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Theory of mind after mild TBI in preschool children : A longitudinal perspective

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Résumé

Les enfants d’âge préscolaire (≤ 5 ans) sont plus à risque de subir un traumatisme crânio-cérébral (TCC) que les enfants plus agés, et 90% de ces TCC sont de sévérité légère (TCCL). De nombreuses études publiées dans les deux dernières décennies démontrent que le TCCL pédiatrique peut engendrer des difficultés cognitives, comportementales et psychiatriques en phase aigüe qui, chez certains enfants, peuvent perdurer à long terme. Il existe une littérature florissante concernant l'impact du TCCL sur le fonctionnement social et sur la cognition sociale (les processus cognitifs qui sous-tendent la socialisation) chez les enfants d'âge scolaire et les adolescents. Or, seulement deux études ont examiné l'impact d'un TCCL à l'âge préscolaire sur le développement social et aucune étude ne s'est penchée sur les répercussions socio-cognitives d'un TCCL précoce (à l’âge préscolaire). L'objectif de la présente thèse était donc d'étudier les conséquences du TCCL en bas âge sur la cognition sociale. Pour ce faire, nous avons examiné un aspect de la cognition sociale qui est en plein essor à cet âge, soit la théorie de l'esprit (TE), qui réfère à la capacité de se mettre à la place d'autrui et de comprendre sa perspective.

Le premier article avait pour but d'étudier deux sous-composantes de la TE, soit la compréhension des fausses croyances et le raisonnement des désirs et des émotions d'autrui, six mois post-TCCL. Les résultats indiquent que les enfants d'âge préscolaire (18 à 60 mois) qui subissent un TCCL ont une TE significativement moins bonne 6 mois post-TCCL comparativement à un groupe contrôle d'enfants n'ayant subi aucune blessure.

Le deuxième article visait à éclaircir l'origine de la diminution de la TE suite à un TCCL précoce. Cet objectif découle du débat qui existe actuellement dans la littérature. En effet, plusieurs scientifiques sont d'avis que l'on peut conclure à un effet découlant de la blessure au cerveau seulement lorsque les enfants ayant subi un TCCL sont comparés à des enfants ayant subi une blessure n'impliquant pas la tête (p.ex., une blessure orthopédique). Cet argument est fondé sur des études qui démontrent qu'en général, les enfants qui sont plus susceptibles de subir une blessure, peu importe la nature de celle-ci, ont des caractéristiques cognitives pré-existantes (p.ex. impulsivité, difficultés attentionnelles). Il s'avère donc possible que les difficultés que nous croyons attribuables à la blessure cérébrale étaient présentes avant même que l'enfant ne subisse un TCCL. Dans cette deuxième étude, nous avons donc comparé les performances aux tâches de TE d'enfants ayant subi un TCCL à ceux d'enfants appartenant à deux groupes contrôles, soit des enfants n'ayant subi aucune blessure et à des pairs ayant subi une blessure orthopédique. De façon générale, les enfants ayant subi un TCCL ont obtenu des performances significativement plus faibles à la tâche évaluant le raisonnement des désirs et des émotions d'autrui, 6 mois post-blessure, comparativement aux deux groupes contrôles. Cette étude visait également à examiner l'évolution de la TE suite à un TCCL, soit de 6 mois à 18 mois post-blessure. Les résultats démontrent que les moindres performances sont maintenues 18 mois post-TCCL. Enfin, le troisième but de cette étude était d'investiguer s'il existe un lien en la performance aux tâches de TE et les habiletés sociales, telles qu'évaluées à l'aide d'un questionnaire rempli par le parent. De façon intéressante, la TE est associée aux habiletés sociales seulement chez les enfants ayant subi un TCCL. Dans l'ensemble, ces deux études mettent en évidence des répercussions spécifiques du TCCL précoce sur la TE qui

persistent à long terme, et une TE amoindrie seraient associée à de moins bonnes habiletés sociales.

Cette thèse démontre qu'un TCCL en bas âge peut faire obstacle au développement sociocognitif, par le biais de répercussions sur la TE. Ces résultats appuient la théorie selon laquelle le jeune cerveau immature présente une vulnérabilité accrue aux blessures cérébrales. Enfin, ces études mettent en lumière la nécessité d'étudier ce groupe d'âge, plutôt que d'extrapoler à partir de résultats obtenus avec des enfants plus âgés, puisque les enjeux développementaux s'avèrent différents, et que ceux-ci ont potentiellement une influence majeure sur les répercussions d'une blessure cérébrale sur le fonctionnement sociocognitif.

Mots-clés : Pédiatrie, Préscolaire, Traumatisme crânio-cérébral, Commotion cérébrale, Cognition sociale, Habiletés sociales, Théorie de l'esprit, Fausses croyances, Long terme, Longitudinal

Abstract

Preschool children (≤ 5 years old) are at particular risk of sustaining traumatic brain injury (TBI) and 90% of these injuries are mild in nature (mTBI). A substantial amount of research has provided evidence of acute and, in more isolated cases, long-term cognitive, behavioral, and psychiatric consequences following mTBI. In the last two decades, there has been an increase in scientific attention dedicated to the social and socio-cognitive (the cognitive functions that underpin socialisation) sequelae of pediatric mTBI; however, research has almost exclusively been conducted with school-aged children and adolescents. Thus, the literature concerning the social repercussions of mTBI remains comparatively sparse in preschool children, with only two studies that have examined social competence following mTBI. No study has investigated the consequences of early (preschool) mTBI on social cognition. Therefore, the overall objective of this thesis was to expand our understanding of the impact of preschool mTBI on social cognition. More specifically, we addressed an aspect of social cognition that typically emerges during the preschool years, that of theory of mind (ToM), known as the capacity to put oneself in others' shoes and understand their perspective.

The first article examined two subcomponents of ToM, that of false belief understanding and desires and emotions reasoning, 6 months post-mTBI. The findings indicate that preschool children (18 to 60 months) who sustain mTBI have significantly poorer ToM skills compared to typically developing peers 6 months post-injury.

The second article focused on the debate in the mTBI literature concerning the most appropriate control group for isolating outcomes that are specific to brain injury. Indeed, it is argued that the choice of the control group (community controls *vs.* injured counterparts) is of paramount importance because it dictates the conclusions that can be drawn in TBI research. It is argued that brain-injury-specific effects constitute a valid conclusion only when compared to injured peers because in general, children who sustain accidental injuries (whether orthopedic or to the head) share certain pre-existing cognitive characteristics (e.g., impulsivity, attentional difficulties) that not only make them more accident-prone but may also be the origin of post-mTBI difficulties. Thus, the aim of the second paper was to determine whether the poorer ToM skills detected in preschool children with mTBI are the result of a general-injury effect or a brain-injury-specific effect. A second goal of this article was to examine the evolution of ToM skills following mTBI, from 6 months to 18 months post-injury. To do so, we compared children with mTBI to both a community control group and an orthopedic injury (OI) control group. The findings indicate that children who sustain mTBI performed worse on the desires and emotions reasoning task 6 months post-injury compared to both injured and uninjured counterparts, and this discrepancy in performance was maintained 18 months post-mTBI. Lastly, the third goal of this study was to investigate the link between performances on ToM tasks and social abilities, as measures by parental questionnaires. Overall, these two studies demonstrate a persistent brain-injury-specific effect on ToM skills following early mTBI, and poorer ToM skills are associated with reduced social functioning.

This thesis provides evidence that early mTBI can interfere with socio-cognitive development, notably in terms of its repercussions on ToM. These findings support the theory according to

which the young, immature brain is more vulnerable to brain insult. Importantly, our studies demonstrate that extrapolation from conclusions drawn with older pediatric age groups may be erroneous because the developmental issues faced by preschool children are fundamentally different. Indeed, neurodevelopmental immaturity may be a driving force that dictates the impact of mTBI on socio-cognitive functioning.

Keywords : Pediatric, Preschool children, Traumatic brain injury, Concussion, Social cognition, Social skills, Perspective taking, Theory of mind, False belief understanding, Long-term

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List of acronyms

ABAS = Adaptive Behaviour Assessment System

ADHD = Attention Deficit Hyperactivity Disorder

ASD = Autism Spectrum Disorder

AOC = Alteration of Consciousness

Bayley–III = Bayley Scales of Infant and Toddler Development, Third Edition

CATCH = Canadian Assessment of Tomography for Childhood Head Injury

CBCL = Child Behavior Checklist

CHALICE = Children's Head Injury Algorithm of Important Clinical Events

CT = Computed Tomography

DAS–4 = Dyadic Adjustment Scale

FAD = Family Assessment Device

FBU = False Belief Understanding

GCS = Glasgow Coma Scale

ICU = Intensive Care Unit

IQ = Intelligence Quotient

LOC = Loss of Consciousness

MRI = Magnetic Resonance Imaging

mTBI = Mild Traumatic Brain Injury

OI = Orthopedic Injury

TBI = Traumatic Brain Injury

TDC = Typically Developing Children

ToM = Theory of Mind

PECARN = Pediatric Emergency Care Applied Research Network

PCS = Postconcussive Symptoms

PSI = Parental Stress Index

PTA = Post Traumatic Amnesia

SWI = Susceptibility Weighted Imaging

WPPSI–III = Wechsler Preschool and Primary Scale of Intelligence, Third Edition

List of abbreviations

e.g.	For example
i.e.	In other words

À Dave,

À l'espoir

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Introduction

Pediatric traumatic brain injury (TBI; i.e, sustained before 18 years of age) is the leading cause of death and disability in children worldwide, and can cause serious disruption to a range of physical, cognitive and social functions. Although mild TBI (mTBI) does not typically result in mortality or serious adverse long-term consequences, the injury can nontheless lead to a constellation of symptoms which may interfere with daily life, especially if left untreated. Considering that approximately 80 – 90% of all pediatric TBIs are mild in nature, the investigation and management of mTBI has become a scientific and medical priority. Increasing scientific inquiry concerning the outcome of mTBI has resulted in a better understanding of the injury, too often considered as “benign” and inconsequential. However, most research in the past decades has focused on the most immediate and obvious sequelae following TBI, such as physical injuries, behavioral disturbances, and cognitive difficulties that appear in the acute phase. It is only in recent years that researchers have begun to examine the social consequences of mTBI in children. The literature concerning the presence and nature of social problems following pediatric TBI is thus comparatively sparse. It is likely that the social aspects of brain injury have received less attention because social difficulties do not tend to appear in the acute phase post-injury, but rather in the long-term when social skills are challenged (i.e, due to the burgeoning of more complex socio-cognitive skills that depend on the integrity of these more basic abilities and/or as a result of increasing environmental demands).

The preschool years (≤ 5 years) constitute a period of intense social development, devoted to the emergence of foundational socio-cognitive milestones that set the stage for adequate social interactions across lifespan. Research has also shown that preschoolers are particularly vulnerable to brain insult because of the unique pathophysiological characteristics of head injury in young children, and the immaturity of their neural system. Therefore, preschool children may be at higher risk of experiencing social difficulties following TBI.

A core socio-cognitive ability that develops during the preschool years is that of theory of mind (ToM), which is the capacity to put oneself in others' shoes and see things from their perspective. The expanding literature on ToM in school-aged children and adolescents following TBI evidences impairments in simple and/or complex forms of ToM (depending on age) and on ToM-related functions (e.g., empathy) in youth who have sustained moderate or severe brain injury. To date, the only study to have examined TBI and ToM skills in preschool children looked at the impact of severe TBI in the acute phase, and difficulties were noted in a subcomponent of ToM (false belief understanding). However, no study has explored the long-term socio-cognitive consequences of mTBI in the preschool population. The goal of this thesis was therefore to examine the long term (6 and 18 months post-injury) impact of preschool mTBI on ToM skills.

In this introduction, the theoretical background supporting the rationale for this study will first be put forth. The definitional, epidemiological and pathophysiological characteristics unique to mTBI in children will be discussed to demonstrate the distinct nature of brain injury in a pediatric population. The cognitive, behavioral, and psychiatric sequelae following TBI in children will then be adressed from a developmental point of view, across the range of injury severities and then more specifically, in relation to mTBI. Social problems following pediatric TBI, as well as the link between these and underlying socio-cognitive functions will then be presented. Lastly, methodological considerations in mTBI research will be discussed, followed by the specific thesis objectives and hypotheses.

Pediatric mild traumatic brain injury

Definition

According to the World Health Organization (WHO) Collaborative Center Task Force on Mild Traumatic Brain Injury, mTBI is defined as: "*an acute brain injury resulting from mechanical energy to the head from external physical forces. Operational criteria for clinical identification include : i) one or more of the following : confusion or disorientation, loss of consciousness for 30 minutes or less, post-traumatic amnesia for less than 24 hours, and/or transient neurological abnormalities such as focal signs, seizure, and intracranial lesion not requiring surgery; ii) Glasgow Coma Scale score of 13 – 15 after 30 minutes post-injury or later upon presentation for healthcare. These manifestations of mTBI must not be due to drugs, alcohol, medications, caused by other injuries or treatment for other injuries (e.g., systemic injuries, facial injuries or intubation), caused by other problems (e.g., psychological trauma, language barrier or coexisting medical conditions) or caused by penetrating craniocerebral injury*" (pp. 115; Carroll et al., 2004).

The American Congress of Rehabilitation Medicine (Mild Traumatic Brain Injury Committee, American Congress of Rehabilitation Medicine, & Head Injury Interdisciplinary Special Interest Group, 1993) and the American Academy of Neurology (1997) also recognize that headaches and memory problems are possible clinical manifestations following mTBI. However, many of these symptoms (e.g., confusion, loss of consciousness, headaches, memory problems) cannot be reliably assessed in young children (Hayden, Jandial, Duenas, Mahajan, & Levy, 2007) and there is no clear definition of what constitutes mTBI in preschool children (V. Chan, Thurairajah, & Colantonio, 2015; Greenes, 2003). Also, studies report that loss of consciousness has a sensitivity ranging between 45 to 68% for older children, and only of 3% for toddlers and preschoolers

(Bonadio, 1989; Dietrich, Bowman, Ginn-Pease, Kosnik, & King, 1993; Greenes & Schutzman, 1999). In light of the lack of clear guidelines, the definition reported by Osmond and colleagues (2010) in their study focusing on the development of a clinical decision rule for the use of computed tomography (CT scan) in children with mTBI was used in the current work. Accordingly, we defined suspected accidental mTBI in preschool children as follows: i) a history of trauma or acceleration-deceleration movement applied to the head *and* ii) a Glasgow Coma Score (GCS) of 13 – 15 at the Emergency Department, adapted for children under the age of five (Ewing-Cobbs et al., 1997; Greenes & Schutzman, 1999; Kuppermann, 2008; Quayle et al., 1997; Schutzman et al., 2001) *and* any of the following: history of loss of consciousness or confusion, irritability according to the parents, persistent vomiting, amnesia or worsening headache in a verbal child. MTBI can be categorized as uncomplicated (i.e., negative neuroimaging results) or as complicated (i.e., positive neuroimaging results; Williams, Levin, & Eisenberg, 1990); the current study focused on the former.

Incidence / Prevalence

In the last decades, pediatric mTBI has earned the descriptives of "silent epidemic" and "serious public health concern", because the overwhelming majority of TBIs are mild in nature (approx. 90%) and are not followed up clinically (Bazarian et al., 2005; Buck, 2011; Cassidy et al., 2004; Congeni, 2009; Feinstein & Rapoport, 2000; Kraus, 1995; Marcotte & Gadoury, 2006; McKinlay et al., 2008; Rickels, von Wild, & Wenzlaff, 2010). Although more boys sustain TBI than girls (approximate ratio of 2:1) in older children and adults, in the preschool population, boys and girls are affected in equal proportions (McKinlay et al., 2008). Thurman (2016) estimates that in 2014, 630 000 children were treated in the Emergency Department (ED), 60 000 required hospitalisation and 7500 died of TBI in the United States. Similarly, a Canadian epidemiological study demonstrated a dramatic increase in the number of ED visits for pediatric mTBI in 2011 (Stewart, Gilliland, & Fraser, 2014). Although this data may be the reflection of a genuine increase in the occurrence of mTBI, it is likely that at least part of this spike is due to heigthened awareness of mTBI and of its possible negative consequences in the general population, resulting in accrued medical consultations. Nonetheless, the number of children who sustain mTBI each year remains high and commands medical attention. Birth cohort data indicate that children between birth and 4 years of age constitute a particularly high-risk group (Langlois, Rutland-Brown, & Thomas, 2005). Consistent with this peak, chart reviews of ED presentations and registries demonstrate that children under 5 have the highest attendance rate for suspected brain injury, mostly due to falls and being dropped (Crowe, Babl, Anderson, & Catroppa, 2009; Faul, Xu, Wald, & Coronado, 2010; Hawley, Ward, Long, Owen, & Magnay, 2003; Rutland-Brown, Langlois, Thomas, & Xi, 2006). Additionally, in the last decade, toppled televisions have become a source of head injury in developed countries, especially in young children (Cusimano & Parker, 2015; Lichenstein et al., 2015).

Early years : Increased plasticity or vulnerability?

Theories

The traditionally-held notion of developmental brain plasticity posits that the young brain is flexible, capable of reorganization, and that children withstand less structural damage and have less functional disabilities as a result of cerebral damage compared to adults. This “plasticity theory”, mistakenly coined the “Kennard principle”, was formulated as an (oversimplified) interpretation of Margaret Kennard’s work with primates in the 1930’s (Dennis, 2010). Dr Kennard, an influential neurologist, sought to explain the factors that predicted outcome (age being one of many factors) and the neural mechanisms that modified the lesioned brain’s functioning. In fact, she readily acknowledged at the moment of her experimentations the complex and multifactoral nature of brain recovery, above and beyond age of injury (Dennis, 2010). Nonetheless, studies of young children with focal brain injuries who went on to develop normal intellectual and cognitive abilities were thought to provide support for and served to popularize the notion that the young brain is more flexible and capable of overcoming insult (Aram & Ekelman, 1986; Ballantyne, Spilkin, Hesselink, & Trauner, 2008; Dennis, 1980; Smith & Sugar, 1975; H. G. Taylor & Alden, 1997b; Teuber & Rudel, 1962). However, conflicting results have since emerged, forcing scientists to reevaluate the theory of increased plasticity of the young brain. Indeed, although young children may have better prognosis compared to older individuals following certain types of injury (e.g., focal injuries), more recent studies demonstrate that early, *generalized* brain injuries, such as traumatic brain injuries, result in *worse* outcomes in children and adolescents (Anderson, Catroppa, Morse, Haritou, & Rosenfeld, 2005; Anderson & Moore, 1995; Anderson, Morse, Catroppa, Haritou, & Rosenfeld, 2004; Anderson, Spencer-Smith, et al., 2009; Donders & Warschausky, 2007; Gronwall, Wrightson, & McGinn, 1997; H. G. Taylor et al., 2002). According to "vulnerability theory", worse outcomes after early childhood TBI can be attributed to the fact that cognitive functions coming online during the first years of life are critically dependent on the integrity of particular brain structures at key developmental stages (Anderson et al., 2005). Of note, it has been shown that difficulties observed following pediatric TBI are often further exacerbated as children mature, because they are faced with increasingly complex responsibilities in the social and academic realms (H. G. Taylor et al., 2002).

Pathophysiology

Vulnerability theory is also supported by the unique pathophysiological characteristics of the developing brain. Young age at injury substantially influences morbidity due to the distinct and specific pathophysiology associated with insult to the immature brain and the unique biochemical, molecular, and cellular changes induced (Ciurea, Gorgan, Tascu, Sandu, & Rizea, 2011; Kochanek, 2006). As mentioned by Raimondi (1972), "children are not young adults […]". Indeed, during early childhood (i.e., before 5 years of age) structural factors such as flexible cranial bones reduce the risk of focal damage because the skull is better-suited to absorb shock. However, the relatively large head and weak neck of young children increase the risk of diffuse brain damage because the neck cannot attenuate the mechanical force applied to the head (Noppens & Brambrink, 2004).

Acute and long-term sequelae of pediatric TBI

Research on the acute and long-term consequences following pediatric TBI has also provided support for vulnerability theory with evidence that children who sustain moderate to severe TBI suffer from a range of neuropsychological, behavioral, psychiatric and academic problems (Catroppa, Anderson, Morse, Haritou, & Rosenfeld, 2007; Fletcher, Ewing-Cobbs, Miner, Levin, & Eisenberg, 1990; Keenan, Hooper, Wetherington, Nocera, & Runyan, 2007; Kinsella, Ong, Murtagh, Prior, & Sawyer, 1999; Mandalis, Kinsella, Ong, & Anderson, 2007; Max et al., 2015; Max et al., 1999; Max, Robertson, & Lansing, 2001; Max et al., 1997; Schwartz et al., 2003; H. G. Taylor et al., 2008; H. G. Taylor et al., 2002; Turkstra, Politis, & Forsyth, 2015). Furthermore, although some cognitive difficulties resolve in the years following the injury, many neuropsychological deficits, behavioral disturbances and psychiatric symptoms persist in the long term (Anderson & Catroppa, 2007; Anderson, Catroppa, Morse, Haritou, & Rosenfeld, 2009;

Catroppa, Anderson, Godfrey, & Rosenfeld, 2011; Catroppa et al., 2007; Ewing-Cobbs et al., 1997; Ewing-Cobbs et al., 2006; G. C. Fay et al., 1994; Gerrard-Morris et al., 2010; Jaffe, Polissar, Fay, & Liao, 1995; Klonoff, Clark, & Klonoff, 1993; Schwartz et al., 2003).

Acute and long-term consequences of pediatric mTBI

Several studies demonstrate the presence of acute consequences following mTBI in children (Bohnen, Jolles, & Twijnstra, 1992; Bohnen, Jolles, Twijnstra, Mellink, & Wijnen, 1995; Levin et al., 2013; Wrightson, McGinn, & Gronwall, 1995), most notably in terms of the presence of postconcussive symptoms (Babikian & Asarnow, 2009; McCauley et al., 2014; Yeates et al., 2009), attention (R. C. Chan, 2000), working memory (McAllister et al., 2001), processing/psychomotor speed (B. L. Brooks, Khan, Daya, Mikrogianakis, & Barlow, 2014; McAllister et al., 2001; McCauley et al., 2014), verbal learning (McCauley et al., 2014) and visual memory (Rieger et al., 2013) problems. Other studies fail to report any group differences in the acute phase following mTBI in children (Grubenhoff, Kirkwood, Gao, Deakyne, & Wathen, 2010; Sroufe et al., 2010), although these studies examined *accuracy* of cognitive performances, rather than the speed of execution, in many domains (e.g., orientation to time, number of words learned, number of digits repeated backwards). Recent meta-analyses and systematic reviews have attempted to reconcile these divergent findings and the conclusion that transpires is that cognitive consequences following mTBI are not infrequent, but these are usually transient and have subsided by 1 to 3 months post-injury for the majority of children (Babikian et al., 2011; Holm, Cassidy, Carroll, & Borg, 2005; Karr, Areshenkoff, & Garcia-Barrera, 2014; Zemek et al., 2016), especially following a single *uncomplicated* mTBI (Babikian & Asarnow, 2009; Kirkwood et al., 2008; Maillard-Wermelinger et al., 2009). Of note, these reviews have focused on the cognitive consequences and have not addressed potential social consequences.

