

After the 6-week intervention, patients' (5/8 with mild TBI) sustained attention ($Z = -2.366, p < .05$) and complex attention ($Z = -2.201, p < .05$) showed significant improvements. Nevertheless, no significant changes were detected in focused attention and tracking. That said, in the tracking task, children with mild TBI showed individual positive progress, whereas children with partial epilepsy did not demonstrate any notable improvements during the 6-week period (unpublished data).

Study IV also demonstrated some long-term positive effects of attention trainings – even 1.63 years after the end of the intervention, patients' reaction time to auditory stimuli was improved ($Z = -2.028, p < .05$). Improvement of reaction time was also noticeable in sustained attention: a slight trend towards faster performance was evident in Symbol Search task ($Z = -1.826, p = .068$) and in Figure Series Search task ($Z = -2.028, p < .05$). In complex attention, positive dynamics were seen in Word Recognition task – the amount of correctly recognized words had increased ($Z = -1.826, p = .068$) and incorrect choices ($Z = -1.753, p = .080$) and missing words ($Z = -1.826, p = .068$) slightly decreased. Again, in focused attention and in tracking, no significant improvements were detected.

The issue of whether the lack of a significant improvement in focused attention and tracking tasks was due to methodological difficulties (e.g., inappropriate task difficulty at baseline, too few trainings) or due to ineffectiveness of the interventions, was not in the scope of the pilot study (Study IV). This will definitely be addressed in future research to improve the overall viability of the presented attention remediation program.

In conclusion, improving attention is the key in the enhancement of all cognitive functions in children. The findings of Study IV suggest that FORAMEN-Rehab Attention module, incorporated into a 6-week, therapist guided computer-

based intervention, is a promising rehabilitation method to improve attention functions in children with mild TBI. Therefore, the research will continue with larger samples. To better address the attention dysfunctions most common in children with mild TBI, continuing improvements in tasks measuring and training tracking, and especially focused attention skills, are much appreciated.

Taken together, these preliminary results suggest that the modern computer-based rehabilitation design could be useful in the remediation of attention in children with mild TBI. Yet, it is acknowledged that continuing systematic research on the effectiveness and applicability of the proposed design is needed.

7. GENERAL SUMMARY AND CONCLUSION

The results of the Study I and Study II presented above improve our knowledge of pre-injury age- and gender-specific differences in social-emotional behavior in children with mild TBI, clearly suggesting that problematic self-regulation and too independent behavior puts young children at an elevated risk for mild TBI. These findings suggest that the differences in social-emotional behavior are not only innate tendencies but can be attributed to an age-related and gender-role development. This knowledge has practical implications. Thus, faced with these differences, knowledge about age- and gender-specific social-emotional behaviors that makes infants and toddlers more vulnerable to early childhood mild TBI should be incorporated into TBI and other accidental injury prevention programs.

The results from the individual studies of the present thesis confirm the viewpoint that children with TBI face various cognitive challenges.

The findings from the Study III and Study IV show that after childhood TBI, different aspects of attention, information processing, visual-spatial planning and memory may be impaired. More so, the results also demonstrate that regarding memory problems, information retrieval difficulties are the most common complaints immediately after injury. In some of the children with TBI, these retrieval difficulties are due to the failure to recall immediate but more often, delayed visual-spatial information. Furthermore, information retrieval difficulty may also be a very common complaint in the following years to come. While injury severity did not seem to have a significant impact on the short- and long-term outcome of retrieval processes, the results of our Study III suggest that compared to moderately/severely injured children, the recovery of visual-spatial recognition is significantly more noticeable in children with mild TBI.

On a more positive note, the results of the Study III suggest that slowness in information processing will likely resolve within two years after the injury. Sadly though, the same recovery trajectory could not be seen in cases of visual-spatial planning deficits. In addition, post-injury attention difficulties, planning problems and memory dysfunction (also replicated in our Studies III and IV) may add on to the mediation of worse social and functional outcomes after mild TBI. Therefore, the exact nature of the effect that a slowed processing speed after mild TBI may have on very young children's social interaction, should be addressed in future research. This knowledge could help to determine and develop the most suitable intervention methods to improve the overall social-emotional and cognitive outcomes after early childhood mild TBI.

The beneficial effect of computer-based and therapist guided cognitive trainings to the overall functional outcome after childhood brain injury are renowned. Whether these positive effects can be substantiated by the active therapist involvement, specific cognitive training tasks, motivation and the time put into intervention, or the interplay of all of these factors, again, will be an area for future research.