Social difficulties following pediatric TBI

In addition to cognitive, behavioral and psychiatric problems, childhood TBI may also be accompanied by challenges on the social front, and impairments have indeed been found in a range of social domains. Most of the research concerning the social repercussions of brain injury has been conducted with school-aged children and adolescents. Specifically, Catroppa and colleagues (2015) provide evidence for a deterioration of social participation 6 months post-injury, particularly for youth who have sustained a more severe injury. Additionally, studies show that these social impairments are often linked to the number and quality of friendships and relationships (Gauvin-Lepage & Lefebvre, 2010; Prigatano & Gupta, 2006; Renstrom, Soderman, Domellof, & Emanuelson, 2012; Roscigno, Swanson, Vavilala, & Solchany, 2011). Across the broad pediatric spectrum (i.e., newborn to late adolescence), survivors of TBI also report a decrease in their involvement, as well as in the intensity and diversity of their social participation in several environments (home, school, community) up to 4 years after sustaining brain injury (Anaby, Law, Hanna, & Dematteo, 2012; Bedell & Dumas, 2004; Bedell, Haley, Coster, & Smith, 2002). Following TBI, children and adolescents have difficulty maintaining peer and intimate relationships and are viewed as less socially competent, more socially isolated, lonelier, and more agressive than non-injured peers (Andrews, Rose, & Johnson, 1998; Dooley, Anderson, Hemphill, & Ohan, 2008; Max et al., 1998). Given these findings, it comes as no surprise that global emotional and social behavior problems have been documented in children and adolescents who have sustained TBI, including conduct problems and disruptive behavior, social problem-solving difficulties, a lack of empathy and poorer moral reasoning, impaired emotional processing and recognition, as well as socio-communicative difficulties (Beauchamp, Dooley, & Anderson, 2013; Dennis, Barnes, Wilkinson, & Humphreys, 1998; Dennis, Purvis, Barnes, Wilkinson, & Winner, 2001; Janusz, Kirkwood, Yeates, & Taylor, 2002; Schmidt, Hanten, Li, Orsten, & Levin, 2010; Tonks et al., 2009; Tonks, Williams, Frampton, Yates, & Slater, 2007; Turkstra, Williams, Tonks, & Frampton, 2008). Unfortunately, the relationship between emotional processing/recognition and social difficulties remains largely unknown in the pediatric population. The only study aimed at bridging the gap between emotion processing and socio-cognitive functioning following pediatric TBI concluded that ToM difficulties may be secondary to impairments in other cognitive functions that underpin perspective taking abilities, such as facial emotion recognition problems (Levy & Milgram, 2016). More research is needed to clarify the nature of the interaction between emotion understanding and socialization after childhood TBI.

Although most research has been conducted with school-aged children and/or adolescents, Yeates and colleagues (2010) also provide evidence of social adjustment and/or social participation difficulties in younger children (3 to 6 years old) who have sustained mild complicated/moderate or severe TBI. In addition, a study conducted with infants and toddlers indicates that even mild injuries can interfere with social development, notably in terms of socio-emotional maturation (Kaldoja & Kolk, 2012), and these difficulties can persist up to 9 months post-injury (Kaldoja & Kolk, 2015).

These findings are especially worrisome given that early childhood consitutes a rich period of social development with the emergence of rudimentary social skills and relationships that set the stage for more complex social interactions (Johnson, Ironsmith, Snow, & Poteat, 2000). The importance of adequate social development early in life is highlighted by research showing that appropriate social functioning has repercussions beyond the social sphere, as it is associated with school readiness and success, as well as emotional well-being (Blair, 2002; Ladd, 1999; Parker &

Asher, 1987). Also, longitudinal studies have demonstrated that social competence in the preschool years has a long-term impact on a child's acceptance by peers, regardless of later improvement in social interaction (e.g., Razza, 2009). Similarly, Jones and colleagues (2015) have provided evidence that socio-emotional skills in kindergarten are associated with multiple outcome markers in adulthood such education, employment, criminal activity, substance use, and mental health. Pertaining to TBI, research shows that children who sustain mTBI are significantly more likely to develop neurodevelopmental and psychiatric conditions (McKinlay, Grace, Horwood, Fergusson, & MacFarlane, 2009) that have been shown to interfere with social functioning (Andrade, Browne, & Tannock, 2014; Culpepper, 2015; DuPaul, Morgan, Farkas, Hillemeier, & Maczuga, 2016). Specifically, McKinlay and colleagues (2009) demonstrate that children who sustain mTBI are at higher risk of showing symptoms of attention deficit hyperactivity disorder (odds ratio = 4.2), conduct disorder / oppositional defiant disorder (odds ratio = 6.2), substance abuse (odds ratio = 3.6), and mood disorder (odds ratio = 3.1).

Hence, the early years of life constitute a crucial period for social development, and any disruption of this developmental trajectory can have long-lasting consequences in a child's life. For children who sustain mTBI during the preschool years, the injury increases their chances of suffering from a neurodevelopmental or psychiatric disorder known to interfere with social functioning. Taken together, these findings suggest that the social repercussions associated with mTBI in preschool children must be taken seriously.

Theoretical model of social dysfunction in pediatric TBI

Several models have been proposed to conceptualize the emergence of social skills in children, as well as the origins of social dysfunction in clinical populations such pediatric TBI (Adolphs, 2009; Beauchamp & Anderson, 2010; Ochsner, 2008; Yeates, 2013). The socio-cognitive integration of abilities (SOCIAL) model, developed by Beauchamp and Anderson (2010), provides an integrative view of the determinants of social competence from a developmental perspective. This framework suggests that the emergence and development of social skills depend on the normal maturation of the brain, cognition, and behavior, within a supportive environment. Indeed, an individual's level of social functioning is determined by a bi-directional and dynamic interaction between neurobiological substrates, socio-cognitive skills, and internal (child) as well as external (environmental) factors (see Figure 1). Specifically, internal and external factors, shaped by biology and the environment, interact to influence the emergence of cognitive and affective functions. These processes then directly dictate an individual's ability to navigate social environments (Beauchamp & Anderson, 2010). At the heart of this model, we find socio-cognitive skills, which emerge as a result of brain development and underpin social competence. Precisely, social cognition, referred to as socio-emotional skills in the model, consists of an ensemble of cognitive processes specifically dedicated to making sense of the social world. Examples of social-cognitive skills include face and emotion perception, attribution (of intent, causes, behavior), theory of mind, empathy, and moral reasoning. One can therefore imagine that brain injury, resulting in disruption to brain integrity, compromises the development of socio-cognitive skills, thereby jeopardizing social functioning.

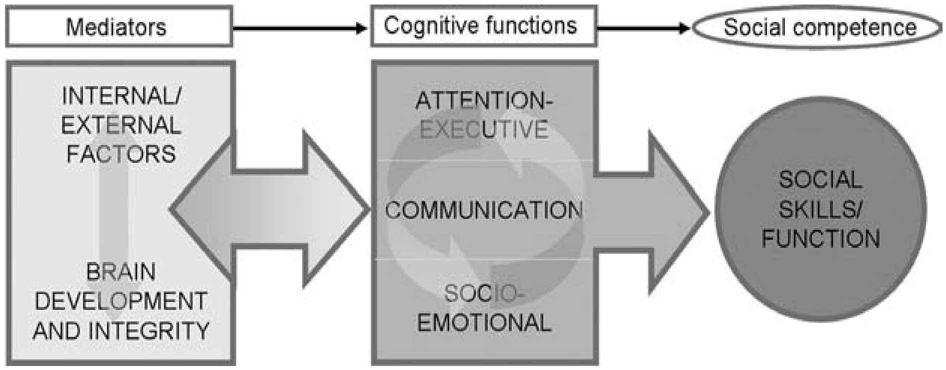

Figure 1. The socio-cognitive integration of abilities model (SOCIAL)

Social cognition and Theory of mind

In order to gain a better understanding of the origins of post-TBI social problems in early childhood, the socio-cognitive underpinnings of social competence have thus become a focus of inquiry. Early childhood is devoted to the burgeoning of a subcomponent of social cognition, that of theory of mind (ToM), characterized as the ability to take on another person's perspective and infer mental states, such as desires, emotions, beliefs, perceptions and intentions in order to predict behavior (Wellman, Cross, & Watson, 2001; Wellman, Fang, & Peterson, 2011). Specifically, ToM enables children to understand that mental states are *representations* of reality (Gopnik & Wellman, 1994; Wellman & Bartsch, 1988). Importantly, extensive research has shown reciprocal associations between ToM and later social competence (e.g., communication, conflict resolution, empathy, etc), in which understanding others' mental states leads to positive social interactions, and in turn, social interactions allow one to learn about the complexity of others' minds (e.g., Astington, 2003; Hughes & Leekam, 2004). As children evolve from an egocentric point of view to a more considerate perspective of the role of internal states on behavior, they are increasingly able to predict and explain the associations between mental states and behavior, and hence become more competent social partners (Razza, 2009). Indeed, Piaget's (1926) influential construct of egocentrism, formulated in the 1920s, is still recognized as being at the heart of mentalistic understanding, and the necessity to decenter from one's own perspective remains the ultimate challenge to understanding others' mental and social worlds (Miller, 2012).

Theory of mind development

During infancy and the preschool years, children progressively develop an understanding of the most basic form of ToM which Miller (2012) describes as "[…] children's ability to think about mental states in themselves and others – thus to think about somebody thinking about something, or feeling something, or wanting something, or whatever the relevant mental state may be" (p. 44). Although the depth of infants' understanding of the mind remains a matter of debate despite extensive study of the subject (e.g., Thoermer, Sodian, Vuori, Perst, & Kristen, 2012), a general developmental sequence of the emergence and acquisition of key ToM concepts prevails (Miller, 2012; Wellman et al., 2011). Specifically, studies have shown that precursors of ToM develop during the first year of life, notably in terms of visual perception, attention and its selective or divided nature (e.g., attentional focus of an agent, joint attention), the social smile, and social referencing (i.e., social understanding guided by others' emotional cues; Feinman, 1992; H. Moll & Tomasello, 2006; Moore & Dunham, 1995; Slaughter & McConnell, 2003; Sodian, Thoermer, & Metz, 2007; Tomasello & Haberl, 2003).

Although several mental states guide human behavior (e.g., desires, beliefs, intentions, emotions), our knowledge of young children's understanding of the mind continues to be primarily extrapolated from literature examining their understanding of beliefs, or rather their understanding of *false* beliefs. It not by chance that false belief understanding (FBU), defined as the understanding that people can hold beliefs that are untrue and nonetheless act on them, is the most studied aspect of ToM in preschoolers. FBU was initially thought to be the first indication that children could distinguish between the mind and the physical world, thus explaining why it is considered a major milestone in ToM development. Specifically, the first studies that looked at FBU led researchers to conclude that children were not capable of perspective taking before the preschool years because of the finding that children younger than 4 years of age systematically failed verbal tasks assessing FBU (Baillargeon, Scott, & He, 2010; Poulin-Dubois, Brooker, & Chow, 2009), such as the classic Sally and Anne task[1] (Baron-Cohen, Leslie, & Frith, 1985). However, a groundbreaking study by Onishi and Baillargeon (2005) challenged this prevailing view, and set the stage for a rich and fertile re-questioning of previously-held assumptions. To do so, the researchers used a violation-of-expectation paradigm, an experimental method extensively used in infant cognitive research, in which children are expected to look reliably longer at situations that violate their expectations. Specifically, they demonstrated that 15-month-olds do hold an *implicit* understanding of false beliefs and of their impact on behavior. Following this seminal study, other researchers have shown, using a variety of non-verbal paradigms (e.g., violation of expectation, anticipatory looking, preferential looking) an implicit competency in increasingly younger children, as young as 10 months of age (Luo, 2011; Luo & Baillargeon, 2007; Tomasello & Haberl, 2003). Although it is true that an *explicit* understanding of false beliefs does not occur before approximately 4 years of age, a rudimentary and implicit comprehension does in fact develop earlier (Baillargeon et al., 2010). Thus, first-order FBU, defined as a child's reflection on someone else's belief ("A thinks that…"), is considered a preschool achievement and is usually fully mastered by the age of five. From this foundational

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[1] The Sally and Anne task is a classic test of FBU in which the following story is presented to children with the help of puppets: Sally takes a marble and hides it in her basket. Sally then leaves the room and goes for a walk. While Sally is away, Anne takes the marble out of Sally's basket and puts it into her own box. Sally is then reintroduced and the child asked "Where will Sally look for her marble? "

layer, more advanced FBU progressively develops (Miller, 2012). Second-order FBU is generally understood by most 7- and 8-year-olds; it involves a child's understanding of someone else's belief about something in the world ("A thinks that B thinks that…"; Miller, 2012). The most complex form of FBU, third-order FBU, is subsequently attained and involves the following recursive reasoning: "A thinks that B thinks that C thinks that…" (Miller, 2012).

A substantial amount of scientific attention has been devoted to children's understanding of how beliefs guide behavior. However, researchers have also mapped the development of children's understanding of how other mental states, such as desires, influence actions. In fact, children understand the impact of desires on behavior before they understand how beliefs dictate one's actions (Wellman, 1993). One of children's first explicit demonstrations that they appreciate the role of desires in guiding behavior occurs at 18 months of age, when they begin to use internal state language such as "want" (Wellman & Bartsch, 1994). It is also by this age that children understand, based on emotional cues, that others can have preferences that differ from their own (Repacholi & Gopnik, 1997). Thus, by 18 months of age, children have some kind of understanding of desires and how emotional cues hint at a person's internal mental state (Poulin-Dubois et al., 2009). At 24 months of age, children are able to talk about different desires of different people (e.g., Anna wants X and Joe wants Y), and by 30 months old, children understand that desires are subjective; that is, different people can have diverging desires concerning the same object (e.g., Anna wants X, but Joe does not want X; Wellman & Bartsch, 1994). And by their third birthday, children understand that an individual's behavior is consistent with his desires, and that different emotions will arise depending on whether a person's desires have been fulfilled (Wellman & Woolley, 1990). Once children have mastered the understanding of the impact of desires on actions, they are then cognitively ready to pursue their development of a "belief – desire psychology" (M. Taylor, 1996) whereby they realize that the interplay between desires *and* beliefs guide behavior (Wellman, 1990; Wellman & Woolley, 1990).

In sum, infancy and the preschool years set the stage for a complex and sophisticated understanding of the workings of the mind, preparing young children to navigate the complex social market that awaits them, as they slowly emerge from the family nest into the outer world. By their second birthday, children have developed a sophisticated, implicit understanding of how others' actions are guided by mental states such as goals, desires, beliefs, intentions, emotions and so on (Baillargeon et al., 2010). They first understand the role of desires in guiding behavior, and later they can appreciate the impact of beliefs as well. Longitudinal research shows that from a child's implicit knowledge of the workings of the mind, an explicit understanding progressively unfolds, thanks to general cognitive advancements, allowing leaps in conceptual understanding of others, in dual representations of reality, and in the expression of their comprehension of the mind (Baillargeon et al., 2010; Devine & Hughes, 2014; Marcovitch et al., 2015; San Juan & Astington, 2012; Thoermer et al., 2012).

Specifically, beyond the preschool years, these socio-cognitive building blocks as well as the maturation of other general cognitive abilities (e.g., language, executive functions) allow children to move away from conceptualizing others' knowledge as an exact copy of reality to a more interpretive, constructivist and subject-oriented ToM (Carpendale & Chandler, 1996; Chandler & Boyes, 1982; Wellman, 1990). Carpendale and Chandler (1996) describe this process as follows: "[…] it is only […] some years after first grasping the possibility of false beliefs, that children are hypothesized to begin gradually consolidating a capacity to appreciate, not only that different persons may have access to different information, but also that different persons can and often do reasonably attach different meanings to one and the same thing" (pp. 1689). Thus, young children's fledgling theory of mind will necessarily be transformed into a more mature, integrative view of other's mental worlds, as they move from a uni-directional to a bi-directional, interactive view of the relation between a person's inner, mental world and physical environment (Miller, 2012; Searle, 1983). Concretely, these developments participate in the emergence of communicative and imaginative abilities and conflict resolution skills, they are necessary to the establishment and maintenance of harmonious relationships, and they are linked to peer-related empathy and popularity (Astington, 2003; Miller, 2012). During the pre-adolescent and adolescent years, progress in ToM allows teenagers to conceptualize role-taking, empathic sensitivity, other and self-perceptions, scientific and moral reasoning, and it allows them to understand irony, metaphors, and idioms (e.g., Baird & Astington, 2004; Caillies & Le Sourn-Bissaoui, 2008; Dunn, Cutting, & Demetriou, 2000; Filippova & Astington, 2008; Happe, 1993; Hillier & Allinson, 2002; Miller, 2012; Winner & Leekam, 1991). Of note, a well-developed ToM can also give way to negative behaviors such as bullying, teasing, and manipulation (e.g., Heerey, Capps, Keltner, & Kring, 2005; Miller, 2012; Polak & Harris, 1999; Talwar, Gordon, & Lee, 2007).

ToM after TBI in children

Several studies document alterations in ToM following childhood TBI. Impairments in more complex forms of ToM (i.e., second-order ToM) and ToM-related functions (e.g., empathy), but not on basic forms (i.e., first-order ToM), have been shown in school-aged children and adolescents who sustain moderate or severe TBI (Dennis, Agostino, Roncadin, & Levin, 2009; Dennis et al., 2013; Dennis et al., 2012; Snodgrass & Knott, 2006; Turkstra, Dixon, & Baker, 2004). In younger children (6- to 8-year-olds), Walz and colleagues (2010a) found first- *and* second-order ToM difficulties following severe TBI. These authors further report that preschool children with severe TBI, when tested within three months of the injury, are impaired on an aspect of first-order ToM, that of FBU, compared to children with moderate TBI and those with orthopedic injuries (Walz, Yeates, Taylor, Stancin, & Wade, 2009). Research on the impact of brain injury on ToM is expanding but it remains comparatively sparse in preschool children. Given that no study has examined the impact of preschool mTBI on ToM skills, the current thesis will explore this avenue of research.

Methodological considerations in pediatric mTBI research

Research examining the consequences of mTBI is plagued by numerous challenges which have been identified as the source of the lack of consensus across studies. Specifically, methodological variations could potentially explain why some studies report postconcussive symptoms and various cognitive, behavioral and psychiatric sequelae following mTBI whereas other do not (Babikian et al., 2011). Notably, Babikian and colleagues (2011) attribute the variability across studies to the following causes : 1) differences in the definition of mTBI and parallel to this problem, the inclusion and exclusion criteria for the participants with mTBI, 2) variability in accounting for premorbid difficulties, 3) breadth of outcome domains explored as well as the type of measures used (parental questionnaires *vs.* formal testing), 4) type of research design used (retrospective *vs.* prospective), and 5) the interval between the injury and assessment.

One other methodological factor that must be considered in mTBI research is the type of control group used (community controls *vs.* injured controls). The choice of the control group is of particular importance because it dictates the conclusions that can be drawn from mTBI research.

Specifically, it allows one to determine if TBI research findings are attributable to a general-injury effect or rather to a brain-injury-specific effect (Babikian et al., 2011).

Community controls, or typically developing children in pediatric research, have practical advantages over injured controls. Specifically, they constitute a convenient group because they are more numerous and more readily available than injured controls, making them less costly to recruit (Mathias, Dennington, Bowden, & Bigler, 2013). Mathias and colleagues (2013) also mention that they are likely comparable to the samples that are used to produce test norms. Also, community controls allow researchers to compare children who have sustained mTBI to peers to whom they will compared to in real life settings. However, community controls do not account for potential pre- and post-injury risk factors and variables that may explain, at least partially, neuropsychological and social performances following TBI. Indeed, it has been shown that children who sustain accidental injury in general are more likely, compared to uninjured children, to be afflicted with premorbid conditions such as attention deficit hyperactivity disorder (ADHD), which render them more injury-prone and could account, at least partially, for their neuropsychological functioning post-injury (Babikian et al., 2011; Bruce, Kirkland, & Waschbusch, 2007; Gerring et al., 1998; McKinlay et al., 2010; Schwebel & Gaines, 2007; Yeates, 2010). Additionally, injured peers have in common the experience of a traumatic injury, which is not the case when comparing an injured group (such as TBI) to uninjured, community samples (Yeates, 2010). Thus, according to several researchers (e.g., Babikian et al., 2011; Yeates, 2010), controlling for such confounds is of paramount importance given that sequelae following mTBI are usually relatively subtle, mostly transient, not always specific to mTBI, are frequent in the general pediatric population (e.g., attention problems, headaches) and could be attributable to pre-existing conditions (Babikian et al., 2011).

To determine if injured peers constitute a better control group than a community sample, Mathias and colleagues' (2013) conducted a large-scale study with an adult population, aged between 18 and 80 years, comparing the performance of community controls to that of injured controls. Contrary to expectations, the results demonstrated that these two groups were strikingly similar demographically (age, socioeconomic status, sex), medically (current medication use and life-time medical diagnoses), psychosocially (fatigue, pain, depression, social support, concussion-like symptoms, community integration) and cognitively (motor and information processing speed; immediate and delayed memory; global, verbal and visuo-spatial intelligence quotient; verbal fluency; test effort). The authors therefore concluded that injured peers did not have a clear advantage over community controls. To our knowledge, the comparison of an injured versus an uninjured control group has never been performed in a pediatric population.

Despite the ongoing debate regarding the most appropriate control group in TBI research, the vast majority of mTBI studies conducted before 2005 have used community controls, with only 15% of research comparing individuals who have sustained TBI to injured counterparts (Frencham, Fox, & Maybery, 2005). A longitudinal study conducted in children with mTBI demonstrated that when controlling for pre-injury factors (i.e., using an orthopedic control group), there is no evidence of long-term cognitive difficulties for the *vast* majority of children who sustain mTBI (Babikian et al., 2011). Babikian and colleagues (2011) thus concluded that their findings provide evidence for a general-injury effect, thereby demonstrating the necessity to use orthopedic controls in mTBI research.

To circumvent the pitfalls inherent to each comparison group, some researchers have integrated both control groups in their study to allow the identification of the sequelae genuinely due to brain injury, and to establish the relative contribution of general-injury and brain-injury-specific effects (Alfano & Satz, 2000; Bijur, Haslum, & Golding, 1990; Dikmen, Ross, Machamer, & Temkin, 1995; Ettenhofer & Barry, 2012; P. S. Satz et al., 1999). Surprisingly, the results have not led to clear conclusions. Two mTBI pediatric studies have been conducted with both control groups. The first used global measures of cognition, achievement and behavior and found no difference between the mTBI group and the two control groups (Bijur et al., 1990). There was also no significant difference between the two control groups (Bijur et al., 1990). As for Asarnow and colleagues (1995), they found that the mTBI and the injured control group both differed from the community controls on one of the five cognitive domains explored (memory); this difference was present one month post-injury, but had resorbed six and 12 months post-injury. Additionally, more pre-injury behavioral problems were reported in the mTBI group. The most recent study conducted with both control groups revealed that university students with mTBI report modestly higher symptom burden; however, when confirmatory factor analyses were conducted, the mTBI group factor structure was indistinguishable from the orthopedic counterparts and uninjured peers (Ettenhofer & Barry, 2012), suggesting a general phenomenon rather than one specific to mTBI. Evidently, these studies do not permit firm conclusions as to the best control group to use in pediatric mTBI research.

The question of the most appropriate control group is all the more relevant when studying very young children. Indeed, what is unique to preschoolers is that they have a short developmental history. We thus know very little about their neuropsychological make-up and whether they will go on to develop neurodevelopmental, psychiatric and/or behavioral conditions. For example, most neurodevelopmental and psychiatric conditions for which children are usually excluded from studies are, for the most part, not yet known in these children. In fact, it is a criteria in the

Diagnostic and Statistical Manual of Mental Disorders (Fifth Edition; American Psychiatric Association, 2014) that many disorders cannot be diagnosed in the early years of life because some conditions, such as learning disabilities, necessitate environmental exposure (e.g., formal education) in order to challenge these abilities and allow the disorder to express itself.

Gap in the literature

Given that the impact of mTBI on social cognition has not been explored in preschool children, we conducted a prospective, longitudinal study examining two important ToM skills that develop during the preschool years (false belief understanding and desires and emotions reasoning) at two fixed, post-mTBI time points (6 and 18 months post-injury). Additionally, given the ongoing debate concerning the most appropriate control group, and considering the inherent particularities of studying preschool children, the mTBI group was compared to both orthopedically injured peers as well as typically developing children. Comparison with children who have sustained an orthopedic injury and the inclusion of baseline measures allowed us to account for possible premorbid difficulties. Lastly, to address the often-noted weakness in pediatric TBI studies concerning the type of measures used, both formal testing (i.e., ToM tasks) and parental questionnaires were included.

Objectives and hypotheses

The thesis is divided into two empirical articles, each with specific aims, and is accompanied by a book chapter on the neural substrates of ToM.

Article 1 aimed to examine post-mTBI ToM skills (false belief understanding and desires and emotions reasoning) by comparing preschool children (18 – 60 months of age) who sustained mTBI to typically developing children, 6 months post-injury. It was expected that the children who sustained mTBI would perform more poorly than typially developing peers on the false belief understanding and desires and emotions reasoning tasks.

Article 2 aimed to explore general-injury versus brain-injury-specific effects in relation to ToM, as well as to map the evolution of ToM skills following preschool mTBI. To do so, we examined ToM skills in preschool children following mTBI compared to two control groups (typically developing peers and orthopedic injured counterparts) and at two time points (6 and 18 months post-injury). It was hypothesized that children who sustained mTBI would obtain worse performances than both control groups 6 months post-injury. However, these differences were expected to have resorbed 18 months after the injury. Article 2 also aimed to examine the link between ToM performance and global and social functioning in order to explore whether poorer ToM skills are related to lower global social functioning.

Article 1

When injury clouds understanding of others:
Theory of mind after mild TBI in preschool children

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Abstract

Objective: There is evidence to suggest that social skills, such as the ability to understand the perspective of others (theory of mind), may be affected by childhood traumatic brain injuries; however, studies to date have only considered moderate and severe TBI. This study aimed to assess theory of mind after early, mild TBI (mTBI). Method: 51 children who sustained mTBI between 18 and 60 months were evaluated six months post-injury on emotion and desires reasoning and false-belief understanding tasks. Their results were compared to that of 50 typically developing children. Results: The two groups did not differ on baseline characteristics, except for pre- and post-injury externalizing behavior. The mTBI group obtained poorer scores relative to controls on both the emotion and desires task and the false-belief understanding task, even after controlling for pre-injury externalizing behavior. No correlations were found between TBI injury characteristics and theory of mind. Conclusion: This is the first evidence that mTBI in preschool children is associated with theory of mind difficulties. Reduced perspective taking abilities could be linked with the social impairments that have been shown to arise following TBI.

Keywords: pediatric, head injury, concussion, social cognition, perspective taking, outcome, social skills.

INTRODUCTION

Preschool children (0 to 5 years of age) constitute a particularly high-risk group for sustaining traumatic brain injury (TBI), with a yearly rate of 1.85 per 100 in children under five years of age (compared to rates of <1.17 in other paediatric age groups; Faul et al., 2010; McKinlay et al., 2008). As with older individuals, preschoolers are most at-risk for sustaining mild TBI (mTBI), constituting 90 % of all injuries (Crowe et al., 2009; McKinlay et al., 2008). Cognitive deficits, delayed school readiness, behavioral and emotional disturbances, and somatic complaints have been documented following early brain injury across the severity spectrum, with evidence of long term persistence of these sequelae (e.g., Garcia, Hungerford, & Bagner, 2014; Li & Liu, 2013; Shay et al., 2014). Although the changes observed following mTBI tend to be more subtle and less pervasive than those associated with severe injuries, the ensuing difficulties can nonetheless interfere with development, notably in terms of school performance and socio-emotional maturation (Kaldoja & Kolk, 2012; Wrightson et al., 1995).

Poor prognosis after early childhood TBI is likely to be attributed to the fact that cognitive functions coming online during the first five years of life are critically dependent on the integrity of particular brain structures at key developmental stages (Anderson et al., 2005; Anderson, Spencer-Smith, et al., 2009; Ryan et al., 2014). These formative years also constitute a rich period of social development with the emergence of rudimentary social skills and relationships setting the stage for more complex social interactions (Johnson et al., 2000). Appropriate social functioning has repercussions beyond the social sphere as it is associated with school readiness and success, as well as emotional well-being (Blair, 2002; Ladd, 1999; Parker & Asher, 1987). Despite the pivotal role of social abilities during the early years and the high prevalence of TBI during this period, little is known of the consequences of preschool TBI on the precursors to adequate social functioning, such as the ability to take the perspective of others (theory of mind).

Global socio-behavioral (e.g., conduct disorders, disruptive behavior), socio-affective, and social participation impairments have been documented after childhood TBI (Anderson et al., 2013; Rosema, Crowe, & Anderson, 2012; Yeates et al., 2004). These problems translate into difficulties maintaining peer relationships, reduced social competence, isolation, loneliness, and increased aggression (Andrews et al., 1998; Baguley, Cooper, & Felmingham, 2006; Max et al., 1998). Although poor social outcome is especially evident after moderate and severe TBI, recent findings indicate that even milder brain injuries can result in social interaction impairments (Kaldoja & Kolk, 2012). Rather than abating, these difficulties may exacerbate as preschoolers transition to later childhood and adolescence, due to the increased pressure and demands of social and academic responsibilities, such as attending school and developing social connections beyond the family (Muscara, Catroppa, Eren, & Anderson, 2009; H. G. Taylor et al., 2002). As such, it has been suggested that social impairments may be the most enduring and debilitating sequelae of childhood TBI (e.g., Beauchamp & Anderson, 2013).

These findings highlight the need to better understand the nature of social dysfunction following early childhood TBI by going beyond the assessment of global social functioning to examine underlying social cognition (i.e., abilities that allow individuals to understand social cues and interact adequately). Theory of Mind (ToM) is a set of basic socio-cognitive skills that emerge in the preschool years and enable individuals to understand another person’s perspective and infer mental states, including desires, emotions, beliefs, and intentions, in order to predict behavior

(Wellman et al., 2011). Extensive research shows that ToM is important for the development and maintenance of social behavior and skills including communication, conflict resolution, empathy, as well as general social competence (Astington, 2003). More precisely, as children evolve from an egocentric point of view to a more considerate perspective of the role of internal states on behavior, they are increasingly able to predict and explain the associations between mental states and behavior, and hence become more competent social partners (Razza, 2009).

Although there are individual differences regarding the specific ages at which key ToM concepts emerge and are fully acquired, a general developmental sequence prevails (Miller, 2012). Studies have shown that precursors of ToM develop during infancy, notably joint attention and social referencing (i.e., social understanding guided by others' emotional cues; e.g., Feinman, 1992; Moore & Dunham, 1995). During the preschool years, children develop a "desire theory" according to which behavior is explained in terms of desires, without any understanding or consideration of the influence of beliefs (Wellman & Woolley, 1990). As such, by three years of age, children understand that people's behavior is guided by their desires. They also appreciate the emotional impact of fulfilled or unfulfilled desires. By the time they reach the age of four, children have typically progressed toward "belief-desire psychology" whereby they realize that both desires and beliefs guide behavior and that people can act on beliefs that are untrue (Wellman, 1990; Wellman & Woolley, 1990). A developmental breakthrough thus occurs during the preschool years, namely that of "false-belief understanding" (FBU). The concept of FBU has long been considered a milestone in the development of ToM because it is one of the first indications that children distinguish between the mind and the physical world, and demonstrate an understanding that these can sometimes be at odds with one another. It is partly for this reason that the earliest form of FBU, first order ToM, is the most widely studied. This concept is defined by Miller (2012) as "[…] children's ability to think about mental states in themselves and others – thus to think about somebody thinking something, or feeling something, or wanting something, or whatever the relevant mental state may be " (p. 44; "A thinks that…"). Considered a preschool achievement, first order FBU is usually mastered by the time children reach the age of five. From this foundational layer, more advanced FBU progressively develops. Second order FBU is generally understood by most seven- and eight-year-olds; it involves someone else's belief about something in the world ("A thinks that B thinks that…"). The most complex form of FBU, third order FBU, is subsequently attained and involves the following recursive reasoning: "A thinks that B thinks that C thinks that…".

Few studies examining ToM after childhood TBI have been conducted to date and they focused primarily on school-aged children. Five studies of individuals between the ages of six and 22 years tested between one and 12 years post injury, found that youth with TBI (especially those with moderate to severe injuries) performed significantly worse than controls on ToM tasks (Dennis et al., 2009; Dennis et al., 2013; Dennis et al., 2012; Snodgrass & Knott, 2006; Turkstra et al., 2004). In these studies, impairments were found on more complex forms of ToM, but not on first-order tasks. In contrast, when children six to eight years of age were tested approximately one year post-injury, first- and second-order ToM deficits were documented in those with severe TBI (Walz et al., 2010a), constituting the first evidence that these fundamental skills may be affected in school-aged children. Only one study to date has examined ToM after preschool TBI, showing that children with severe TBI are impaired on FBU compared to those with moderate TBI and orthopedic controls (Walz et al., 2009). Given a) the evidenced negative socio-cognitive consequences of head injuries in children and b) the high prevalence of TBI, especially mTBI, in children under five years of age, the goal of the present study was to examine first-order ToM skills in preschool children (18 to 60 months) with mTBI. It was expected that children with mTBI would perform significantly worse on ToM tasks compared to typically developing children.

METHOD

Participants

Recruitment

This study was approved by the institutional review board of Ste-Justine Hospital and conducted in accordance with the Helsinki declaration. Informed written parental consent and child assent were obtained prior to participation. Participants were recruited as part of a prospective longitudinal cohort for a project aiming to study cognitive and social outcomes of early TBI. Data are presented pertaining to the 6-month post-injury timepoint. Children with mTBI, excluding mild complicated TBI, were recruited via the Emergency Room between 2011 and 2014, using the definition proposed by Osmond and colleagues (2010). Inclusion criteria were a) age at injury between 18 and 60 months of age, b) closed head injury with a Glasgow Coma Scale (GCS) between 13 and 15 (Teasdale & Jennett, 1974), c) at least one of the following symptoms: loss of consciousness, excessive irritability, persistent vomiting (more than two times), confusion, headaches that worsen over time, drowsiness, dizziness, motor difficulties or balance problems, blurred vision, hypersensitivity to light, and/or the presence of seizures; d) child and at least one parent fluent in French or English. Exclusion criteria were: a) non-accidental head injuries, b) diagnosed congenital, neurological, developmental, psychiatric, or metabolic condition, c) less than 36 weeks of gestation, d) prior TBI, and e) evidence of intracranial lesion on clinical CT or MRI (i.e, mild complicated TBI).

Typically developing children (TDC) were recruited via advertisements posted in daycare centers. In order to ensure that children in the TDC group would be age-matched to the mTBI group at 6-months post-injury, inclusion criteria for the control group were: a) aged between 24 and 66 months, b) child and at least one parent fluent in French or English. The same exclusion criteria applied.

Final Sample

Of the 63 children who sustained mTBI and the 51 TDC initially recruited, 6 participants (all mTBI) dropped-out before completing T1. Additionally, 7 participants (6 mTBI, 1 TDC) were excluded at T1 because they had TBI-like symptoms that were better explained by another medical condition (1), lacked mastery of French or English undetected at screening (3), or were identified as having a developmental disorder (3). Data from 51 children with mTBI and 50 TDC were therefore used in the analyses.

PROCEDURE

mTBI

At enrolment (Time point 0, T0), parents were asked to complete a pre-injury questionnaire booklet including sociodemographic information, developmental milestones, behavioral and adaptive functioning, and family characteristics. They were asked to report on their child's behavior and adaptive skills as well as their familial situation in the weeks *preceding* the injury, in order to provide an estimate of baseline characteristics. Six months post-injury (Time point 1, T1), children completed a socio-cognitive assessment battery administered by neuropsychology doctoral candidates and trained research assistants and parents completed the same questionnaire booklet (without the sociodemographic and developmental milestone questions) along with the Postconcussive Symptom Interview (PCS-I; Mittenberg, Wittner, & Miller, 1997; Yeates et al., 2012) in an interview format. At this time point, parents were instructed to assess their child's behavior and their family characteristics in the last four weeks prior to the testing session. Testing occurred in a single three-hour session with regular breaks.

Controls

Given the absence of injury, the children were tested as soon as possible after recruitment using the same socio-cognitive battery, and parents completed the same questionnaires and PCS-I as the one filled out by mTBI parents at T1, along with the sociodemographic and developmental milestone questionnaire.

MEASURES

Questionnaires

Case Report Form

General medical information was obtained from medical files including: cause of mTBI, lowest GCS, and neurological symptoms: headaches, irritability, persistent vomiting (more than two times), hematoma (forehead or scalp), drowsiness, dizziness, seizures, visual symptoms (blurred vision, hypersensitivity to light), and balance/motor problems. Loss of consciousness (LOC) was measured according to the following categories: none, <1 minute, <5 minutes, <1 hour, 1 to 24 hours, >24 hours, suspected, unknown. Where possible, alteration of consciousness (AOC, i.e., confusion) was also assessed as follows: none, <1 hour, 1 to 24 hours, >24 hours, suspected, unknown. Results of clinical neuroimaging were obtained when available to verify exclusion criteria “e” (mild complicated TBI).

Postconcussive Symptom Interview

The PCS-I (PCS-I; Mittenberg et al., 1997; Sady, Vaughan, & Gioia, 2014; Yeates et al., 2012) is a parental report questionnaire consists of 15 symptoms from the following domains: Physical, Cognitive, Affective and Sleep; parents must say if the symptoms were present (1) or absent (0) at any time during the week prior to testing and within the last six-months. The form was slightly reworded to be age-appropriate and to reflect a third-person perspective. A score out of 15 was calculated both for symptoms observed in the last week and in the six months post-injury.

ABCs Laboratory Sociodemographic Questionnaire

Parents completed an in-house developmental and demographic questionnaire. The following developmental information was recorded: highest APGAR score, age of first words, and age of first steps. Familial socioeconomic status was calculated using the Blishen Socioeconomic Index (Blishen, Carroll, & Moore, 1987), which attributes a socioeconomic score according to caregiver occupation. For double-earner families, the highest socioeconomic score was used. Parental education was also tabulated according to eight levels (1 = Doctoral level studies – 8 = less than seven years of education). Mother and father’s highest educational attainment were averaged.

Adaptive Behavior Assessment System

The Adaptive Behavior System (ABAS; 0 to 5 years old version; Harrison & Oakland, 2003) is a 241-item assessment of everyday adaptive skills parents are asked to rate their child on a 4-point scale according to the frequency at which he or she *correctly* demonstrates a behavior, *without help*, when such behavior is necessary. The Global Adaptive Composite (GAC) as well as the Social Composite are reported (standard score, M = 100, SD = 10). The Social Composite evaluates children's ability to interact socially, engage in play, initiate and maintain friendships, and express and recognize emotions.

Child Behavior Checklist

The Child Behavior Checklist (CBCL; 18 months to 5 years old version; Achenbach & Rescorla, 2000) is a 100-item questionnaire asks parents to rate various aspects of their child's behavior on a 3-point scale according to the degree to which the statement describes their child. Two global scores are obtained by grouping the subscales: Internalizing Behavior (Emotionally reactive, Anxious/depressed, Somatic complaints, and Withdrawn subscales) and Externalizing Behavior (Attention problems and Aggressive behavior subscales).

Family Assessment Device – General family functioning subscale

The Family Assessment Device – General family functioning subscale (FAD; N. B. Epstein, Baldwin, & Bishop, 1983) requires the primary caregiver to rate the degree to which each of the twelve statements describes their general family functioning using a 4-point scale (e.g., "We can express feelings to each other", "Planning family activities is difficult because we misunderstand each other"). Higher scores indicate poorer levels of family functioning.

Parental Stress Index

The Parental Stress Index (PSI-brief; Abidin, 1995) is a 24-item questionnaire filled out by the primary caregiver aims to identify dysfunctional parent-child systems (e.g., “When I do things for my child, I get the feeling my efforts are not appreciated very much”) . Two subscales were used: parental distress and parent-child dysfunctional interactions, in which a higher score indicates increased distress or dysfunction.

Dyadic Adjustment Scale

The Dyadic Adjustment Scale (DAS-4; Spanier, 1976) is a 4-item self-report measure filled out by the primary caregiver and it assesses the degree of satisfaction couples are experiencing (e.g., “In general, how often do you think that things between you and your partner are going well?”).

Intellectual functioning

Intellectual functioning and verbal ability were measured for descriptive purposes. Children between the ages of 24 and 30 months completed the Bayley Scales of Infant Development Cognitive and Language subscales (Bayley-III; Bayley, 2005). Children 31 months and older completed the Wechsler Preschool and Primary Scale of Intelligence (WPPSI-III; Wechsler, 2002) and scores were calculated for the Verbal, Performance and Global Indices. The Cognitive Composite of the Bayley-III and the Global Index of the WPPSI-III were used as measures of intellectual functioning, whereas the Bayley Language Composite and the WPPSI-III Verbal Index were used as approximations of verbal ability. Percentile ranks were used to allow direct comparisons between assessment tools.

Theory of mind

ToM tasks were selected to assess two aspects of ToM that develop during the preschool period: emotion and desires reasoning, and FBU. For emotion and desires reasoning, participants were administered age-appropriate variations of such tasks. All children completed the same FBU task.

Discrepant desires task

The discrepant desires task (24 to 36 months of age; Repacholi & Gopnik, 1997) is a task of emotion and desires reasoning involves giving the child the choice between two foods, one typically liked by children (e.g., cookies) and one that is generally less preferred (e.g., broccoli).The experimenter expresses a preference for the children's non-preferred food and then asks them to give her another food item because she is still hungry. The goal of the task is to assess whether children will answer egocentrically or will consider the experimenter's preferred food. A total of four food combinations are presented, for a maximum of four points; z- scores are used.

Desires task

The desires task (36 months of age and older; Pears & Moses, 2003) is a more advanced task assessing children's understanding of how fulfilled and unfulfilled desires might affect a character's feelings was administered. The stories describe a character's search for a desired object in a particular location with three possible endings to the story, each presented twice: 1) the character finds the desired object, 2) he finds nothing, or 3) he finds a different object, not initially sought after. The child is asked to speculate on the character's feelings (happy or sad) in these three situations. A score out of a possible six points is calculated and z-scores are used.

False belief task

For the false belief task (Hughes, Ensor, & Marks, 2011), children are presented with a peep-through picture book which incorporates a deceptive element and are then asked to recall their own initial belief about what they saw, as well as predict another's belief via two forced-choice questions. For example, children are made to believe that they see an eye through the peep-through hole, but they find out at the end of the story that it is a spot on a snake. They are then asked: "Before we turned the page, what did you think it was, an eye or a snake?" and [Turn back to initial page, before the child saw it was a spot and not an eye] "This is Leo, he has never read this book, what does he think it is, an eye or a snake?" A control question is also included "What is it really, an eye or a snake?". For both scenarios, children receive credit (one point) only if they are able to answer the corresponding control question, for a maximum of two points.

Statistical analyses

All data were analyzed using SPSS statistical software (version 21.0; SPSS, Inc., Chicago, IL) and screened for violations of normality. The degrees of freedom associated with equal variance not assumed are reported for t-tests when Levene's test for Equality of Variances was significant. An alpha level of $p < 0.05$ was considered significant and effect sizes were calculated using Cohen's d (small effect d = 0.2, medium effect d = 0.5, large effect d =0.8; Cohen, 1988).

Group comparisons (mTBI vs. TDC) were conducted via independent samples t-tests for the following variables: age at testing; intellectual functioning (Bayley-III Cognitive Composite or WPPSI-III Global Index); verbal abilities (Bayley-III Language Composite or WPPSI-III Verbal Index); socioeconomic status; parental education; pre- and post-injury global and social behavior (CBCL, ABAS) and family characteristics (FAD, PSI-brief, DAS-4); and postconcussive symptoms (PCS-I; one week and six months prior to T1 assessment). A Chi-square analysis was conducted to determine whether there was a sex difference between the two groups (mTBI vs. TDC).

Percentages and frequencies are reported for the following TBI injury characteristics: lowest GCS, cause of the accident, presence of loss of consciousness (LOC) and alteration of consciousness (i.e., confusion; AOC). The mean and standard deviation is reported for the number of neurological symptoms reported in the case report form.

Group analyses (mTBI vs. TDC) were first conducted using independent samples t-tests. The false belief task total raw score and the emotion and desires tasks combined z scores were used as outcome variables. An analysis of covariance (ANCOVA) was also performed to control for pre-existing group differences (externalizing behavior as measured by the CBCL; see below).

Correlations were computed between performance on the ToM tasks and the following TBI injury characteristics: lowest GCS, number of neurological symptoms reported in the case report form, and number of postconcussive symptoms (PCS-I).

RESULTS

Sample descriptives

The two groups did not differ in terms of baseline intellectual, behavioral, developmental and family characteristics (see Table 1), except for pre- and post-injury externalizing behavior, as measured by the CBCL. Accordingly, pre-injury externalizing behavior was used as a covariate in the main analyses. There was no significant sex difference between the mTBI and TDC groups, X^2 (1, N = 101) = 2.98, p = .08. At T1, the two groups differed on the number of postconcussive symptoms reported within the last six months, as would be expected.

[INSERT TABLE 1]

mTBI injury characteristics

The majority of children (90%) had a GCS score of 15. The most frequently documented neurological symptoms in the case report form were headaches (35%), persistent vomiting (49%), haematoma (49%), drowsiness (46%), and dizziness (18%). Seizures were reported in only one participant. The majority (96%) of mTBIs were caused by an accidental fall. Other injuries included bumping head on furniture (1) and knee hit on head (1). Nine children reportedly lost consciousness. The LOC lasted either for less than one minute (5), for less than five minutes (1) or it was suspected (3). Eight other participants experienced an alteration in consciousness (AOC). The AOC lasted either less than one minute (7) or between one and 24 hours (1). See Table 2.