That said, the results of our pilot study (Study IV) indicate that after our computer-based therapist guided attention remediation program, patients' sustained attention and complex attention improved. Moreover, parents and teachers of participating patients also stated positive changes in behavior and increase in academic achievement, suggesting the generalized effect of the intervention.

The proposed intervention method used in the pilot study had some shortcomings (e.g., the task training tracking and focusing of visual and/or auditory attention did not seem to be the best fit for children with mild TBI). In the continuing cognitive intervention research, these shortcomings are being amended as appropriate and diagnosed-specific attention dysfunctions (mainly the slowed processing speed and deficits in focusing visual and/or auditory attention in children with mild TBI) are taken into consideration.

To sum up, mild TBI in early childhood may have a negative impact on the ongoing social-emotional and cognitive development. Therefore, the prevention of such injuries is crucial. Even in early ages, different age- and gender-specific social-emotional risky behaviors for mild TBI can be detected. To improve mild TBI prevention during early childhood, parents and caregivers of infants and toddlers should be informed and educated about these risky behaviors. Regardless of the causes, if a child sustains mild TBI, timely detection of emerging or ongoing social-emotional and cognitive difficulties along with appropriate intervention is important.

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SUMMARY IN ESTONIAN

Lapseea kerge ajutrauma: traumaeelne sotsiaal-emotsionaalne käitumine, sotsiaal-emotsionaalne käitumine ja kognitiivsed võimed ajutraumajärgselt ning soovitud tähelepanuhäirete rehabilitatsiooniks

Traumaatiline ajukahjustus ehk ajutrauma on üks sagedasemaid laste invaliidisuse põhjuseid. Eestis on laste ajutrauma esinemissagedus eriti kõrge (369: 100 000) ja kõige rohkem esineb ajutraumasid kuni nelja aasta vanuste poiste hulgas.

Kuigi enamik ajutraumaga lastest paraneb hästi, võivad osadel lastel siiski pärast traumat ilmneda erinevad neuroloogilised, kognitiivsed või sotsiaal-emotsionaalsed probleemid. Sagedased on probleemid nii tähelepanu, mälu, õppimise kui ka impulsikontrolliga. Nimetatud häired ei pruugi avalduda kohe pärast ajutraumat, vaid oluliselt hiljem, kui laps on vanemaks saanud.

Lapseeas saadud ajutrauma korral tekkinud kõrvalekalded kognitiivsetes võimetes ja sotsiaal-emotsionaalsetes protsessides on väga hästi käsitletud Beauchampi ja Andersoni (2010) *SOCIAL*-mudelil. See mudel on ka käesoleva doktoritöö üheks olulisimaks teoreetiliseks aluseks. Beauchamp ja Anderson usuvad, et pärast ajutraumat sõltub lapse üldine toimetulek just aju bioloogilisest küpsusest, ajukahjustuse raskusest, tähelepanust ja täidesaatvatest funktsioonidest, sotsiaal-emotsionaalsetest ja kommunikatiivsetest protsessidest, isiksuse eripäradest ning ümbritseva keskkonna ja käitumise vastastikmõjust.

Beauchampi ja Andersoni mudelist lähtudes keskendutigi käesolevas doktoritöös ajutraumaga laste sotsiaal-emotsionaalsete protsesside ja kognitiivsete võimete täpsemale uurimisele. Doktoritöö fookuses on eelkõige lapseea kerge ajutrauma ning doktoritöö käigus läbi viidud uuringutes pöörati erilist tähelepanu nii kerge ajutraumaga seotud võimalikele vanuse- ja soospetsiifilistele sotsiaal-emotsionaalsetele probleemkäitumistele kui ka erinevatele kognitiivsetele ja sotsiaal-emotsionaalsetele häiretele ajutraumajärgselt. Lisaks tutvustatakse doktoritöös põhjalikumalt ühte kaasaegset arvutipõhist tähelepanufunktsioonide arendamiseks mõeldud treeningprogrammi ja selle sobilikkust ajutraumaga laste tähelepanufunktsioonide parandamiseks.