[INSERT TABLE 2]

Theory of mind performances

The mTBI group performed significantly worse than the TDC group on both the desires and emotions tasks ($t(93) = -2.81$, $p = .006$, $d = -.58$) and the false belief task ($t(93) = -2.40$, $p = .02$, $d = -.49$). The analyses of covariance (ANCOVA) revealed that when pre-injury externalizing behavior was entered as a covariate, the main effect of externalizing behavior was not significant in either case ($F(1,89) = .67$, $p = .41$; $F(1,89) = .05$, $p = .83$), while the main effect of group remained significant for both tasks (Desires task: $F(1,89) = 4.61$, $p = .03$, $d = -.53$; False belief task: $F(1,89) = 2.47$, $p = .03$, $d = -.49$). See Table 3.

[INSERT TABLE 3]

Correlations between mTBI injury characteristics and theory of mind performances

Analyses were conducted to verify if the lowest GCS, the number of neurological signs (as recorded in the case report form), and the number of postconcussive symptoms within the last week and within the last six months were associated with ToM. No correlations were found to be significant. See Table 4.

[INSERT TABLE 4]

DISCUSSION

The primary goal of this study was to examine the six-month post-injury effects of mTBI on first-order ToM abilities in two to five year-old children. First-order ToM deficits of moderate magnitude were observed in children who sustained mTBI compared to their uninjured peers, and were characterized by poorer performance on tasks assessing desires and emotions reasoning as well as false belief understanding, even after controlling for pre-existing differences between the two groups (i.e., externalizing behavior). To our knowledge, this is the first time that poorer ToM is detected following mTBI in the preschool population. Only one other study has examined post-TBI ToM in an overlapping age group (three- to five-year-olds). Walz and colleagues (2009) found that children with severe TBI had difficulties in understanding false beliefs; however, reasoning about desires and emotions was not assessed, nor was mTBI.

Inconsistent effects of brain injury on cognitive and behavioral outcomes are reported following mTBI (Kirkwood et al., 2008). Some studies document specific neuropsychological weaknesses (e.g., poorer performance on some aspects of attention, memory, language, visuoperception; Anderson, Catroppa, Morse, Haritou, & Rosenfeld, 2001; Wrightson et al., 1995), whereas others suggest that mTBI is associated with minimal or no adverse consequences, especially in the long term (Babikian & Asarnow, 2009; Babikian et al., 2011; Kirkwood et al., 2008; Maillard-Wermelinger et al., 2009; Petersen, Scherwath, Fink, & Koch, 2008). Importantly, Hessen and colleagues (2007; 2006) suggest that even children with mTBI are are at increased risk for chronicity of neuropsychological impairment and that outcomes may vary depending on the severity of symptoms (P. Satz et al., 1997). However, most mTBI studies have focused on general aspects of cognition, and little is known about the impact of mTBI on the social domain. It is increasingly clear that moderate to severe TBI in older children is associated with global social repercussions such as social isolation, reduced participation in daily activities, psychosocial difficulties and affective disorders (Anderson et al., 2013; Rosema et al., 2012; Yeates et al., 2004), and one study in preschool children provides evidence that socio-emotional difficulties can occur following mild injuries (Kaldoja & Kolk, 2012). Our findings specifically suggest that mTBI in very young children may have negative consequences on at least one aspect of social cognition, namely ToM.

In keeping with this, vulnerability theory posits that sustaining a brain injury at a young age can disturb functions that are coming online at the moment of injury, whereas well-consolidated skills are more resilient to damage (Anderson et al., 2005; Anderson, Spencer-Smith, et al., 2009; Hessen et al., 2007; Ryan et al., 2014). For example, data from school-aged children indicate that first- and second-order ToM deficits are present following severe TBI (Walz et al., 2010a). In older children and adolescents, second-order ToM deficits have been found following moderate to severe TBI, in the absence of first-order ToM impairments (Dennis et al., 2009; Dennis et al., 2013; Dennis et al., 2012; Snodgrass & Knott, 2006; Turkstra et al., 2004). These studies thus suggest that functions developing at the moment of the injury are most at risk of disruption. Given that preschool children are in the process of acquiring the most fundamental concepts and abilities, their developing socio-cognitive skills, such as ToM, may be more fragile and less resistant to disruption. This increased vulnerability is worrisome given the potentially cumulative effects of early injury and the possibility that difficulties may be magnified in the long term with increasingly demanding and complex social environments. Our results lend support to the idea that early brain injuries may disrupt important socio-cognitive processes that are emerging and developing. However, a longitudinal follow-up is necessary to track the post-TBI progressiom of theory of mind (FBU and desires and emotions reasoning) in the longer term and to examine whether more widespread, cumulative ToM deficits reveal themselves or if the difficulties resorb over time.

TBI injury characteristics and theory of mind performance

No correlations were found between the TBI injury characteristics and theory of mind performance. Given that children with mild complicated TBI were excluded from this study, skull fractures or brain lesions (visible on CT or MRI scans) cannot be held responsible for poorer ToM. However, it is also possible that the clinical measures typically collected after mTBI are not sensitive enough to detect subtle variations in injury severity that may influence outcome. In addition, it is difficult to obtain reliable information on the presence and duration of LOC and AOC, and amnesia is impossible to evaluate in such young children due to their inability to clearly verbalize what they are experiencing. With respect to neuroimaging, there is evidence that CT and conventional MRI are relatively insensitive to small haemorrhagic lesions and that only more advanced techniques, such as susceptibility weighted imaging, are able to detect subtle brain changes that may influence outcome (Beauchamp et al., 2011, 2013). Mild brain injuries may also result in functional brain disturbances (e.g., abnormal metabolism, decreased blood flow, impaired neural transmission; Ewing-Cobbs et al., 2000; MacKenzie et al., 2002; Umile, Sandel, Alavi, Terry, & Plotkin, 2002; Wozniak et al., 2007), better assessed through advanced neuroimaging techniques and biomarkers (Papa, Lewis, Falk, et al., 2012; Papa, Lewis, Silvestri, et al., 2012).

Other studies indicate that environmental factors are more predictive of social outcomes post-TBI than clinical factors,(Anderson et al., 2013; Crowe, Catroppa, Babl, & Anderson, 2012; Rosema et al., 2012). Research shows that positive parental behavior, adequate family functioning, and higher quality of home environment are linked to better recovery (Crowe et al., 2012; Wade et al., 2011; Yeates et al., 2004; Yeates et al., 2010). The family characteristics assessed in the current study, namely general family functioning, parental stress, and parental marital satisfaction do not provide evidence for this hypothesis in our sample. However, a more exhaustive assessment of environmental and family characteristics may be necessary to capture all aspects of family dynamics and other environmental variables, which may play a role in the link between mTBI and ToM.

Everyday social implications of theory of mind difficulties

Disruptions to ToM skills can have a variety of negative socio-emotional consequences, such as difficulty taking another's perspective, less sensitivity towards others' feeling and misfortunes (i.e., empathy), or mistaken intent attribution and decoding of socio-emotional cues, which can all result in reduced social competence and is likely to elicit unfavorable reactions from peers. This is of concern given the well-documented importance of peer relationships for children's subsequent emotional, social, and academic adjustment. For instance, studies show that young children who have more or better-quality friendships are likely to present better socio-emotional adjustment (Ladd & Troop-Gordon, 2003) and school adjustment (Ladd, 2003; Ladd, Kochenderfer, & Coleman, 1996), and are less likely to drop out of school in subsequent years (Srebnik & Elias, 1993). Thus, early social deficits emanating from poor ToM could have lasting consequences for children's developmental pathways.

LIMITATIONS

In the TBI literature, the issue of the appropriate control group (typically developing children vs. orthopedic injured peers) remains controversial (Babikian et al., 2011; Mathias et al., 2013). Children with orthopedic injuries are thought to provide a better control for child characteristics that could put individuals at-risk for TBI (e.g., attention and behavior problems; Babikian et al., 2011) though a recent study, albeit in adults, suggests that orthopedic injury control groups do not have any clear advantages over community control groups (Mathias et al., 2013). A typically developing (community) control group was used here to compare children with mTBI to the peers they are likely to interact with and be compared to in everyday life. While we cannot entirely rule out the possibility that group differences are inherent to the TBI population, it is notable that the two groups in this study had comparable (TBI pre-injury) socioeconomic status, developmental milestones, intellectual functioning, verbal skills, adaptive functioning, parental stress, parental marital satisfaction and family functioning. They differed only on the increased presence of pre-injury externalizing behavior problems in the mTBI group, which is consistent with other studies (e.g., Garcia et al., 2014; Li & Liu, 2013). When this difference was controlled for in the analyses, the results remained robust with medium effect sizes, suggesting that differences in ToM may be more attributable to TBI than to pre-existing behavioral differences. Another limitation in this study related to age effects. Given that ToM develops rapidly during the preschool years, future work with larger samples should seek to investigate ToM performance in smaller age bands, in order to capture more subtle changes and differences in social cognition.

CONCLUSIONS

As the first evidence that mTBI is associated with ToM difficulties in very young children, the findings have substantial implications for clinical management. However, to devise appropriate interventions, we must first establish if the difficulties observed in the current study are associated with more extensive social impairments in the longer term, or whether they will resorb as a result of ongoing neurocognitive development, as some studies have shown for other cognitive functions (e.g., Anderson, Catroppa, Godfrey, & Rosenfeld, 2012; Anderson, Godfrey, Rosenfeld, & Catroppa, 2012; Beauchamp, Catroppa, et al., 2011). Additionally, given the complex and multidimensional nature of ToM, it will be important to establish, especially in the preschool population, if ToM skills are uniformly affected or if some components are more resilient to injury. Future studies should assess a wider range of ToM (e.g., intent attribution) and associated socio-cognitive skills (e.g., empathy) using longitudinal designs to obtain a clearer profile. Lastly, the link between mTBI and ToM skills may be the result of a complex orchestration of various cognitive functions not limited to ToM (e.g., attention, executive skills) and the relation may be modulated by other variables (e.g., fatigue, motivation) not considered in this study. Nonetheless, considering the impact that social difficulties may have on daily functioning, the current findings point to the necessity of assessing and monitoring social cognition after early TBI, even when injuries are mild. Elucidation of the putative causes and consequences of ToM impairments in this population will be helpful in guiding health practitioners in their management and follow-up of young children with mTBI who exhibit persistent socio-cognitive difficulties.

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Table 1. Sample descriptives

	mTBI	TDC	***t* / *F***	***p***	***d***
N	51	50	—	—	—
Demographics					
Sex [male], n (%)	26	17	2.98	.08	—
SES[a], M (SD)	57.36 (11.83)	59.54 (13.08)	-.85	.40	-.17
Parental education, M (SD)	3.17 (1.10)	2.87 (.82)	1.51	.13	.31
TBI-related variables					
Age at TBI (months), M (SD)	36 (11.19)	—	—	—	—
Time post-TBI (months), M (SD)	6.51 (.83)	—	—	—	—
Age at testing (months), M (SD)	42.51 (11.17)	44.44 (11.94)	-.84	.40	-.17
PCS[b] (last wk), M (SD)	.54 (1.23)	.61 (1.24)	-.32	.75	.08
PCS[b] (last 6 mos), M (SD)	2.08 (2.58)	.45 (.98)	4.18	**<.0001**	.84
Cognitive & behavioral variables					
Intellectual functioning (%ile rank), M (SD)	59.96 (25.79)	57.33 (24.90)	.51	.61	.10
Verbal abilities (%ile rank), M (SD)	51.46 (28.05)	51.94 (24.83)	-.09	.93	.02
Pre-injury ABAS[c], GAC (raw score), M (SD)	96.63 (15.82)	100.29 (18.81)	-1.02	.31	.21
Post-injury ABAS[c], GAC (raw score), M (SD)	97.82 (16.53)	100.29 (18.81)	-.69	.49	.14
Pre-injury ABAS[c], Social (raw score), M (SD)	21.48 (5.03)	22.98 (6.88)	-1.23	.22	.25
Post-injury ABAS[c], Social (raw score), M (SD)	21.71 (4.23)	22.98 (6.88)	-1.10	.28	.22
Pre-injury CBCL[d] Externalizing Scale (raw score), M (SD)	14.63 (6.49)	11.35 (7.08)	2.40	**.019**	.48
Post-injury CBCL[d] Externalizing Scale (raw score), M (SD)	16.62 (10.29)	11.35 (7.08)	2.98	**.004**	.60
Developmental milestones					
APGAR, M (SD)	9.29 (.46)	9.31 (.58)	-.23	.82	-.04
Age first words, M (SD)	10.22 (3.44)	11.16 (3.38)	-1.23	.22	-.28
Age first steps, M (SD)	12.55 (2.28)	12.39 (2.16)	.34	.74	.07

Family characteristics					
Pre-injury PSI[e] – Parental distress, M (SD)	1.95 (.71)	2.02 (.65)	-.46	.65	-.10
Post-injury PSI[e] – Parental distress, M (SD)	1.92 (.63)	2.02 (.65)	-.77	.44	-.16
Pre-injury PSI[e] – Parent-child dysfunctional interactions, M (SD)	1.50 (.41)	1.39 (.33)	1.38	.17	.30
Post-injury PSI[e] – Parent-child dysfunctional interactions, M (SD)	1.50 (.42)	1.39 (.33)	1.36	.18	.29
Pre-injury FAD[f], M (SD)	3.35 (.44)	3.45 (.41)	-1.11	.27	-.24
Post-injury FAD[f], M (SD)	3.42 (.49)	3.45 (.41)	-.30	.76	-.07
Pre-injury DAS[g], M (SD)	4.01 (.86)	4.19 (.75)	-1.03	.31	-.22
Post-injury DAS[g], M (SD)	4.10 (.75)	4.19 (.75)	-.58	.56	-.12

Note: [a]SES = Socioeconomic status, Blishen Socioeconomic Index, 1981; [b]PCS = Postconcussive symptoms; [c]ABAS = Adaptive Behavior Assessment System; [d]CBCL = Child Behavior Checklist; [e]Parental Stress Index; [f]Family Assessment Device; [g]Dyadic Adjustment Scale.

Table 2. mTBI injury characteristics

Lowest GCS[a], (n, %)[a]	14 (5, 10%), 15 (46, 90%)
Number neurological signs[b], M (SD)	2.25 (1.52)
Cause of mTBI [accidental fall], n (%)	49 (96%)
Neuroimaging[c], n (%)	5 (10%)
LOC[d], n (%)	<1 min (5, 10%), < 5 mins (1, 2%), Susp. (3, 6%)
AOC[e], n (%)	<1 min (7, 14%), 1-24 hrs (1, 2%)

Note: [a]GCS = Glasgow Coma Scale; [b]Neurological signs include the presence of the following symptoms: Headaches, irritability, persistant vomiting (more than two times), hematoma, drowsiness, dizziness, convulsions, visual symptoms (e.g. blurred vision), balance or motor problems (e.g. crooked walking); [c]Neuroimaging: All were found to be negative. [d]LOC = Loss of consciousness (Susp. = suspected); [e]AOC = Alteration of consciousness.

Table 3. Performance on theory of mind tasks according to group

TASKS	**mTBI**	**TDC**	**Confidence intervals (95%)**
	n = 51	n = 50	
Desires tasks combined[a], M (SD)	-.31 (1.12)	.27 (.84)	**mTBI** : -.62 – -.02
			TDC : -.02 – .57
False belief task, M (SD)	.53 (.69)	.87 (.75)	**mTBI** : .34 – .76
			TDC : .64 – 1.07

Note: [a]Standardized scores of the discrepant desires task and the desires task; tabulated as z-scores.

Table 4. Correlations between ToM performance and mTBI injury characteristics

Task	Injury characteristic	*r*	*p*
False belief understanding	PCS[a] last week	-.01	.96
	PCS[a] last 6 months	-.20	.18
	Lowest GCS[b]	.16	.27
	No. neuro. signs	.08	.57
Emotion and desires reasoning	PCS[a] last week	-.05	.77
	PCS[a] last 6 months	-.10	.51
	Lowest GCS[b]	-.06	.67
	No. neuro. signs	.01	.93

Note: [a]PCS = Postconcussive symptoms; [b]GCS = Glasgow Coma Scale.

Article 2

Long-term brain-injury-specific theory of mind differences after mild TBI in preschool children

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Abstract

A previous study conducted by our group found theory of mind (ToM) differences in preschool children who sustained mild traumatic brain injury (mTBI) compared to typically developing peers, six months post-injury. The goals of the current longitudinal study were to determine if these findings are the result of a brain-injury-specific effect or rather a general-injury effect, to examine the long-term evolution of ToM skills following preschool mTBI, as well as to investigate the links between ToM abilities and general social functioning. To do so, 72 children who sustained mTBI between the ages of 18 and 60 months were evaluated 6 and 18 months post-injury on ToM tasks including desires and emotions reasoning and false belief understanding. They were compared to 58 participants who sustained an orthopedic injury (OI) and 83 typically developing children (TDC). The three groups did not differ on demographic and baseline characteristics. The mTBI group obtained poorer scores relative to both comparison groups on the desires and emotions reasoning task, both at 6 and 18 months injury. No correlations were found between injury characteristics and ToM performance. For the mTBI group, associations were found between ToM performance and global social competence. These findings suggest a brain-injury-specific effect on ToM that persists in the long term following mTBI in preschool children.

Keywords: pediatric, traumatic brain injury, concussion, social cognition, theory of mind, false belief understanding, perspective taking, longitudinal, social skills.

INTRODUCTION

Early in life children begin to develop the rudimentary skills necessary to become adequate social partners, setting the stage for a rich social life. For most children, this occurs in a natural and flawless way, following a typical developmental trajectory. However, underneath the seemingly effortless acquisition of social skills is a vast and well-orchestrated neural network responsible for understanding and participating in the world (e.g., Adolphs, 2009). Unsurprisingly, disruption to the integrity and/or maturation of this "social brain" can have a negative impact on children's social competence. As such, social and behavioral problems have been documented in several neurodevelopmental disorders including autism, fetal alcohol syndrome and ADHD (e.g., Baron-Cohen, 2000; Fahie & Symons, 2003; Hughes, Dunn, & White, 1998; Turkstra et al., 2004). Global socio-behavioral (e.g., conduct disorder, disruptive behavior), socio-affective, and social participation impairments have also been reported after acquired injuries, such as moderate and severe pediatric traumatic brain injury (TBI; Anderson et al., 2013; Rosema et al., 2012; Yeates et al., 2004). Although changes in the social realm following mild TBI (mTBI) tend to be more subtle and less pervasive than those associated with severe injuries, the ensuing difficulties can nonetheless interfere with development, notably in terms of socio-emotional maturation (Kaldoja & Kolk, 2012), and these socio-emotional problems can persist up to nine months post-injury (Kaldoja & Kolk, 2015).

Identifying potential social difficulties after pediatric TBI may be especially important given research showing that social functioning is also associated with school readiness and success, as well as emotional well-being (Blair, 2002; Ladd, 1999; Parker & Asher, 1987).

Additionally, social problems can have lasting consequences. Longitudinal studies have demonstrated that social competence in the preschool years has a long-term impact on a child's acceptance by peers, regardless of later improvement in social interaction (Razza, 2009). Jones and colleagues (2015) also provided evidence that early socio-emotional skills are associated with multiple outcome markers in adulthood such as education, employment, criminal activity, substance abuse, and mental health.

In order to gain a better understanding of the origins of post-TBI social problems, and to identify potential loci of intervention, neuropsychologists have begun to explore the cognitive underpinnings of social competence, known as social cognition. Social cognition is an umbrella term that refers to the backstage skills necessary for adequate interaction on the social scene. Early childhood is devoted to the burgeoning of a subcomponent of social cognition, known as theory of mind (ToM), which refers to one's understanding that humans are beings with mental states (i.e., desires, beliefs, feelings, intentions; Wellman et al., 2001; Wellman et al., 2011) that shape and predict one's behavior. During the preschool period, children develop an understanding of the most basic form of ToM, known as first-order ToM, which Miller (2012) describes as "[…] children's ability to think about mental states in themselves and others – thus to think about somebody thinking about something, or feeling something, or wanting something, or whatever the relevant mental state may be" (p. 44).

Several studies document alterations in ToM following childhood TBI. Impairments in more complex forms of ToM (i.e., second-order ToM : a child's understanding of someone else's belief about something in the world) and ToM-related functions (e.g., empathy), but not in basic forms (i.e., first-order ToM), have been shown in school-aged children and adolescents who have sustained moderate or severe TBI (Dennis et al., 2009; Dennis et al., 2013; Dennis et al., 2012; Snodgrass & Knott, 2006; Turkstra et al., 2004). In younger children (6- to 8-year-olds) who sustained severe TBI, Walz and colleagues (2010a) found first- *and* second-order ToM difficulties. These authors further reported that preschool children with severe TBI, when tested within three months of the injury, are impaired on an aspect of first-order ToM, that of false belief understanding (FBU: the understanding that people can hold beliefs that are untrue and nonetheless act on them), compared to children with moderate TBI and those with orthopedic injuries. Our group subsequently extended these findings in the most mildly injured preschool children, by showing that children between 18 and 60 months of age who sustain mild, uncomplicated TBI perform more poorly on ToM tasks (FBU and desires and emotions reasoning) six months post-injury, even after controlling for pre-injury behavioral differences (Bellerose, Bernier, Beaudoin, Gravel, & Beauchamp, 2015). At first glance, these results may seem somewhat unexpected given studies demonstrating that mild, uncomplicated TBI does not typically result in long-term neurocognitive sequelae (e.g., Babikian et al., 2011; Holm et al., 2005; Karr et al., 2014). Indeed, there is some debate concerning brain-injury-specific effects versus general-injury effects after mild TBI, whereby some have found that chronic postconcussive symptoms or abnormal neuropsychological scores following mTBI are due to premorbid or environmental determinants that are common to many types of injuries (Babikian & Asarnow, 2009; Babikian et al., 2011; Kirkwood et al., 2008; Maillard-Wermelinger et al., 2009; Rohling, Larrabee, & Millis, 2012; Yeates, 2010).

However, there is evidence that there is a particular "vulnerability" to brain injury during the early years of life. Studies conducted in the last decades have provided evidence for worse outcomes following early childhood TBI, which is argued to be attributable to the fact that during the first years of life, children are developing their cognitive repertoire, critically dependent on the integrity of particular brain structures at key developmental stages (Anderson et al., 2005; Anderson & Moore, 1995; Anderson, Spencer-Smith, et al., 2009; Donders & Warschausky, 2007; Gronwall et al., 1997; H. G. Taylor et al., 2002). Thus, children appear to be at increased risk of suffering brain-injury-related sequelae because of their immature and fragile neural system. Despite mounting evidence suggesting greater vulnerability of the young brain, no study has specifically addressed the persistence of socio-cognitive difficulties in young children, and research concerning preschoolers remains sparse comparatively to older children.

Thus, the primary goal of the current study was to investigate whether ToM difficulties after mild, uncomplicated preschool TBI are specific to brain injury, or whether they are the result of a general injury effect. To do so, we compared preschool children who sustained mTBI to an orthopedic comparison group and we expected to find a brain-injury-specific effect. The second aim was to track the evolution of ToM skills in the long-term, from 6 months to 18 months post-injury. Given the mildness of the brain injuries in our sample, it was hypothesized that the 6-month ToM difficulties would resorb by the 18-month time point. Third, we sought to examine the relation between ToM skills 6 months post-injury and more global social functioning at 6 and 18 months post-injury. It was expected that poorer ToM skills at 6-months post-injury would be associated with lower social functioning at the 6- and 18-month time points.

METHOD

Participants

Recruitment

This study was approved by the ethics review board of Sainte-Justine Hospital and conducted in accordance with the Helsinki declaration. Informed written parental consent was obtained prior to participation. Participants were recruited as part of a prospective longitudinal study of cognitive and social outcomes after early TBI (see Bellerose et al., 2015). Data are presented pertaining to the 6- and 18-month post-injury time points. Children with mTBI were recruited *via* the Emergency Room between 2011 and 2015, using the definition proposed by Osmond and colleagues (2010). Inclusion criteria were a) age at injury between 18 and 60 months, b) closed head injury with a Glasgow Coma Scale (GCS) between 13 and 15 (Teasdale & Jennett, 1974), c) at least one of the following symptoms: loss of consciousness, excessive irritability, persistent vomiting (more than two times), confusion, headaches that worsen over time, drowsiness, dizziness, motor difficulties or balance problems, blurred vision, hypersensitivity to light, and/or the presence of seizures; d) child and at least one parent fluent in French or English. Exclusion criteria were: a) suspicion of non-accidental injuries, b) diagnosed congenital, neurological, developmental, psychiatric, or metabolic condition, c) less than 36 weeks of gestation, d) prior TBI, and e) for the purposes of the analyses presented here, evidence of intracranial lesion on clinical CT or MRI (i.e, mild complicated TBI).

A convenience sample of children with an orthopedic injury (OI) excluding the head was also recruited *via* the Emergency Room between 2011 and 2015. The following orthopedic injuries were considered: fracture, sprain, contusion, laceration, and any other orthopedic injury such as a pulled elbow. The same inclusion criteria (except for b and c) and the same exclusion criteria applied.

Typically developing children (TDC) were recruited via advertisements posted in daycare centers. Inclusion criteria for this comparison group were: a) aged between 24 and 66 months, b) child and at least one parent fluent in French or English. The same exclusion criteria applied.

Procedure

mTBI & OI groups

At enrolment (Time point 0, T0), parents were asked to complete a pre-injury questionnaire booklet including sociodemographic information. They were asked to report on their child's adaptive skills in the weeks *preceding* the injury, in order to provide an estimate of baseline functioning. The research team also completed a Case Report Form. Six and eighteen months post-injury (Time points 1 (T1) and 2 (T2)), children completed a socio-cognitive assessment battery administered by doctoral candidates in neuropsychology or research assistants trained and supervised by a qualified neuropsychologist. Parents completed the same questionnaire booklet as at T0. At T1 and T2, parents were instructed to assess their child's adaptive skills in the last four weeks. They also completed the Postconcussive Symptom Interview (PCS-I; Mittenberg et al., 1997; Yeates et al., 2012) whereby they were asked to reflect on the presence of symptoms in the week prior to testing as well as since the injury. Testing occurred either in a single three-hour session or in two shorter sessions with regular breaks.

Typically Developing Comparison (TDC) group

Given the absence of injury, the children in the TDC group completed T1 as soon as possible after recruitment, using the same socio-cognitive battery and parental questionnaires (including the Postconcussive Symptom Interview; see Measures section for details) as those used for the mTBI and OI groups. Twelve months later (T2), the same procedure was repeated.

Measures

Case Report Form

General medical information was obtained from medical files including the following for the mTBI group: cause of mTBI, lowest GCS, and neurological symptoms: headaches, irritability, persistent vomiting (more than two times), haematoma (forehead or scalp), drowsiness, dizziness, seizures, visual symptoms (blurred vision, hypersensitivity to light), and balance/motor problems. Loss of consciousness (LOC) was measured according to the following categories: none, <1 minute, <5 minutes, <1 hour, 1 to 24 hours, >24 hours, suspected, unknown. Where possible, alteration of consciousness (AOC, i.e., confusion) was also assessed as follows: none, <1 hour, 1 to 24 hours, >24 hours, suspected, unknown. Results of clinical neuroimaging were obtained when available to verify exclusion criteria "e" (mild complicated TBI). For the OI group, the following information was obtained from the medical files: cause of OI, diagnosis (fracture, sprain, contusion or laceration) and severity of injury. The severity of the injury was established according to the Abbreviated Injury Scale as follows: Minor = no treatment required, Moderate = outpatient treatment required, Serious = admission required but not in Intensive Car Unit (ICU), Severe = ICU admission and/or basic treatment required, Critical = intubation, mechanical ventilation or vasopressors required (Wang & Gennarelli, 2009).

Postconcussive Symptom Interview (PCS-I; Mittenberg et al., 1997; Sady et al., 2014; Yeates et al., 2012): This parental report questionnaire consists of 15 symptoms from the following domains: Physical, Cognitive, Affective and Sleep. Parents must say if the symptoms were present (1) or absent (0) at any time during the week prior to testing and since the injury (T1: last 6 months, T2: last 18 months). A score out of 15 was calculated both for symptoms observed in the last week and since the injury.

ABCs Laboratory Sociodemographic Questionnaire: Parents completed an in-house developmental and demographic questionnaire including, for example, information on the child's age, sex and ethnicity. Parental education (i.e, number of years of schooling completed) was also obtained, and mother and father highest educational attainment were averaged.

Adaptive Behavior Assessment System (ABAS; 0 to 5 and 5 to 21 years old versions; Harrison & Oakland, 2003): In this 241-item assessment of everyday adaptive skills parents are asked to rate their child on a 4-point scale according to the frequency at which he or she *correctly* demonstrates a behavior, *without help*, when such behavior is necessary. The Global Adaptive Composite (GAC) as well as the Social Composite are reported (standard score, M = 100, SD = 10). The Social Composite evaluates children's leisure activities as well as their ability to interact socially, engage in play, initiate and maintain friendships, and express and recognize emotions.

Intellectual functioning

Intellectual functioning and verbal ability were measured for descriptive purposes. Children between the ages of 24 and 30 months completed the Bayley Scales of Infant Development Cognitive and Language subscales (Bayley-III; Bayley, 2005). Children 31 months and older completed the Wechsler Preschool and Primary Scale of Intelligence (WPPSI-III; Wechsler, 2002) and scores were calculated for the Verbal, Performance and Global Indices. The Cognitive Composite of the Bayley-III and the Global Index of the WPPSI-III were used as measures of intellectual functioning, whereas the Bayley Language Composite and the WPPSI Verbal Index were used as approximations of verbal ability. Percentile ranks were used to allow direct comparisons between assessment tools.

Theory of mind

ToM tasks were selected to assess two aspects of ToM that develop during the preschool period: desires and emotions reasoning and FBU. For desires and emotions reasoning, participants were administered age-appropriate variations of such tasks. Of note, some children completed the same desires and emotions reasoning task at both time points whereas others completed different tasks given their age. All children completed the same FBU task at both time points.

Discrepant desires task (24 to 35 months of age; Bellerose et al., 2015; Repacholi & Gopnik, 1997): This task of desires and emotions reasoning involves giving the child the choice between two foods, one typically liked by children (e.g., cookies) and one that is generally less preferred (e.g., broccoli). The experimenter expresses a preference for the children's non-preferred food and then asks them to give her another food item because she is still hungry. The goal of the task is to assess whether children will answer egocentrically or will consider the experimenter's preferred food. A total of four food combinations are presented, for a maximum of four points; Z-scores are used. This task was used only at T1 because all children were 36 months or older at T2.

Desires task (36 months of age and older; Bellerose et al., 2015; Pears & Moses, 2003): For older children, a more advanced task assessing children's understanding of how fulfilled and unfulfilled desires might affect a character's feelings was administered. The stories describe a character's search for a desired object in a particular location with three possible endings to the story, each presented twice: 1) the character finds the desired object, 2) he finds nothing, or 3) he finds a different object, not initially sought after. The child is asked to speculate on the character's feelings (happy or sad) in these three situations. Each possible ending is presented twice, for a total of six stories. A score out of a possible six points is calculated and z-scores are used.

False belief task (Bellerose et al., 2015; Hughes et al., 2011): Children are presented with a peep-through picture book which incorporates a deceptive element and are then asked to recall their own initial belief about what they saw, as well as predict a puppet's belief via two forced-choice questions. For example, children are made to believe that they see an eye through the peep-through hole, but they find out at the end of the story that it is a spot on a snake. They are then asked: "Before we turned the page, what did you think it was, an eye or a snake?" and [Turn back to initial page, before the child saw it was a spot and not an eye] "This is Leo, he has never read this book, what does he think it is, an eye or a snake?" A control question is also included "What is it really, an eye or a snake?". For both scenarios, children receive credit (one point) only if they are able to answer the corresponding control question, for a maximum of two points.

Statistical analyses

All data were analyzed using SPSS statistical software (version 23.0; SPSS, Inc., Chicago, IL) and screened for violations of normality. An alpha level of $p < 0.05$ was considered significant.

Group comparisons (mTBI *vs.* OI *vs.* TDC) for the following variables were conducted via univariate analyses of variance (ANOVAs): age at T1 and T2, parental education, postconcussive symptoms (PCS-I; within the last week and in the last six months at T1), ABAS Global and Social scores. Cohen's *d* is reported as the effect size. For the injured groups (TBI *vs.* OI), independent t-tests were computed for age at injury and time post-injury at T1 and T2; partial eta squared is used as a measure of effect size. Chi-square analyses were also conducted for sex and ethnicity. Lastly, mixed linear analyses were performed for the ABAS Global and Social scores. Preliminary analyses were conducted to examine group differences at the three time points; it also provided evidence of stable adaptive skills between T1 and T2 for the TDC group, and therefore T1 ABAS data was used as a proxy for T0.

Percentages and frequencies are reported for the following mTBI characteristics: cause of the accident, lowest GCS, occurrence of neuroimaging, presence of loss of consciousness (LOC) and alteration of consciousness (i.e., confusion; AOC). The mean and standard deviation is reported for the number of neurological symptoms obtained from the case report form. Concerning the OI group, percentages and frequencies are given for the following variables: cause of OI, severity of the injury and diagnosis.

Main group analyses (mTBI *vs.* OI *vs.* TDC) on ToM performance at the two time points (6 and 18 months post-injury) were conducted using a mixed linear model to examine the evolution of ToM skills as well as to determine, in the case of group differences, whether the findings are the result of a general-injury or a brain-injury-specific effect. Pre-existing group differences that could potentially influence the outcome (e.g., IQ, verbal abilities, adaptive skills) were considered as covariates. Confidence intervals (95%) were used as estimates of the effect size.

Correlations were computed between injury characteristics (number of neurological signs provided in the Case Report Form and postconcussive symptoms as measured with the PCS-I) and performance on both ToM tasks at both time points (T1 and T2). Additionally, correlations were conducted to examine the relation between scores on both ToM tasks and scores on the ABAS (Global and Social scores) at T1 and T2; correlations were first run including all participants and then in the mTBI group only.

RESULTS

Final Sample

The recruitment and follow-up of participants are detailed in Figures 1 and 2. The attrition rate between T0 and T1 is 5% for the mTBI group and 11% for the OI group. Also, 10% of mTBI, 2% of OI, and 6% of TDC participants who completed T1 did not return for follow-up at T2. The final sample at T1 consisted of 72 mTBI, 58 OI, and 83 TDC participants. At T2, 41 mTBI, 23 OI and 43 TDC had been retested at the time of data extraction.

Sample characteristics

For the mTBI and OI groups, there was no difference in terms of age at injury (mTBI: $t(1, 198) = .40$, $p = .69$; OI: $t(1, 120) = .07$, $p = .95$) and sex (mTBI: X^2 (1, $N = 199$) = .101, $p = .80$; OI: X^2 (1, $N = 212$) = .03, $p = .88$) between those who participated and those who refused to participate in the study. Similarly for the TDC group, there was no age (at recruitment: $t(1, 107) = 1.26$, $p = .21$) or sex differences related to participation status (X^2 (1, $N = 106$) = 2.61, $p = .16$). The three groups did not differ in terms of intellectual and cognitive variables, nor were they different in terms of demographics (sex, parental education and ethnicity; see Table 1). For behavioral variables (Global and Social composites of the ABAS), the Group x Time interaction was not significant (Global: $F(4, 300) = .13$, $p = .97$; Social: $F(4, 302) = 1.00$, $p = .41$). There was no main effect for Group (Global: $F(2, 216) = 1.22$, $p = .30$; Social: $F(2, 216) = .80$, $p =.45$), but a significant main effect was found for Time (Global: $F(2, 300) = 4.05$, $p = .02$; Social: $F(2, 302) = 2.96$, $p = .05$). For the ABAS Global composite, post-hoc analyses revealed that the scores obtained at T1 and T2 were significantly higher than those obtained at T0 (T0 to T2, $p = .02$; T01 to T2, $p = .04$). For the ABAS Social composite, T2 scores were significantly higher than T0 only ($p = .05$). Despite significant improvement from T0 to T2 on

ABAS Global and Social composites, the scores remained in the average range (mean = 100 ± 15) at all time points and for all groups. Concerning the medical variables, differences were found for PCS-I since the injury (i.e., last six months) at T1 ($F(2,199) = 7.83$, $p = .001$), with post hoc analyses revealing that the mTBI group reported significantly more postconcussive symptoms than both comparison groups (mTBI *vs.* OI $p = .02$, mTBI *vs.* TDC $p < .001$). Of note, despite significant group differences, all groups had, on average, less than two symptoms. See Table 1.

[INSERT TABLE 1]

[INSERT TABLE 2]

Injury Characteristics

mTBI

The vast majority of mTBIs were caused by an accidental fall (93%), resulting in a GCS score of 15 in 92% of cases. The most frequently documented neurological signs and symptoms in the case report form were drowsiness (54%), hematoma (50%), persistent vomiting (42%) and headaches (35%). Seizures were reported in only one participant. Eight children reportedly lost consciousness (LOC), either for less than one minute (6, 8%) or between one to five minutes (2, 3%). LOC was also suspected in six other participants. Additionally, twelve other participants experienced an alteration in consciousness (AOC), lasting either for less than one hour (10) or between one and 24 hours (2). See Table 2.

OI

For the OI group, most injuries were also caused by an accidental fall (64%). Other causes include other accidental injuries (18%) such as while playing in inflatable games or while jumping on a trampoline. In another 5% of cases, there were no witnesses at the moment of injury. Most injuries were minor (41%) or moderate (55%) in severity and resulted in a diagnosis of fracture (55%), contusion (9%), laceration (2%) or another orthopedic injury (pulled elbow, luxation; 34%). See Table 2.

[INSERT TABLE 2]

Theory of Mind (ToM) Performance

Given the absence of group differences in terms of intellectual and verbal ability, pre-injury behavioral variables and demographics, no covariates were used in these analyses. Concerning the Desires and emotions reasoning tasks, there was also no Group X Time interaction ($F(2, 147) = .32$, $p = .72$), but there was a main effect for Group ($F(2, 191) = 4.93$, $p = .01$). Post hoc analyses revealed a significant overall difference both between the mTBI and TDC groups ($p = .03$) and between the mTBI and OI groups ($p = .02$). As displayed in Table 3 and in Figure 3, the mTBI group performed significantly more poorly than OI and TDC groups, at both time points. For the FBU task, there was no Group X Time interaction ($F(2, 171) = 1.28$, $p = .28$) and there were no main effects, either for Time ($F(1, 172) = .03$, $p = .86$) or for Group ($F(2, 188) = 2.76$, $p = .07$), although the latter approached significance.

[INSERT TABLE 3]

[INSERT FIGURE 3]

Correlations between injury characteristics and ToM performance at T1 and T2 for the mTBI group

The injury characteristics (lowest GCS, number of neurological symptoms as reported in the case report form and postconcussive symptoms at T1) did not correlate with the FBU and the Desires and emotions reasoning tasks at either time point. See Table 4.

[INSERT TABLE 4]

Correlations between ToM performance (both time points) and ABAS scores (T1 and T2)

Correlations were first conducted including all participants; analyses revealed no significant associations between both ToM task performances at T1 and ABAS Global and Social composite scores both at T1 and T2. Similarly, no relations were found between both ToM task performances at T2 and ABAS Global and Social composite scores at T2. When correlational analyses were conducted in the mTBI group only, significant associations were found between the ToM and general functioning variables such that performance on both tasks at T1 was positively correlated with the ABAS Social composite score at T1 (FBU task: $r(61) = .31$, $p = .02$; Desires and emotions reasoning task: $r(65) = .25$, $p = .04$). Additionally, FBU task performance at T1 was positively associated with both the ABAS Global and Social composite scores at T2 ($r(40) = .44$, $p = .004$; $r(40) = .42$, $p = .01$). See Table 5.

[INSERT TABLE 5]

DISCUSSION

In our previous paper (Bellerose et al., 2015), we observed first-order ToM differences following preschool mTBI compared to typically developing peers, six months post-injury. The primary goal of the current study was to verify whether these findings are the result of a brain-injury-specific effect or a general-injury effect. Given the particular vulnerability associated with sustaining brain injury at an early age, we expected a brain-injury-specific effect at 6 months post-injury. The study also aimed to explore the evolution of ToM skills following mTBI. As such, it was expected that ToM difficulties present 6 months post-injury would resorb in the long term (i.e., 18 months post-injury). Our results support our brain-injury-specific hypothesis such that children who sustained mTBI obtained significantly lower results on a desires and emotions reasoning task compared to their OI counterparts, at 6 months post-injury. However, contrary to our expectations, the group differences on this task were maintained 18 months post-injury. To our knowledge, this is the first evidence of persistent brain-injury-specific effects following mild, uncomplicated TBI.

These results may seem counterintuitive given the literature concerning older children and adolescents, which indicates that acute neurocognitive consequences following mTBI are not infrequent, but are usually transient and subside by 1.5 to 3 months post-injury following a single mild, uncomplicated pediatric TBI (Holm et al., 2005; Karr et al., 2014; Kirkwood et al., 2008; Rohling et al., 2012). However, several reasons may explain why the mTBI participants in this study demonstrate long-term brain-injury-specific effects. First, we know very little about the impact of brain injury in preschool children given that the vast majority of studies have focused on school-aged children and adolescents. It may be that brain injury has differential effects in very young children compared to older peers. In fact, the last decades have provided increasing evidence of an "early vulnerability" view of TBI. Specifically, this theory posits that the young brain is more vulnerable to insult because the immature neural system cannot ensure the intact development of basic cognitive functions typically emerging during the early years, on which more complex skills depend (Anderson et al., 2005). Of note as well, because children are still in the process of developing basic skills, it may be more challenging for some of them to "catch up" to their peers after mTBI given the constant progression of their typically developing counterparts. Thus, long-term, brain-injury-specific socio-cognitive effects after preschool mTBI may be the result of an increased risk associated with sustaining a brain injury during the early years while the brain is still immature and has consolidated very few skills and compensatory means. Precisely, this neural immaturity makes it more difficult to "overcome" a disruption, and once developmental progression resumes, children have to theoretically "speed up" their developmental acquisitions to come back to par with peers who have pursued their development in the meantime.

In line with this developmental view, the particularities of the young, developing brain may also explain why not all ToM aspects are affected uniformly by brain injury, especially following a mild, uncomplicated TBI. Socio-cognitive processes recruit a vast neural network (Adolphs, 2009; Bellerose, Beauchamp, & Lassonde, 2011; Blakemore & Frith, 2004; U. Frith & Frith, 2003; Gallagher & Frith, 2003b) and injuries at a young age result in more diffuse injuries given the biomechanical factors specific to young children (Ciurea et al., 2011; Kochanek, 2006; Noppens & Brambrink, 2004). It is therefore possible that mild injuries, known to result in more diffuse damage in young children, combined with widespread socio-cognitive substrates results in subtle, non-uniform ToM changes. Specifically, diffuse damage to the vast neural network that underpins socio-cognitive functioning will probably not affect the functionality of the entire network but more plausibly, it will lead to subtle and more selective disruption of the neural system, and thus of certain aspects of theory of mind.

Pre-injury, child and environmental factors

Alternatively, several researchers argue that chronic postconcussive complaints or abnormal scores on neuropsychological tests following pediatric mTBI are the result of pre-existing psychological factors such as psychosocial/environmental variables (e.g., family environment, socioeconomic status), behavioral problems, neurodevelopmental conditions (e.g., ADHD) as well as premorbid cognitive ability (Anderson et al., 2006; Babikian & Asarnow, 2009; Bonfield, Lam, Lin, & Greene, 2013; Holm et al., 2005; Kinsella et al., 1999; Max et al., 1998; Max et al., 1997; Rohling et al., 2012; Schwartz et al., 2003; H. G. Taylor et al., 1999; H. G. Taylor et al., 2002; Yeates et al., 1997; Yeates et al., 2012; Yeates et al., 2010). Given this literature, the current study measured children's global IQ, verbal IQ, ethnicity, pre-injury behavioral and social abilities as well as parental education; no group differences were found on any of these variables. Despite these findings, it is plausible that other factors known to be related to and/or predictive of theory of mind development need to be considered. Notably, studies have shown that child temperament and executive functions are predictive of theory of mind in early childhood, even after controlling for sex, age, and receptive language abilities (e.g., Benson, Sabbagh, Carlson, & Zelazo, 2013; Devine & Hughes, 2014; Mink, Henning, & Aschersleben, 2014). Additionally, other aspects of language such as a child's use of mental-state vocabulary have been shown to predict later ToM. For example, Brooks and Meltzoff

(2015) report that children who use more mental-state words at 2.5 years are more successful on ToM tasks at 4.5 years, even when general language, maternal education, and nonsocial attention are controlled for. Bianco and colleagues (Bianco, Lecce, & Banerjee, 2015) also found that the accuracy of mental-state attribution, as opposed to the frequency of the use of such words, mediates the relation between conversational experience and mental-state reasoning even when age, family affluence, vocabulary and executive functions were entered as covariates. It is possible that general measures of language ability such as verbal IQ used here, may not capture the specific aspects of language that promote theory of mind development and maturation. Thus, it cannot be excluded that pre-existing difficulties and/or child as well as environmental determinants may play a role in the persistent symptomatology and difficulties following mTBI. Given that we have not proceeded with an exhaustive exploration of all possible pre-injury factors, future work should definitely consider additional cognitive and behavioral factors that have been shown to influence ToM. However, once again, it must be noted that all of the studies arguing in favor of the role of factors unrelated to the brain injury in mTBI outcome were conducted with older children. As such, the findings may not apply to younger children, or possibly, pre-injury, child and environmental determinants may have a differential impact on mTBI outcome in preschoolers. Additionally, Kaldoja and Kolk (2012) found that that pre-existing socio-emotional difficulties were exacerbated by a mild brain injury in children. The authors demonstrate that the injury can potentially modify children's developmental trajectory, thereby providing evidence that mild brain injuries during the first years of life are not inconsequential.