Doktoritöö esimeses osas uuriti, kas kerge ajutraumaga lastel esineb juba enne traumat tavapärasest enam sotsiaal-emotsionaalseid probleeme. Uuringutes I ja II osales 35 kolme kuu kuni viie aasta ja viie kuu vanust kerge ajutraumaga last, kes ajavahemikul 2005. a detsember kuni 2009. a mai olid hospitaliseeritud SAs Tartu Ülikooli Kliinikumi Lastekliinik. Uuringusse kaasatud ajutraumaga laste vanemad täitsid kohe pärast lapse hospitaliseerimist „Vanuste ja staadiumide küsimustiku” iseloomustades oma lapse käitumist kahe nädala jooksul enne õnnetust. Ajutraumajärgse sotsiaal-emotsionaalse käitumise kaugtulemuste hindamiseks täitsid vanemad lapse vanusele vastava uue küsimustiku üheksa kuud pärast ajutraumat. Kontrollgrupp koosnes 70 sama vanast

ja samast soost normarenguga lapsest. Ka kontrollgruppi kuulunud laste vanemad täitsid lapse vanusele vastava „Vanuste ja staadiumide küsimustiku” kahel korral – uuringu alguses ning üheksa kuud pärast esimese küsimustiku täitmist.

Meie uuringu tulemustest selgus, et kerge ajutraumaga imikute ja väikelaste hulgas on juba enne traumat sagedasemad erinevad sotsiaal-emotsionaalsed probleemid. Seejuures eristasid just kehvem enesekontroll ja liigne iseseisvus kerge ajutrauma grupi lapsi kontrollgruppi kuulunud eakaaslastest (uuring I). Veelgi enam, väga selgelt eristusid ajutrauma gruppi kuulunud laste vanuse- ja soospetsiifilised sotsiaal-emotsionaalsed probleemid. Nii näiteks on ajutraumadest (eriti kukkumistest) ohustatumad afektiivsete probleemidega 12 kuu vanused imikud, suhtlemis- ja enesekontrolliraskustega 30 kuu vanused väikelapsed ja liiga iseseisvad ja sõltumatud 5-aastased lapsed. Sagedamini esineb ajutraumasid ka liiga iseseisvatel ja/või kehvema enesekontrolliga poistel ja eakohasest nõrgemate adaptiivsete võimetega tüdrukutel. Ka üheksa kuud pärast õnnetust ilmnis kerge ajutrauma läbi teinud lastel tervete eakaaslastega võrreldes rohkem sotsiaal-emotsionaalseid probleeme. Nii näiteks olid ajutrauma läbi teinud poisid jätkuvalt kehvema enesekontrolliga ning liiga iseseisvad ja sõltumatud. Lisaks oli ajutraumajärgselt nii väikestel poistel kui ka väikestel tüdrukutel aga välja kujunenud raskused teistega suhtlemisel.

Seega näitavad meie uuringu tulemused, et varases lapseas saadud ajutrauma järgselt kahjustub oluliselt just teistega suhtlemise võime. Beauchampi ja Andersoni (2010) käsitluste järgi on sotsiaalse suhtlemise häired vähemalt osaliselt seotud ajutraumast tingitud kognitiivsete häiretega (sh info aeglasema töötuse kiiruse ja mäluhäiretega).

Infotöötuse kiiruse ja mälu olulist halvenemist pärast ajutraumat kinnitasid ka meie III uuringu tulemused. 2005. a detsembrist kuni 2009. a maini SA Tartu Ülikooli Kliinikumi Lastekliiniku neuroloogia ja neurorehabilitatsiooni osakonnas läbi viidud uuringus osales 38 ajutraumaga (sh 21 kerge ajutraumaga) last vanuses 6–16 aastat, kelle infotöötuse kiirust, visuaalruumilist planeerimisvõimet ja visuaalset mälu hinnati nii trauma akuutses faasis kui ka kaks aastat pärast traumat Rey-Osterrieth'i kompleksse kujundi testiga.

Uuringu tulemustest selgus, et kohe pärast ajutraumat esines ligi pooltel ajutrauma läbi teinud lastest visuaalse mälu häireid, ühel kolmandikul oli raskusi visuaalruumilise planeerimisega ja üks kolmandik lastest töötles visuaalset informatsiooni eakohasest aeglasemalt.

Mäluprobleemide täpsemal uurimisel selgus, et ajutrauma läbi teinud lastele valmistas raskusi nii visuaalse info kohene kui ka hiline vaba meenutamine, samas kui visuaalse info äratundmisega olulisi raskusi ei olnud. Kerge ajutraumaga laste põhjalikumal uurimisel selgus, et trauma akuutses faasis oli visuaalne mälu häiritud 61,5% uuringus osalenud kerge ajutraumaga lapsest – suur osa nendest lastest oli hädas visuaalse info taastamisega. Raskused visuaalse info salvestamise või visuaalse info kodeerimisega olid pigem harvad ja esinesid vaid üksikutel kerge ajutraumaga lastel.