Injury characteristics and ToM performance

No correlations were found between brain injury characteristics and theory of mind performances. This lack of association may be due to the relative insensitivity of current clinical measures to detect subtle variation in injury severity that may influence outcome. For example, the GCS is not a discriminative measure when working with a mild, uncomplicated TBI population given that there is little possible variability (i.e., score between 13 and 15); in our sample, less than 10% of participants scored under 15. LOC is also less relevant following mild, uncomplicated TBI, especially in young children, because studies have shown that LOC has a sensitivity of only 3% for toddlers and preschoolers (Bonadio, 1989; Dietrich et al., 1993; Greenes & Schutzman, 1999). Additionally, the measurement of postconcussive symptoms is particularly challenging in preschool children for two reasons. Firstly, it is difficult to obtain reliable information on the presence of several symptoms in children, such as the presence and duration of LOC, AOC, dizziness, and headaches, and parents have very limited means to detect these manifestations. Amnesia is also challenging to evaluate due to the inability of young children to clearly verbalize what they are experiencing. Secondly, it is likely that the postconcussive symptoms measure used here is inappropriate for this age group as it has not been validated in children under five years of age (Sady et al., 2014). In the absence of any validated measure, we chose to explore its use in our group despite its clear limitations. Finally, retrospective reporting of postconcussive symptoms is subject to parental bias. Hence, before firm conclusions can be drawn on the link between injury characteristics and ToM, research is needed to establish which clinical measures are most useful and suitable for documenting postconcussive symptoms and injury characteristics in the mTBI preschool population.

Theory of mind performances and global social functioning measures

In line with our hypothesis, in children with mTBI, poorer ToM performance was associated with lower social functioning 6 months post-injury; poorer ToM performance was also related to lower global and social functioning 18 months post-injury. The average scores are not suggestive of significant social deficits; however, it is important to note that better ToM is associated with more general social competence after TBI, suggesting that more severe injuries may potentially be associated with reduced social functioning.

Limitations & future studies

As previously mentioned, one of the limitations inherent to the current study is the paucity of sensitive and adapted clinical measures for the preschool mTBI population. Additionally, although the goal of the current study was to examine the long term socio-cognitive skills following mTBI, it would have been useful to collect acute ToM data to allow a more accurate depiction of the evolution of these skills following brain injury. A further limitation is the fact that the typically developing children were tested as soon as they were recruited, whereas the two injury groups were tested 6 months post-injury. T0 adaptive behavior data was therefore not available for the typically developing children, and T1 data was used as proxy for T0 in this group. Of note, analyses at T2 included only a subset of children present at T1 given that not all of them had reached the 18-month, post-injury time point at the moment of data extraction. Also, our sample size did not allow us to examine ToM performances in smaller age ranges; this will need to be addressed in future studies in order to capture more subtle developmental changes in social cognition following mTBI.

Further work could seek to elucidate the impact of the first-order ToM difficulties presented here on later-developing, increasingly complex ToM skills (e.g., second- and third-order ToM) as children who sustained mTBI pursue their social development. Future studies could also investigate a wider array of socio-cognitive abilities (e.g., intention attribution, empathy) following preschool mTBI to examine the extent to which these skills are affected by mTBI. It is possible that some aspects are more resilient to injury than others. Lastly, as noted by Yeates (2010), most research on the consequences of mTBI focuses on group outcomes. However, group data is of limited clinical value because the reasons for the persistence of difficulties, whatever they are, are likely to vary across individuals. Using a "person-centered" research approach in mTBI studies may help elucidate more specific individual determinants that increase a child's risk of suffering from a range of persistent symptoms and/or difficulties after a mild, uncomplicated TBI (Yeates, 2010).

Conclusion

Preschool children who sustain mTBI demonstrate significantly poorer ToM skills compared to both typically developing peers and orthopedic counterparts in a task assessing a subcomponent of ToM, that of desires and emotions reasoning, suggesting a brain-injury-specific effect. These difficulties were present 6 months post-injury and persisted in the long term (i.e., 18 months following the injury). We cannot exclude the possibility that the results of the current study are driven by a subset of children who present with persistent ToM difficulties, either due to the injury itself or to a combination of injury and/or environmental/child factors. To gain a better understanding of the impact of mTBI in young children, the clinical markers of mTBI must first be refined and adapted to suit the preschool mTBI population. Continued exploration of the vast array of environmental and child factors that may influence the presence and persistence of socio-cognitive difficulties is needed. These findings and future directions could inform about the socio-cognitive outcomes after early mTBI, and permit the identification of children at-risk for social difficulties early in development. They may also inform clinicians of the necessity to assess socio-cognitive functioning following mTBI in young children.

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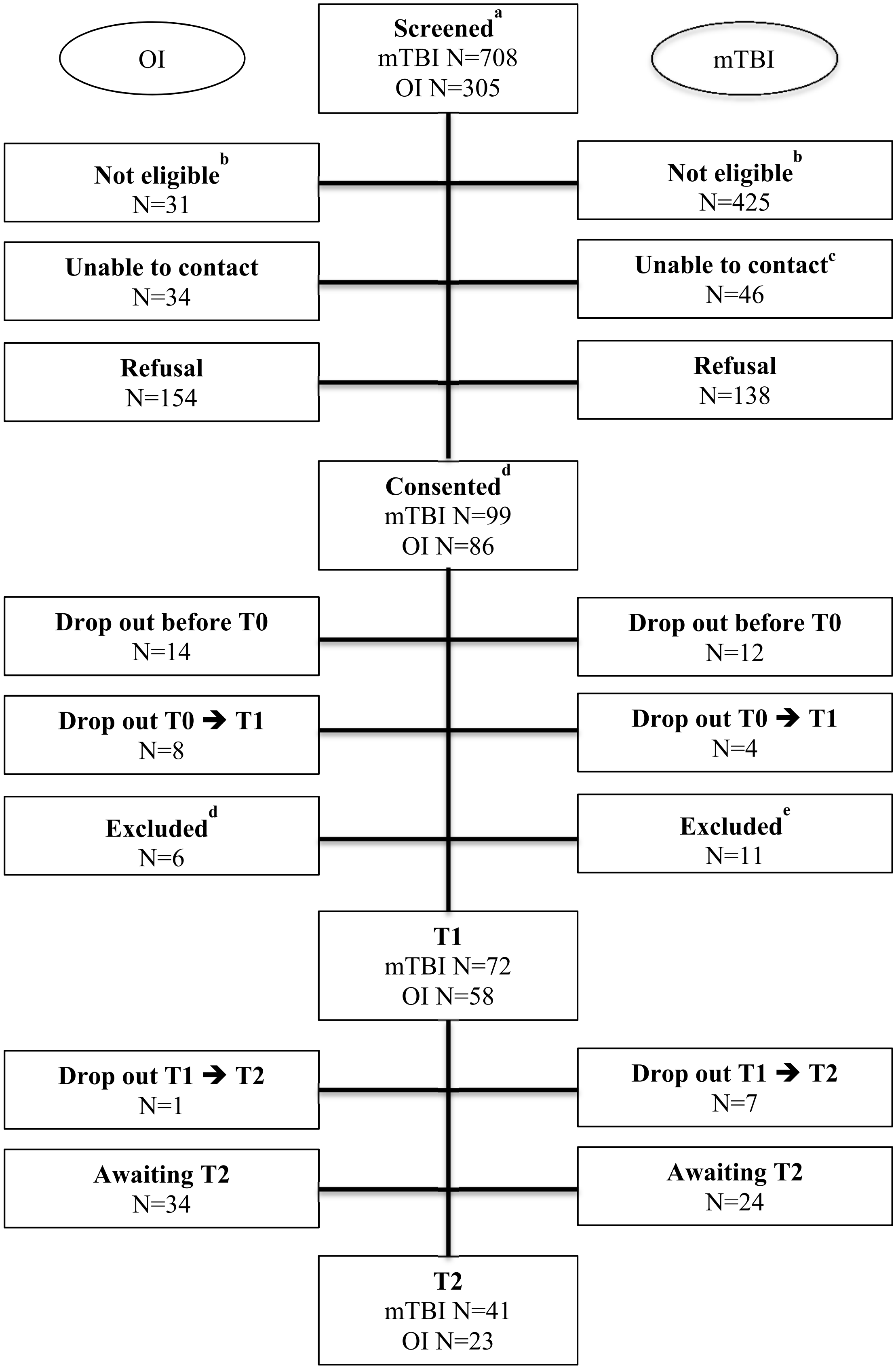
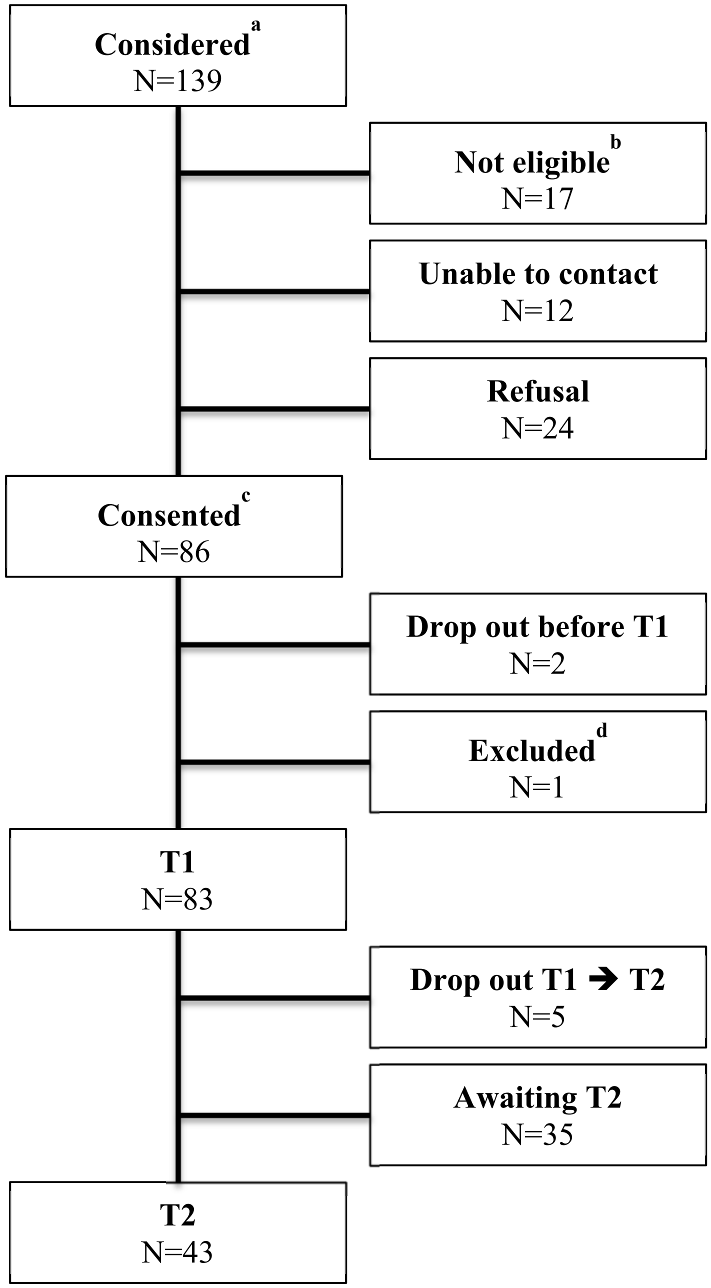
Figure 1. Recruitment and follow-up flowchart for the two injury groups



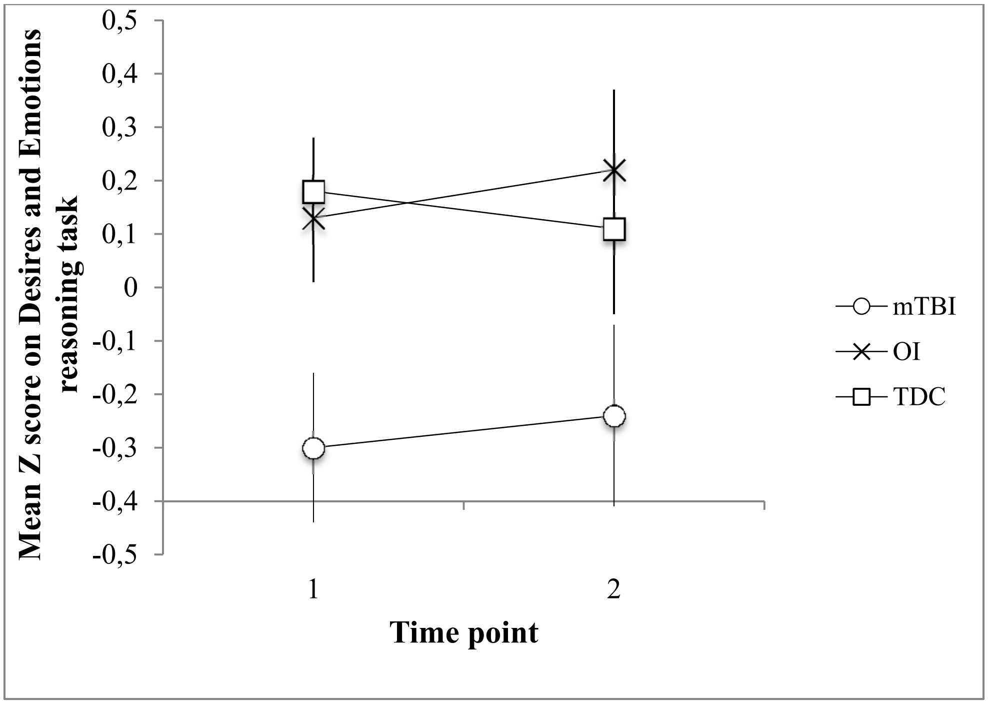
Note. [a]The following Emergency Room screening codes were considered for participation in the study: *mTBI group* : traumatic brain injury, head fracture, concussion, intracranial bleeding/hemorrhage, polytrauma ; *OI group* : Orthopedic trauma leading to a diagnosis of fracture, sprain, contusion, laceration or any non-specific trauma to an extremity. [b]Potential participants were not eligible because they did not satisfy an inclusion and/or exclusion criteria.[c]*Unable to contact* refers to one of two situations : 1) the parents were approached by a research nurse at the ED and consented to being contacted by our research team, but we were never able to reach them *or* 2) the family was sent a study pamphlet, but we were never able to contact them. In both cases, the research team attempted to reach the parents 6 times and left 3 voice mail messages, when possible, before concluding that the participant was unable to be reached. [d]*Consented* refers to those participants whose parents signed a consent form. [e]These participants were excluded at T1 because they did not satisfy an inclusion and/or exclusion criteria that had not been detected prior to testing.

Figure 2. Recruitment and follow-up flowchart for the typically developing children



Note. [a]*Considered* refers to participants whose parents were given a study pamphlet at the daycare and who consented that we call them. [b]Potential participants were not eligible because they did not satisfy an inclusion and/or exclusion criteria. [c]*Consented* refers to those participants whose parents signed a consent form. [d]These participants were excluded at T1 because they did not satisfy an inclusion and/or exclusion criteria that had not been detected prior to testing.

Figure 3. Graphic representation of the mean (Z-score ± SEM) ToM performances at both time points



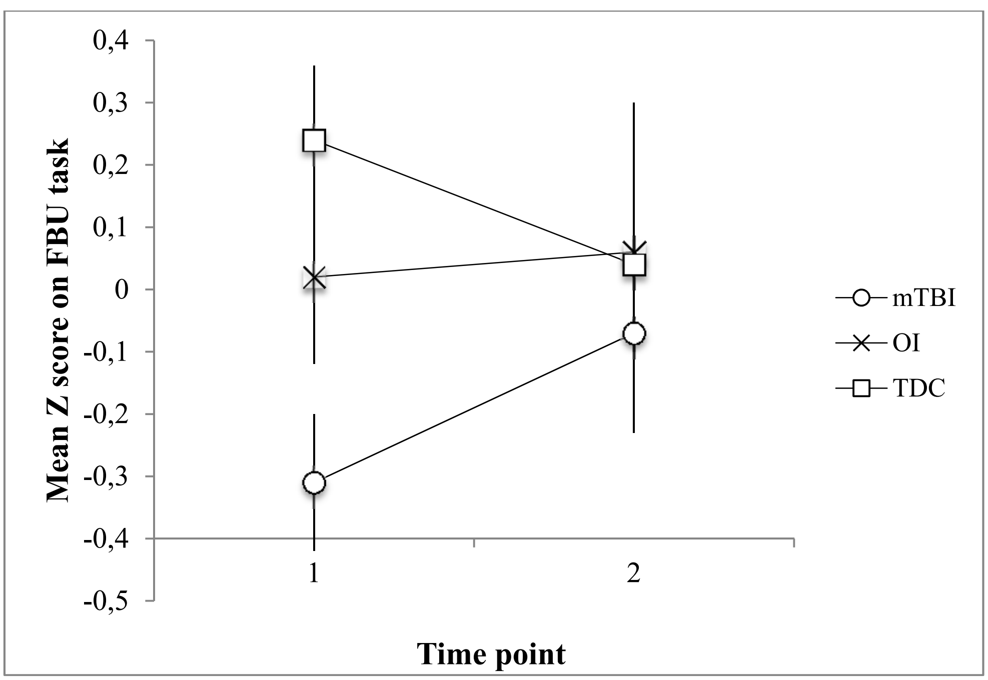


Table 1. Sample descriptives

	mTBI	OI	TDC	*t/F*	*p*	d/η^2
N	72	58	83	—	—	—
Demographics						
Sex [Male], n (%)	38 (53)	29 (50)	42 (51)	.12	.94	—
Parental education (number of years of education), M (SD)	15.53 (2.74)	15.79 (2.28)	16.20 (1.92)	1.67	.19	.02
Ethnicity [Caucasian], n (%)	61 (86)	45 (80)	65 (80)	7.35	.50	—
Injury-related variables						
Age at injury (months), M (SD)	35.57 (11.59)	34.47 (10.53)	—	.56	.58	.10
Time post-injury at T1 (months), M (SD)	6.74 (1.02)	6.98 (1.23)	—	-1.24	.22	.21
Time post-injury at T2 (months), M (SD)	18.88 (.99)	19.65 (1.27)	—	-2.70	**.01**	.68
Age at T1 (months), M (SD)	42.31 (11.60)	41.52 (10.41)	43.28 (11.71)	.42	.66	.004
Age at T2 (months), M (SD)	55.65 (10.90)	56.61 (10.74)	55.58 (12.17)	.07	.93	.001
PCS[b] T1 (last wk), M (SD)	.60 (1.21)	.71 (1.17)	.70 (1.29)	.17	.84	.002
PCS[b] T1 (since injury), M (SD)	1.79 (2.28)	.93 (1.43)	.64 (1.54)	7.83	**.001**	.07
Cognitive & behavioral variables						
Intellectual functioning (%ile rank), M (SD)	56.81 (25.77)	59.57 (24.11)	60.77 (24.93)	.48	.62	.01
Verbal abilities (%ile rank), M (SD)	48.94 (28.67)	55.78 (27.70)	56.11 (25.87)	1.51	.22	.02
Pre-injury ABAS[c], GAC (standard score), M (SD)	96.03 (11.44)	95.60 (12.21)	98.44 (11.91)	1.21	.30	—
Pre-injury ABAS[c], Social (standard score), M (SD)	102.33 (14.06)	102.02 (13.82)	104.02 (16.13)	.38	.68	—
Post-injury T1 ABAS[c], GAC (standard score), M (SD)	96.94 (12.23)	96.09 (11.06)	98.44 (11.91)	.70	.50	—
Post-injury T1 ABAS[c], Social (standard score), M (SD)	102.61 (14.86)	103.53 (13.16)	104.02 (16.13)	.17	.84	—
Post-injury T2 ABAS[c], GAC (standard score), M (SD)	100.33 (13.05)	99.22 (11.64)	100.76 (13.46)	.10	.90	—
Post-injury T2 ABAS[c], Social (standard score), M (SD)	104.60 (14.91)	106.96 (13.40)	107.37 (12.29)	.45	.64	—

Note: [a]SES = Socioeconomic status, Blishen Socioeconomic Index, 1981; [b]PCS = Post-concussive symptoms; [c]ABAS = Adaptive Behaviour Assessment System.

Table 2. mTBI and OI injury characteristics

mTBI group	
Cause of mTBI [accidental fall], n (%)	67 (93)
Lowest GCS[a], (n, %)[a]	13(2, 3), 14 (4, 5), 15 (66, 92)
Number neurological signs[b], M (SD)	2.26 (1.40)
Occurrence of neuroimaging[c], n (%)	10 (14)
LOC[d], n (%)	None (57, 80), <1 min (6, 8), < 5 mins (2, 3), Susp. (6, 8), Unknown (1, 1)
AOC[e], n (%)	None (57, 80), <1 hr (10, 13), 1-24 hrs (2, 3), Unknown (3, 4)
OI group	
Cause of OI [accidental fall], n (%)	37 (64)
Severity of injury[f], (n,%)	Minor (24, 41), Moderate (32, 55), Serious (1, 2), Unknown (1, 2)
Diagnosis, (n,%)	Fracture (32, 55), Pulled elbow or Luxation (20, 34), Contusion (5, 9), Laceration (1, 2)

Note: [a]GCS = Glasgow Coma Scale; [b]Neurological signs include the presence of the following symptoms: Headaches, irritability, persistent vomiting (more than two times), hematoma, drowsiness, dizziness, convulsions, visual symptoms (e.g. blurred vision), balance or motor problems; [c]Neuroimaging: All were found to be negative; [d]LOC = Loss of consciousness (Susp. = suspected); [e]AOC = Alteration of consciousness; [f]According to the Abbreviated Injury Scale: Minor = no treatment required, Moderate = outpatient treatment required, Serious = admission required (but not in ICU), Severe = ICU admission and/or basic treatment required, Critical = intubation, mechanical ventilation or vasopressors required.

Table 3. Performance on theory of mind tasks according to group

TASKS	T1			T2			Post-hoc analyses	
	mTBI	OI	TDC	mTBI	OI	TDC	*mTBI vs. OI*	*mTBI vs. TDC*
Desires task combined[ab], M (SEM[c]) *Confidence interval (95%)*	-.29 (.12) *-.52 – [-.05]*	.12 (.14) *-.15 – .39*	.17 (.11) *-.05 – .39*	-.25 (.15) *-.55 – .05*	.24 (.20) *-.15 – .64*	.07 (.15) *-.22 – .37*	*p* = .02	*p* = .03
False belief task, M (SEM[c]) *Confidence interval (95%)*	-.31 (.12) *-.55 – [-.06]*	.02 (.14) *-.26 – .29*	.24 (.11) *.01 – .46*	-.09 (.16) *-.40 – .22*	.07 (.20) *-.33 – .47*	.03 (.15) *-.27 – .33*	*p* = .44	*p* = .066

Note: [a]At T1: Z-scores on the discrepant desires task and the desires task; At T2: Z-scores scores of the desires task; [b]At T1: Children who completed the Discrepant desires task: mTBI = 20, OI = 16, TDC = 21; Children who completed the Desires task: mTBI = 47, OI = 36, TDC = 55; [c]SEM = Standard error of the mean.

Table 4. Correlations between injury characteristics and ToM performances for mTBI group

Task	Injury characteristic	*r*	*p*
FBU T1	PCS T1 last week	-.01	.93
	PCS T1 last six months	-.13	.32
	Lowest GCS	.16	.21
	Number neurological signs	.15	.26
FBU T2	PCS T1 last week	.20	.25
	PCS T1 last six months	-.09	.61
	Lowest GCS	-.01	.96
	Number neurological signs	.09	.59
Desires T1	PCS T1 last week	.06	.62
	PCS T1 last six months	-.13	.29
	Lowest GCS	.15	.22
	Number neurological signs	-.001	.99
Desires T2	PCS T1 last week	.09	.61
	PCS T1 last six months	.02	.90
	Lowest GCS	.28	.08
	No. neuro. signs	-.08	.63

Note: [a]PCS = Postconcussive symptoms; [b]GCS = Glasgow Coma Scale.

Table 5. Correlations between ToM performances and ABAS scores

		All participants		mTBI only	
Task	**ABAS**	***r***	***p***	***r***	***p***
FBU T1	ABAS GAC T1	-.03	.74	.24	.07
	ABAS Social T1	.11	.15	.31	**.02**
	ABAS GAC T2	.10	.36	.44	**.004**
	ABAS Social T2	.11	.28	.42	**.01**
FBU T2	ABAS GAC T2	.10	.33	.09	.62
	ABAS Social T2	.16	.13	.11	.52
Desires T1	ABAS GAC T1	.05	.48	.15	.24
	ABAS Social T1	.11	.13	.25	**.04**
	ABAS GAC T2	.10	.33	.22	.19
	ABAS Social T2	.08	.45	.14	.40
Desires T2	ABAS GAC T2	.15	.13	.20	.22
	ABAS Social T2	.07	.50	.17	.31

Discussion

Young children are at increased risk of sustaining TBI and of experiencing difficulties following brain injury due to the immaturity of their neural system. Although the cognitive, behavioral, and psychiatric sequelae of preschool mTBI have been explored to some extent, less is known of its social consequences and their socio-cognitive underpinnings. The current thesis thus aimed to examine the impact of preschool mTBI on one aspect of social cognition, theory of mind (ToM). The primary objective was to establish if there are ToM difficulties – precisely, false belief understanding and desires and emotions reasoning – following preschool mTBI, and if so, whether they are the result of a brain-injury-specific effect or rather a general-injury effect. A second goal was to map the evolution of ToM skills from 6 months to 18 months post-injury. The association between social cognition and global social functioning was also investigated. The results obtained will first be discussed and contextualized within the current literature. Future research avenues as well as the clinical significance of the findings will then be presented. Lastly, the limitations of the thesis will be addressed.

Theory of mind skills following mTBI in preschool children

The first thesis article brings to light significantly lower performances, of moderate magnitude, on both the false belief understanding and desires and emotions reasoning tasks in preschool children who sustain mTBI compared to typically developing peers, 6 months post-injury, even after controlling for pre-existing externalizing behavior differences between the two groups.

The second thesis article illustrates that desires and emotions reasoning difficulties present 6 months post-injury are maintained 18 months following preschool mTBI, compared to both orthopedically injured and non-injured peers. Of note, all three groups were equivalent on a number of potentially confounding variables such as parental education, sex, ethnicity, general intellectual and verbal abilities, as well as pre-injury global and social functioning. Taken together, our findings suggest a long-term brain-injury-specific socio-cognitive effect of preschool mTBI. These results contrast with the general consensus according to which symptoms and difficulties that arise following mild forms of TBI typically resorb within 1 to 3 months for the majority of children (Babikian et al., 2011; Holm et al., 2005; Karr et al., 2014; Kirkwood et al., 2008; Zemek et al., 2016). In the following discussion, a neurodevelopmental account will be presented to explain why young children may experience more persistent changes in socio-cognitive functioning following mTBI. Child and environmental factors will also be addressed in light of our findings, as possible modulators of the impact of brain injury on socio-cognitive skills. Finally, brain injury characteristics and their link to socio-cognitive outcomes, as well as the association between social cognition and social functioning will be discussed.

Neurodevelopmental considerations

A neurodevelopmental account could explain why socio-cognitive skills following preschool mTBI do not follow the typical evolution reported in older children and adolescents, that is, normalization of neurocognitive functioning within 1 to 3 months post-injury. Although the theory according to which young children are more resilient to brain insult ("plasticity theory") has been in vogue since its inception in the 1960s, the last two decades have demonstrated that despite typically faring better than adults following *focal* injuries, children experience *worse* outcome as a result of *generalized* brain injury ("vulnerability theory"), such as TBI. Thus, even though long-term, neurocognitive brain-injury-specific effects have not been found in school-aged children and adolescents following mTBI, this may be the case in younger children because of an increased vulnerability to brain insult. Additionally, it may be that children who sustain brain injury early in life have difficulty "catching up" to their peers, who are constantly progressing in their acquisition of new skills and knowledge. In fact, Kaldoja and Kolk (2015) provide support for the theory of vulnerability in young children who sustain minor brain injury with evidence that mTBI in infants and toddlers disrupts socio-emotional development, and that these difficulties can persist up to 9 months after the injury.

Research with typically developing children has established that each developmental stage consists of unique neurodevelopmental realities and challenges that need to be studied independently. Yet, too often, research questions pertaining to young children continue be framed according to knowledge gained from older children and adolescents, partly due to the lack of theoretical models to support hypotheses formulated in young children. Thus, often the wrong research questions are asked or the questions eclipse an important aspect of the studied phenomena. In this vein, some authors suggest that a consideration of developmental particularities could provide valuable knowledge concerning the impact of pediatric TBI. For example, Taylor and Alden (1997a) propose that "[t]he critical issue […] is not whether there are sequelae, but the extent to which normal development is possible in spite of early brain insult" (H. G. Taylor & Alden, 1997a, p. 556). Indeed, examining difficulties following pediatric TBI should be accompanied by an investigation of how these interfere with developmental trajectories. We attempted to incorporate this complementary perspective in the current thesis with the use of a longitudinal design and via correlational analyses to examine the association between social cognition and social functioning. Pertaining to the implications of TBI in young children, Anderson and McKinlay (2013) also propose that “what is often being evaluated are the deficits in potential rather than the decline in existing function”. Although older children have acquired a small skills set and have developed a certain cognitive repertoire, this is less true of young children for whom injury potentially compromises developmental potential more than consolidated abilities. Undisputably, evaluating “normal development” and “cognitive potential” is an inherent challenge in the preschool population given the very short developmental histories of young children. However, nothwithstanding these methodological issues, Taylor and Alden as well as Anderson and McKinlay highlight that the relevant questions to explore following *early* (preschool) mTBI may differ from the questions that are pertinent in older children.

Child factors

It can be further argued that child factors modulate or account for post-injury outcome in this young age group. This proposition emanates from research showing that children who sustain accidental injury display higher levels of pre-existing cognitive, behavioral, and/or psychiatric problems, making them more accident-prone and possibly accounting for post-mTBI neurocognitive difficulties (Babikian et al., 2011; Bruce et al., 2007; Gerring et al., 1998; McKinlay et al., 2010; Schwebel & Gaines, 2007; Yeates, 2010). We therefore considered several child factors that have been shown to be related to outcome following TBI, such as sex, ethnicity, global intellectual and verbal abilities, as well as pre-injury global and social functioning; notably, our groups were not found to be different on any of these variables. However, group equivalencies may not provide the full story given that certain factors may have a differential impact on mTBI. For example, post-TBI outcome can be modulated by the child's sex, such that females consistently report more postconcussive symptoms following mTBI (Dillard et al., 2016; Heyer et al., 2016; Zemek et al., 2016). Although there is not a clear consensus in the literature regarding sex differences in terms of ToM skills, several studies report a "female advantage" (e.g., Calero, Salles, Semelman, & Sigman, 2013; Charman, Ruffman, & Clements, 2002; Hughes & Dunn, 1998). Thus, a more thorough examination of the influence of child factors may be needed to clarify their impact on social cognition following early mTBI.

Additionally, a broader exploration of the integrative, biopsychosocial perspective proposed by Beauchamp and Anderson's (2010) SOCIAL model (see Figure 1 in Introduction) may be necessary to elucidate the reasons behind the persistance of socio-cognitive difficulties following preschool mTBI. As previously mentioned, several variables known to influence mTBI outcome were taken into consideration in our studies; however, there are other factors that influence ToM following mTBI that have not been extensively examined in this thesis. For example, studies show that language (Astington & Jenkins, 1999; Im-Bolter, Agostino, & Owens-Jaffray, 2016; Milligan, Astington, & Dack, 2007) is an important correlate of ToM. The role of language in ToM development is undisputable given that it is the primary means of communication and of knowledge acquisition, especially when it comes to abstract, unobservable concepts like mental states. However, the exact ways in which language promotes ToM, particularly which aspects of language are relevant, remains a matter of debate

(Hughes et al., 2005). It is possible that general vocabulary and/or verbal reasoning abilities, as measured in our studies, do not capture aspects of language that are essential to the burgeoning of ToM skills. Recent research demonstrates that a child's choice of mental state words (R. Brooks & Meltzoff, 2015), as well as the accuracy of mental state attribution (Bianco et al., 2015) mediate the relation between conversational experience and mental-state reasoning. As a vehicle of our inner thoughts and feelings, language and the words chosen to convey inner meaning are indeed one of the manifestations of ToM understanding in children. Thus, the qualitative and quantitative analysis of mental state words (e.g., *like, know, want, sad, happy*) employed by children, during play for example, may be a complementary, ecological way of assessing ToM skills after early mTBI.

Moreover, semantics and syntax may be important language-based correlates of ToM development (Im-Bolter et al., 2016). Specifically, semantics allow one to represent physically unobservable concepts such as mental states, and syntax provides a structure for representing and tracking mental states (Im-Bolter et al., 2016). Research supports the presence of a dose-response relationship concerning language difficulties following pediatric TBI, both in terms of knowledge-based (e.g., vocabulary) and functional (e.g., grammar) aspects (Morse et al., 1999). Despite the absence of group differences between mild, moderate and severe TBI groups on some general language measures and linguistic competencies, the group means on various tasks incrementally decrease as injury severity increases, with the presence of comprehension, syntactic, and pragmatic difficulties reported following more severe TBI in children (e.g., Morse et al., 1999; Turkstra et al., 2015). To our knowledge, there is no evidence of such difficulties after preschool mTBI. However, without constituting frank deficits, we could speculate that subtle variations in semantic, syntactic, and pragmatic maturity following early mTBI could influence socio-cognitive outcome. In sum, many aspects of language still need to be explored in relation to socio-cognitive prognosis following mTBI in young children.

Executive functioning (EF), defined as an ensemble of functions that serve to regulate and coordinate thought, action and emotion (e.g., Garon, Bryson, & Smith, 2008; Miyake et al., 2000), has also been extensively studied in relation to ToM because of their similar developmental trajectories and shared neural substrates (Austin, Groppe, & Elsner, 2014; Carlson & Moses, 2001; Devine & Hughes, 2014; Im-Bolter et al., 2016). Although EF has been shown to be robustly linked to ToM, it is still unclear whether EF development precedes the emergence of ToM or vice versa, or whether they emerge in parallel (Benson et al., 2013; Carlson, Mandell, & Williams, 2004; Hughes, 1998; Hughes & Ensor, 2007; Marcovitch et al., 2015; Muller, Liebermann-Finestone, Carpendale, Hammond, & Bibok, 2012; Perner & Lang, 1999, 2000; Russell, 1997; Schneider, Lockl, & Fernandez, 2005). Although there is evidence that EF development precedes ToM emergence (e.g., Marcovitch et al., 2015), this controversy nonetheless remains even after a meta-analytic study covering the last 20 years of research on the subject (Devine & Hughes, 2014). This finding demonstrates the complex and possibly multifactorial nature of the association between EF and ToM, whereby the relation between the two constructs is akin to a symbiotic dance involving reciprocal influence (Austin et al., 2014). Subcomponents of EF such as attentional shifting/cognitive flexibility, inhibition, and working memory have been shown to be particularly relevant to ToM (especially false belief understanding) in 3- to 5-year-old children (Devine & Hughes, 2014). Specifically, ToM presumably requires that children engage in perspective taking by putting aside their own perspective (inhibition) to examine reality from another person's point of view (attentional shifting/cognitive flexibility), all the while holding in mind and monitoring these various elements (working memory) in order to draw conclusions and inferences (Doherty, 2009). Thus, EF seems to play a role in the mental tracking and updating of various mental states (Im-Bolter et al., 2016) and appears to be another important factor that needs to be investigated in relation to socio-cognitive outcome following preschool mTBI.

Environmental determinants

Aside from child factors, children's environments have also been shown to play a role both in post-mTBI outcome and in shaping their socio-cognitive understanding. Young children are indissociable from their family environment and as such, the family system is possibly an important environmental determinant of ToM skills following early mTBI. In our studies, we considered parental education/socioeconomic status, general family functioning, parental stress as well as marital satisfaction and no group differences were found. However, these variables do not constitute an exhaustive exploration of all potential family factors that may influence ToM skills following mTBI. Indeed, numerous studies have demonstrated an association and/or moderating effect of other family environment factors on post-TBI outcome, such as quality of the home environment, parenting style, and caregiver mental health (Ryan, van Bijnen, et al., 2016; Wade, Zhang, Yeates, Stancin, & Taylor, 2016; Yeates et al., 2012; Yeates et al., 2010). Similarly, research indicates that mother-child talk (Ensor & Hughes, 2008; Sung & Hsu, 2014), as well as, mothers' mental state references predict individual differences in preschoolers' false belief understanding (Ensor, Devine, Marks, &

Hughes, 2014; Ruffman, Slade, & Crowe, 2002). Likewise, siblings seem to exert an important influence, such that in general, having more than one sibling has been shown to enhance ToM development (e.g., McAlister & Peterson, 2013; Miller, 2012; C. C. Peterson, 2000; Randell & Peterson, 2009). Thus, it is clear that a more thorough examination of the role of the family in relation to social outcomes following early mTBI is needed. Hypothetically, family may play a greater role, or rather a different one, in mTBI outcome in very young children, compared to school-aged peers and adolescents, given preschoolers' lesser degree of autonomy and the near absence of social networks beyond the family.

Brain injury characteristics and ToM skills

Research has demonstrated that brain injury characteristics can be useful predictors of TBI outcome, especially following moderate to severe brain injuries in older children. These include clinical indicators such as the Glasgow Coma Scale (GCS), the presence of postconcussive symptoms (PCS), the duration of post-traumatic amnesia (PTA) and the length of alteration and/or loss of consciousness (AOC/LOC). Physical evidence and neuroimaging data also aid in determining the presence and extent of structural brain damage (e.g., skull fracture, intracranial hemorrage, edema, white matter damage), which have been shown to be important determinants of outcome in moderate to severe brain injuries (e.g., Kinnunen et al., 2011; Medana & Esiri, 2003). We therefore examined the link between brain injury characteristics (PCS in the week preceding the evaluation and since the injury, lowest GCS, and number of neurological signs and symptoms) and ToM performance in our sample of preschool children; however, no associations were found. Although this finding potentially suggests that ToM following preschool mTBI is unrelated to indicators of injury severity, methodological considerations must first be examined before firm conclusions can be drawn concerning the link between brain injury markers and socio-cognitive outcome in preschool children. Current clinical tools lack discriminative ability when it comes to the mTBI spectrum. For example, AOC/LOC, PTA, and seizures are very rarely reported in individuals who experience mTBI. If AOC/LOC is present following mTBI, it is typically of very short duration, which renders its detection challenging. Additionally, young children are typically unable to communicate overt manifestations of brain injury including symptoms such as AOC/LOC, PTA, as well as dizziness, headaches, and visual disturbances (e.g., hypersensitivity to light, double vision). Parallel to these issues, previous research has highlighted the limited use of some of these injury characteristics both in young children and following mild injuries (Shore et al., 2007). For example, the GCS is rarely correlated with any outcome measure in young children (Durham et al., 2000; Marion & Carlier, 1994; Segatore & Way, 1992). Another concern is the lack of age-appropriate and validated measures of PCS for the preschool population, as well as the fact that existing postconcussive symptom questionnaires do not take into account the particularities inherent to young children, such as their limited verbal and introspective ability. The two most widely used pediatric PCS measures, the Postconcussive Symptoms Interview (PCS-I; Mittenberg et al., 1997) and the Health and Behavior Inventory (Yeates et al., 1999), are not very useful in preschoolers, as neither tool has been validated in child under 5 years of age. Despite these limitations, the PCS-I was employed in our studies given the absence of other measures better-suited to assess postconcussive symptoms in preschool children.

Given the inherent limited predictive power of current clinical tools following early mTBI, other clinical markers, such as blood serum biomarkers, have been explored and continue to be investigated by other groups. The utility of serum biomarkers resides in the correlation between the concentrations and/or peak times of specific biomarkers and the severity of organ damage (Shore et al., 2007). Biomarkers such as S100B, neuron-specific enolase (NSE), and glial fibrillary acidic protein, have shown to be potentially useful in predicting outcome following severe and possibly mild TBI in adolescents and adults (see review by Berger, 2006; Hayakata et al., 2004; Pleines et al., 2001). However, research pertaining to infants and children is limited (see review by Berger, 2006), and one study shows that biomarkers are worse than conventional clinical markers, such as the GCS, in predicting outcome following severe TBI in young children (Shore et al., 2007). Of note, no biomarker study has been conducted with young children who have sustained accidental mTBI. Thus, more research is needed to establish the prognostic value of serum biomarkers and their potential association with social outcomes following early mTBI.

Another active area of research concerning prediction of outcome following mTBI is that of advanced imaging techniques. For example, susceptibility weighted imaging (SWI) has been shown to be more sensitive than CT and MRI in detecting subtle subtle hemorrhagic brain lesions (Beauchamp, Ditchfield, et al., 2011). As such, Beauchamp and colleagues (2013) found that SWI combined with GCS explained a significant, albeit small, proportion of the variance in intellectual outcome across the TBI spectrum in 5- to 16-year-olds. Similarly, pathology detected with SWI has been shown to be related to socio-cognitive outcome in adolescents between the ages of 10 and 15, but not in younger children (5 to 9 years old; Ryan et al., 2015). Ryan and colleagues (2016) also propose that volumetric change in the "social brain network" may be a useful imaging marker for predicting social impairment following pediatric brain injury. These authors put forth the notion of "age-dependent socio-cognitive difficulties", such that ensuing problems and the best predictors of outcome may differ depending on age (i.e., developmental stage; Ryan, Catroppa, et al., 2016; Ryan et al., 2015). However, none of these studies included children younger than 5 years of age.

While neuroimaging data would be interesting to document in children who present to the Emergency Room with suspected brain injury, there are obvious health and financial reasons to limit the acquisition of such information in young children. Notably, clinical decision algorithms have been implemented in most pediatric medical centers to determine the necessity of Computed Tomography (CT) neuroimaging following brain insult in children in order to minimize exposure of the immature, developing brain to radiation. The most widely used clinical decision protocols include the Canadian Assessment of Tomography for Childhood Head Injury rule (CATCH; Osmond et al., 2010), the Pediatric Emergency Care Applied Research Network rule (PECARN; Kuppermann et al., 2009), and the Children's Head Injury Algorithm of Important Clinical Events (CHALICE; Dunning et al., 2006). For example, the PECARN rule provides a sensitivity of 100% in identifying patients with clinically important brain injury (Easter et al., 2014). As a result of the application of clinical decision rules, only a minority of children (~ 37%) who present to the Emergency Room with suspected brain insult undergo CT imaging. Clinically, these empirically derived tools are major advancements. However, from a research perspective, the low scanning rate constitutes an obstacle to further our understanding of the impact of minor brain injuries on brain integrity. To minimize radiation exposure, and given the research showing that standard CT imaging does not detect subtle brain abnormalities associated with mTBI (e.g., Beauchamp, Beare, et al., 2013; Ryan, Catroppa, et al., 2016; Ryan et al., 2015), MRI could be used as the first line imaging technique. However, the high costs associated with this medical procedure preclude this solution from being economically viable in clinical settings. In research settings, examining brain structure and functional integrity via MRI in young, nonsedated children (< 5 years old) presents additional practical/procedural issues (e.g., child's anxiety, motivation and cooperation, movement restriction, parents' anxiety) as well as technical obstacles (availability of child-appropriate equipment and of appropriate analysis methods such as pediatric brain templates) which renders neuroimaging research in this population particularly challenging (Bookheimer, 2000; Poldrack, Pare-Blagoev, & Grant, 2002; N. Raschle et al., 2012). Solutions have been developed to minimize and circumvent these limitations, such as pediatric experimental imaging protocols (Dean et al., 2014; N. M. Raschle et al., 2009; Sanchez, Richards, & Almli, 2012) and strategies (e.g., mock scanner, play therapy, behavioral training and simulation, basic relaxation techniques; Byars et al., 2002; J. N. Epstein et al., 2007; Slifer, 1996; Slifer, Bucholtz, & Cataldo, 1994). Applying these technical innovations and behavioral strategies to the neuroimaging of early mTBI may constitute a fruitful avenue of research.

Despite the continued exploration of various clinical markers, it remains unclear what the best indicators of outcome are in very young children who sustain mTBI. Future research will need to determine what are the best prognostic tools following early mTBI.

Tom skills and social competence

Although there is ongoing research concerning the specific contribution of ToM to general social functioning (e.g., C. Peterson, Slaughter, Moore, & Wellman, 2016), it nonetheless appears clear that there is a link between ToM and social competence, such that more advanced ToM is associated with better social communication and conflict resolution, more sophisticated pretend play, superior teacher ratings of social functioning, and increased popularity with peers (Astington, 2003; Astington & Jenkins, 1995; Devine, White, Ensor, & Hughes, 2016; Ding, Wellman, Wang, Fu, & Lee, 2015; Dunn, 1996; C. Peterson et al., 2016). The associations between ToM and social functioning in typically developing children are further supported by research with various clinical populations, such as children with Down syndrome, autism spectrum disorder (ASD), attention deficit/hyperactivity disorder (ADHD), language impairment, intellectual disabilities, and psychiatric disorders, who demonstrate both disruption of socio-cognitive skills and reduced social competence (Andres-Roqueta, Adrian, Clemente, & Villanueva, 2016; Bakopoulou & Dockrell, 2016; Bora & Pantelis, 2016; Marton, Abramoff, & Rosenzweig, 2005; Miranda-Casas, Baixauli-Fortea, Colomer-Diago, & Rosello-Miranda, 2013; Nader-Grosbois, Houssa, & Mazzone, 2013; C. C. Peterson, Garnett, Kelly, & Attwood, 2009; Stanton-Chapman, Justice, Skibbe, & Grant, 2007; Timler, 2003; Yirmiya, Erel, Shaked, & Solomonica-Levi, 1998). Of note, however, socio-cognitive perturbations and social functioning alterations differ qualitatively and/or quantitatively across disorders. For example, impaired social cognition and social functioning are hallmarks of autism. Specifically, these children present, to varying degrees, general ToM difficulties that lead to “mind blindness” and give way to behaviors that are inappropriate in social contexts, to a difficulty or inability to understand non-literal language and to “read” emotions, and to the establishment of few relationships that are devoid of reciprocal exchanges (American Psychiatric Association, 2014). Comparatively, research shows that socio-cognitive difficulties in ADHD are more circumscribed (i.e., less pervasive) and less severe than in ASD, and often involve the pragmatics of social interactions (e.g., waiting your turn, not interrupting; Bora & Pantelis, 2016; Miranda-Casas et al., 2013).