Paljude laste jaoks olid kirjeldatud kognitiivsed häired püsivad – kaks aastat pärast ajutraumat oli ühel kolmandikul ajutraumaga lastest ikka raskusi visuaalruumilise planeerimisega ja ligi pooltel esines visuaalse mälu häireid.

Kui dünaamikas ei ilmnenu kerge ega ka mõõduka/raske ajutraumaga laste visuaalse info koheses ja hilises meenutamises olulisi muutusi, siis visuaalse info äratundmine paranes märgatavalt just kerge ajutraumaga lastel, aga mitte mõõduka ja raske ajutraumaga lastel. Need tulemused on osaliselt kooskõlas ka Andersoni ja tema kolleegide uuringutulemustega, kes juba 1999. aastal avaldatud uurimuses väitsid, et kui ka trauma akuutses faasis ei esine kerge, mõõduka ja raske ajutraumaga laste mälu funktsioonides olulisi erinevusi, siis aasta pärast ajutraumat on kergema ajutraumaga laste mälu funktsioonid oluliselt paremad, võrreldes raskema ajutrauma läbi teinud lastega. Veel selgus meie III uuringu tulemustest, et visuaalse info töötamise kiiruse häired on iseloomulikud vaid trauma akuutses faasis – kaks aastat pärast õnnetust oli uuringus osalenud laste infotöötamise kiirus eakohane.

Lisaks visuaalse mälu, visuaalruumilise planeerimisvõime ja visuaalse info töötlemise kiiruse häiretele võivad ajutraumajärgselt ilmneda ka raskused keskendumisel visuaalsetele ja/või auditoorsetele stiimulitele (IV uurimus). IV uuringus leidsime, et ülesannetes, kus tuleb tähelepanu koondada visuaalsetele või auditoorsetele stiimulitele, on ajukahjustusega lapsed tervetest eakaaslastest aeglasemad. Ajavahemikul märts 2010 kuni aprill 2012 läbi viidud seksu-uuringus osales kaheksa 10–12 aasta vanust ajukahjustusega (viis kerge ajutrauma ja kolm epilepsia diagnoosiga) last ning 18 samaealist normarenguga last. Kuue nädala kestel, iga nädal kahel korral, võtsid uuringusse kaasatud ajukahjustusega lapsed osa arvutipõhisest erinevaid tähelepanufunktsioone arendavast treeningust *ForamenRehab*. Selleks, et treeningute efektiivsust ja laste motivatsiooni suurendada ja õpitut paremini igapäevaellu rakendada, toimus treeningu terapeudi juhendamisel. Pärast kuus nädalat kestnud treeningut ilmnes ajukahjustusega laste tähelepanu püsivuses ja komplekses tähelepanus oluline positiivne dünaamika. Ajukahjustusega laste fokuseeritud tähelepanu ja seiramise võime selle aja jooksul aga oluliselt ei paranenud. Kas treeningutejärgselt kerge ajutraumaga laste fokuseeritud tähelepanu ja seiramise võime tõesti ei parane või ei võimaldanud kasutatud uuringumetoodika paranemise olemust piisavalt täpselt hinnata, sellele püüame vastuse leida jätkuuringutes.

Nii laste kui ka lastevanemate subjektiivne tagasiside ja pilootuuringu esmased tulemused kinnitasid aga treeningute positiivset mõju – terapeudi juhendamisel *ForamenRehab* programmiga tähelepanufunktsioonide treenimine parandab kerge ajutraumaga laste tähelepanuvõimet.

Lõpetuseks, ka kerge ajutrauma varases lapseas võib avaldada negatiivset mõju lapse edasisele sotsiaal-emotsionaalsele ja kognitiivsele arengule. Üheks parimaks viisiks selliseid soovimatuid tagajärgi ära hoida, on ajutraumat ennetada. Meie uuringutulemustest selgus, et juba varases eas on võimalik tuvastada erinevaid soole ja vanusele omaseid ajutraumaga seotud sotsiaal-emotsionaalseid riskikäitumisi. Lapsed, kellel sellised käitumisjooned ilmnevad, vajavad erilist tähelepanu ja suunamist. Seega on oluline teavitada vane-

maid ja ka teisi väikelastega tegelevaid täiskasvanuid erinevate vanusele ja soole omaste sotsiaal-emotsionaalsete probleemkäitumiste osas. Laps, kes siiski õnnetusse satub ja kerge ajutrauma saab, vajab aga olemasolevate ja/või tekkinud sotsiaal-emotsionaalsete ja kognitiivsete probleemide kiiret märkamist ning sobilike sekkumisstrateegiatega rakendamist juba probleemide ilmnemise varases etapis.

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