In our studies, we found that in preschool children who sustained mTBI, poorer ToM skills were associated with poorer social functioning 6 months post-injury, as well as with poorer global adaptive and social functioning 18 months post-mTBI. Despite this association, it is important to mention that global adaptive and social functioning scores remained in the average range at both time points, suggesting that poorer ToM skills did not translate into obvious social dysfunction in our sample. Nonetheless, given the literature showing both altered ToM and social functioning in more severe pediatric brain injuries (e.g., Robinson et al., 2014; Ryan, Catroppa, et al., 2016), we could speculate that a dose-response relationship exists, whereby a certain degree of ToM impairment is needed to result in overt social disturbances.

Although not directly examined in the current thesis, it is possible that altered development of basic socio-cognitive skills, such as first-order ToM, may jeopardize the emergence of more complex socio-cognitive abilities (e.g., second- and third-order ToM) in the longer term. Hypothetically, socio-cognitive difficulties may translate into more global social functioning problems only once this cascading effect has taken place. Also, alterations may become apparent to the child's entourage only once this deviation from the typical developmental trajectory begins to interfere with daily social functioning. Thus, longitudinal research is needed to acertain the impact of early ToM difficulties on future socio-cognitive development.

In sum, our findings suggest a long-term brain-injury-specific sociocognitive effect following preschool mTBI. Nonetheless, the literature demonstrating the influence of child and environmental factors in relation to pediatric mTBI prognosis suggests that outcome is probably modulated by a multitude of determinants, that potentially vary across individuals. For example, Fay and colleagues (2010) report that postconcussive symptoms are moderated jointly by cognitive reserve capacity (as measured by cognitive ability) and injury severity. Hypothetically, there may be an additive or cumulative effect of vulnerability (or resiliency) factors that dictate a child's trajectory following mTBI. As suggested by Yeates (2010), this knowledge of multifactorial determination of mTBI outcome commands that the field moves from a variable-centered approach guided by group means to a person-centered approach revealing risk factors of less favorable prognosis following mTBI. Interestingly, this view is in the spirit of Dr Margaret Kennard's *avant-garde* work as she readily acknowledged, back in the 1960s, the multifactorial nature of post-TBI outcome.

Future research avenues

The findings of this thesis have led to the formulation of future research questions that will need to be explored to further elucidate the impact of preschool mTBI on social cognition and general social development and functioning. Several suggestions have already been proposed above concerning language and post-mTBI outcome. Another interesting avenue related to language would be the exploration of the influence of bilingualism on post-mTBI ToM skills.

The idea of a cognitive superiority resulting from speaking more than one language appeared in the literature in the 1960s when Peal and Lambert (1962) reported that “Intellectually [the bilingual child’s] experience with two language systems seems to have left him with a mental flexibility, a superiority in concept formation, a more diversified set of mental abilities” (p. 20). In the following 50 years, research has further specified this “bilingual advantage”, notably in terms of inhibition, cognitive flexibility and selective attention in children as young as 24 months of age (e.g., Bialystok, Craik, & Luk, 2012; Carlson & Meltzoff, 2008; Crivello et al., 2016; Poulin-Dubois, Blaye, Coutya, & Bialystok, 2011). The posited explanation for this executive functioning enhancement in bilinguals is that speaking more than one language implicitly exercises general switching and inhibitory processes, as individuals alternate between languages, and constantly inhibit one of the two (or more) languages (e.g., Buchweitz & Prat, 2013). Numerous studies have sought to examine if this advantage generalizes to other cognitive domains that require switching/inhibitory underpinnings. Unfortunately, there is still a lack of consensus regarding the generalizability of the bilingual executive functioning superiority, notably because of a publication bias in favor of studies that demonstrate a bilingual advantage (see meta-analysis by de Bruin, Treccani, & Della Sala, 2015). Nonetheless, numerous studies have provided support for an advantage of bilingualism in terms of understanding mental states in children (Berguno & Bowler, 2004; Bialystok & Senman, 2004; Goetz, 2003; Kovacs, 2009; Nguyen & Astington, 2014) and adults (e.g., Rubio-Fernandez & Glucksberg, 2011), with evidence that this advantage is modulated by factors such as proficiency in both languages (Gordon, 2015). Developmental research has thus established that, at least for some individuals, bilingualism can enhance the development of other cognitive functions such as ToM. The field is now ripe for the examination of the impact of bilingualism on ToM following pediatric brain injury. Research with aging populations has shown that bilingualism constitutes an element of cognitive reserve known to prevent cognitive decline related to normal aging, and to delay the onset of neurodegenerative conditions such as Alzheimer's disease (Bialystok, Craik, & Freedman, 2007; Bialystok et al., 2012; Craik, 2010; Schweizer, Ware, Fischer, Craik, & Bialystok, 2012). Could it be that bilingualism has a similar impact following pediatric TBI, such that speaking more than one languages buffers cognitive abilities, including socio-cognitive functions, from being altered following pediatric TBI? Specifically, we could hypothesize that children reap the benefits of bilingualism, in terms of cognitive reserve, as early as the preschool years. This line of research could provide a more sophisticated and nuanced outlook of the impact of brain injury on cognitive functioning during the early years of life.

Lastly, as a socio-cultural construction, language development cannot be evacuated from its context and environmental influences. Although children's mastery of language is undeniably important in ToM development, so is the use of language by children's first role models, their parents and immediate family (e.g., Rollo & Sulla, 2016). Therefore, both children's linguistic skills as well as their "linguistic environments" (e.g., family discourse about feelings, psychological lexicon) play a role in ToM development, and could be studied in relation to post-mTBI socio-cognitive outcome.

These language analyses could be complemented with naturalistic observations in a context that is familiar to children, such as during play. In addition to the ecological value of play in comparison to experimental tasks, it is also more suitable for children whose vocabulary is not developed enough and for whom language-based methodologies are not appropriate. Indeed, pretend play, defined by Youngblade and Dunn (1995) as “a subcategory of play in which actions, objects, persons, places or other aspects of the here and now are transformed or treated nonliterally” (p. 1476), can be used to explore ToM in children of all ages. Although play can and often does involve utterances, it also consists of many non-verbal representations of children's understanding of the mind. For example, gestures, gaze and physical proximity are all meaningful expressions of children's perspective taking abilities. Only one exploratory study has investigated the impact of acquired brain injury on the amount and sophistication of pretend play in a case series of three children between the ages of 3 and 6 years. The authors report that for two of the three children, the engagement in make-believe scenarios was below age-appropriate expectations (Fink, Stagnitti, & Galvin, 2012). However, no study has specifically examined ToM skills in relation to pretend play following preschool mTBI. Thus, future studies should take advantage of the richness of children’s socio-cognitive knowledge that is displayed while engaged in pretend play. As such, Youngblade and Dunn’s (1995) study investigating individual differences in pretend play and its association with children’s relationships with their mothers and siblings could be reproduced in a sample of preschool mTBI children. This study is particularly interesting because of the various aspects of pretend play that were measured, such as the diversity of themes, the type of interactions (child only, child – sibling dyadic play, as well as child, sibling and mother interactive play), participation in scenario negociation, and role enactment (e.g., pretending to be the doctor or teacher). Although it is true that children do not verbalize or demonstrate all that they know or understand, it is assumed that the sample gleaned from a play session is representative of the depth and extent of their understanding of others’ minds.

On a different note, the current thesis examined only two aspects of a multi-faceted construct (ToM; i.e., false belief understanding and desires and emotions reasoning). Future studies should therefore explore the impact of early mTBI on other subcomponents of ToM, such as the understanding of intentions, as well as other aspects of social cognition such as moral reasoning. Moral judgement is particularly interesting because its developmental trajectory is similar to that of ToM (Loureiro & Souza, 2013). Also, both ToM and moral reasoning concern the interpretation of behavior; whereas ToM consists of distinguishing between true and false, moral reasoning involves the discrepancy between right and wrong (Loureiro & Souza, 2013). In fact, an understanding of desires and beliefs is necessary to attribute intentions and motives, the underlying mental states needed to reason about the morality of actions. Given the parallel development and similarities between the two concepts, many studies have investigated the influence of ToM on moral reasoning development as well as the reciprocal associations between these two constructs in typically developing preschool children (i.e., 5 years and younger; e.g., Lane, Wellman, Olson, LaBounty, & Kerr, 2010; Loureiro & Souza, 2013; Smetana, Jambon, Conry-Murray, & Sturge-Apple, 2012). Recent research has demonstrated that understanding of desires, beliefs and goals in early childhood is predictive of later moral reasoning (Sodian et al., 2016). Thus, moral reasoning as well as the link between ToM and the judgement of morality should also be examined in preschool children who have sustained mTBI, particularly given research showing that adolescents who sustain mTBI show reduced moral reasoning skills (Beauchamp, Dooley, et al., 2013).

Additionally, future longitudinal studies spanning several years will help clarify the impact of preschool socio-cognitive difficulties (first-order ToM) on the emergence of more complex socio-cognitive abilities, such as second- and third-order ToM, intent attribution as well the understanding of non-literal language (metaphors, irony, sarcasm, humor), that presumably depend on these more basic skills to develop.

Lastly, as previously mentioned, research with preschool children consists of inherent limitations related to their short developmental histories, such that some of the children in our sample may already have altered brain development due to neurodevelopmental conditions (e.g., ADHD, learning disabilities) that have not yet become manifest. Given the higher proportion of neurodevelopmental disorders in children who sustain injury in general (Bruce et al., 2007; Schwebel & Gaines, 2007), we speculate that there should not be more children with neurodevelopmental conditions in our mTBI than in our OI group. Future research should acertain this empirically by retrospectively excluding the children who go on to develop a neurodevelopmental condition. Alternatively, this could be done by comparing the rate of neurodevelopmental diagnoses between the mTBI and OI groups. However, regardless of the solution adopted, it remains a challenge to tease apart purely neurodevelopmental conditions from difficulties that may be secondary to mTBI. Rates of premorbid and secondary ADHD have been published for children between the ages of 4 and 19 (Gerring et al., 1998), but these estimates may not apply to younger children.

Clinical significance

Standard pediatric neuropsychological assessment does not typically include an evaluation of social cognition, despite years of research demonstrating the importance of socialization in child development, and the deleterious consequences of many childhood central nervous system disorders on social skills. This thesis thus underscores the necessity of developing clinically useful assessment measures that could be incorporated into standard evaluations of children who present with neurodevelopmental conditions and/or acquired injuries such as TBI. Until such measures are more widely available, this research highlights the importance of remaining atuned, as clinicians, to possible social and/or socio-cognitive effects of pediatric brain insult, by questioning parents thoroughly concerning social difficulties or changes they may have noticed in their child, and/or by relying on global, standardized questionnaires.

If future research supports the presence of a cascading effect of early mTBI on social skills whereby alterations in basic sociocognitive skills lead to disruptions in more complex abilities and potentially interferes with daily social functioning, a long-term vision of medical care following preschool mTBI will need to be adopted to deal with social problems that arise years after the injury. The challenge of connecting future problems with injury that occurred several years before thus commands long-term vigiliance and follow up after early mTBI. If professional, long-term follow up is possible, there should be a particular emphasis on transitions (e.g., daycare and/or school entry) in which increased environmental demands (e.g., getting along with classmates) may serve to shed light on potential socio-cognitive difficulties. Unfortunately, long-term follow up is probably not within the reach of the majority of children who sustain mTBI given the limited resources of public medical systems and the high costs of private services.

Despite the political and economic realities of medical care, this thesis stresses the importance of translating research findings into clinically useful information that can serve to better inform both clinicians and the general population. The goal is not to create panic concerning the consequences of mTBI, but rather to provide policymakers, clinicians and medical professionals, as well as parents with the most accurate and up-to-date findings in order to manage mTBI in the most responsible and informed manner as possible. Parents are the first guardians of children's well-being and thus, they should have privileged, lay access to information emanating from research.

Limitations

This thesis is not without its limitations. As previously mentioned, the assessment of postconcussive symptoms was ill-suited to the particularities inherent to the mTBI preschool population. The PCS-I was used because no validated preschool measure exists. However, it is possible that as a result, the symptoms displayed by young children following mTBI were not fully captured. Secondly, the representative nature of our sample is probably limited due to the likelihood that not all children who sustain mTBI present to the Emergency Room for medical evaluation. Parents' knowledge of brain injury and its repercussions, as well as individual characteristics and beliefs (e.g., easily worried, distrust of medical authority) play a role in the decision to seek medical advice following children's injuries. Thirdly, we cannot exclude the possibility that some children in the mTBI group sustained a mild complicated TBI because most children did not undergo clinical neuroimaging. Of note as well, the sample size precluded analyses according to smaller age bands. Such future analyses may provide a better understanding of the impact of preschool mTBI on ToM across the preschool age range, given the speed at which this socio-cognitive skill develops during the early years. Lastly, the assessment of ToM relied exclusively on experimental measures. Convergence of results obtained with complementary measures (e.g., observations measures during pretend play) with the current findings will provide a clearer picture of the impact of preschool mTBI on socio-cognitive functioning.

Conclusion

This thesis constitutes the first evidence of a brain-injury-specific socio-cognitive effect following preschool mTBI. These findings provide support for vulnerability theory according to which the young, immature brain is at increased risk of sustaining sequelae as a result of brain insult. Neurodevelopmental immaturity thus appears to be a driving force in the prognosis of mTBI socio-cognitive outcome. As such, these studies highlight the necessity to study preschool children given that extrapolation from results obtained with older pediatric age groups may prove to be misleading. Indeed, children are not “little adults”, nor are they likely to be “little adolescents”! The neurodevelopmental challenges they face are unique and therefore require customized theoretical models and methodologies suited to their reality.

References – Introduction & Discussion

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Appendix I

New insights into neurocognition provided by brain mapping:

Social cognition and theory of mind

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Introduction

Social cognition refers to the mental processes that are used to perceive and process social cues, stimuli, and environments, and has traditionally been studied by social, developmental, and neuro-psychologists from conceptual and behavioural perspectives. Advances in brain imaging technology within the last two decades have also provided a means of investigating the neural underpinnings of these three interrelated concepts. Researchers from the field of social neurosciences have recently started to map abstract socio-cognitive concepts in the brain, and the value and practical applications of this cortical mapping are wide-ranging, diverse, and profound. In particular, greater insight into the neural substrates of social cognition is beneficial to medical practice in explaining the socio-cognitive deficits that may result from neurosurgical interventions for conditions such as epilepsy and brain tumors. Furthermore, knowledge of the brain regions and circuits that underlie uniquely human social skills can deepen our understanding of neurological and psychiatric illnesses in which the presenting symptoms include socio-emotional and socio-cognitive deficits, such as in autism or schizophrenia. To illustrate these points, the following chapter will focus on two central components of social cognition, theory of mind and moral reasoning, in the context of human brain mapping. These concepts will first be defined and distinguished from one another, before we turn to a study of their development and neural substrates. External factors that have bearing on neurocognition, such as culture and gender, will also be highlighted. Lastly, to underscore the importance of these issues for the clinical community, we will illustrate how socio-cognitive abilities are affected in a range of neurological and psychiatric conditions, what implications such impairments may have for our understanding of neurocognition, and how knowledge of socio-cognitive substrates may help inform clinical practice, such as neurosurgery.

Scourfield and colleagues (Scourfield, Martin, Lewis, & McGuffin, 1999) define social cognition as "those aspects of higher cognitive function which underlie smooth social interactions by understanding and processing interpersonal cues and planning appropriate responses." As such, it includes a vast range of functions. Within these, one of the processes most central to appropriate social and emotional functioning is theory of mind (ToM), or "mentalizing", which is the ability to attribute mental states (beliefs, intents, desires, pretending, knowledge) to oneself and others, and to understand that others have mental states that are different from one's own. ToM is a subcomponent of social cognition because it refers specifically to inferences about other people's mental states, and is distinct from other social cues such as eye gaze and gestures, which can also be used to make judgments in social situations (Carrington & Bailey, 2009). ToM has been found to influence and subserve many other socio-cognitive abilities, in particular, moral reasoning and cognitive empathy.

Neuroanatomical and neurofunctional substrates of socio-cognitive functions

Given the centrality of ToM and related cognitive functions to appropriate social cognition, knowledge of their neural substrates is key to understanding how disruptions in brain structure and function can cause social problems throughout development. Yet, neuroimaging studies attempting to elucidate the brain regions involved in socio-cognitive abilities have yielded some discrepancies across studies. In general, studies have shown that the anterior temporal lobes are activated in a wide range of social cognition tasks. In addition, electrophysiological studies in monkeys have shown that the superior temporal cortex, the orbitofrontal cortex and the amygdala are reliably involved in social cognition (Brunet-Gouet & Decety, 2006). However, more specificity is needed to distinguish particular socio-cognitive processes from each other, as functions such as ToM, empathy and moral reasoning may be differentially affected by brain disruption. After reviewing a large number of ToM studies, Carrington and Bailey (Carrington & Bailey, 2009) posit that there may be "core" regions activated for most ToM abilities and more "peripheral" regions recruited based on the specific demands of some ToM tasks. This suggestion is based on the observation that methodological variability does not account for the varied results produced by neuroimaging studies thus far (Blakemore, 2008; Carrington & Bailey, 2009). The following regions have been identified as "core" or critical structures sustaining ToM abilities: medial prefrontal cortex (mPFC, including anterior-medial regions (amFC)), superior temporal sulcus (STS), temporo-parietal junction (TPJ), as well as the para- and anterior-cingulate cortices (Carrington & Bailey, 2009; Spengler, von Cramon, & Brass, 2009). Additionally, Carrington and collaborators posit that the control of shared representations is involved in ToM abilities. The concept of shared representations stems from the study of "mirror neurons", through which it has been suggested that the brain systems involved in representing one's own mental states may be the same as those representing others' mental states. Mirror neurons were first discovered in monkeys whereby it was observed that a monkey's premotor cortex was activated both when the animal engaged in a motor action as well as when it observed another monkey performing a motor action (di Pellegrino, Fadiga, Fogassi, Gallese, & Rizzolatti, 1992; Gallese, Fadiga, Fogassi, & Rizzolatti, 1996). Scientists studying social cognition in humans have since extrapolated that there may also be mirror neurons for socio-cognitive abilities that fire when mental representations are shared (e.g., theory of mind). Indeed, there is some evidence that the same brain circuits are activated when one is thinking about one's own mental states as well as when one is reflecting on another person's mental states (Kaplan & Iacoboni, 2006; Rizzolatti & Fabbri-Destro, 2008). In fact, scientists have suggested that this similarity in activation is what makes us capable of ToM. If this is true, then there must be a way of differentiating between one's own mental states and that of others, and the amFC and TPJ may play a crucial role in this regard. Specifically, the amFC appears to control shared representations while the TPJ seems to govern self-other differentiation (Spengler et al., 2009). Other studies corroborate this idea, demonstrating that the mPFC and the TPJ (especially the right TPJ) show the most consistent activation across a variety of ToM tasks (1,2). The mPFC is activated in 90% of ToM studies (Brunet-Gouet & Decety, 2006). Of note, studies conducted by Gallagher and Frith (C. D. Frith & Frith, 2006; Gallagher & Frith, 2003a) found that ToM solicits the following brain areas: the mPFC, STS, TPJ, and the temporal poles. Of note, although the amygdala seems to play a role in ToM, it is not consistently activated across studies. Carrington and Bailey (Carrington & Bailey, 2009) speculate that the amygdala may be involved in the development of ToM, but may not be as necessary for the maintenance of this ability later in life. This suggestion partly stems from the observation that early damage to the amygdala has been linked with deficits in ToM (Shaw et al., 2004). The temporal poles have also shown some activation during ToM tasks, but once again, not in a consistent way and their specific role (whether it be critical or part of a larger circuitry that gives rise to ToM) remains ill-defined. So far, researchers have identified the role of the temporal poles within ToM as being activated when individuals are presented with complex social stimuli (e.g. a story or social vignette), in which they must evaluate another person's intentions, beliefs, and emotions (Olson, Plotzker, & Ezzyat, 2007). In essence, knowledge gained from neuroimaging studies of ToM suggest that although there appears to be a core circuit related to this process, the brain areas recruited are also task-dependent. In addition, individuals interested in mapping the neural substrates of ToM must keep in mind that even though all ToM tasks assess some aspect of ToM function, variations in task design may result in additional regions being recruited, such as those related to linguistic abilities.

ToM is closely linked to a number of other socio-cognitive abilities. In particular, it underlies moral reasoning, which allows individuals to consider the world around them and to make decisions about right and wrong. Moral reasoning is tightly linked to ToM because for individuals to engage in appropriate moral behaviours, they must have the ability to understand and represent another person's perspective (ToM). Although both ToM and moral reasoning refer to consideration of other's mental states, in moral reasoning the focus is on considering intention and justification for moral action, rather than on understanding another's beliefs. Research into the neural correlates of moral reasoning to date has shown that the mPFC, TPJ, orbitofrontal regions, cingulate cortices, STS, and the amygdala are involved when making moral judgments about a social situation (J. Moll, de Oliveira-Souza, Bramati, & Grafman, 2002; Van Overwalle, 2008; Young, Cushman, Hauser, & Saxe, 2007; Young & Saxe, 2009). Since these brain regions are recruited specifically for moral versus non-moral information, it is likely that one automatically infers mental states in order to process moral facts (Young & Saxe, 2009). This is an interesting conjecture given that many of the regions recruited during moral reasoning are also recruited during ToM tasks (see Figure 1).

In an attempt to reconcile the somewhat heterogeneous neuroimaging findings generated in relation to ToM and moral reasoning, some researchers have looked to other internal and external factors, such as development, gender, and culture that may influence social cognition. Singer (Singer, 2006) provides a good argument for focusing on developmental aspects of social cognition: a child's mentalizing abilities develop by the age of four years old, clearly much before the brain regions sustaining those abilities have fully matured. Indeed, the behavioural aspects of ToM development are well-established and there is ample evidence in the literature that ToM abilities change qualitatively during childhood and well into the teenage years. First-order beliefs (attributing a belief to another person) generally develop by four years of age, while second order beliefs (attributing a belief about another person's belief) generally emerge between the ages of six and ten. However, given that scientists, especially those in the field of social neuroscience, have only begun to look at the neural underpinnings of ToM development, studies that have looked at this aspect specifically are scarce. Interestingly, Kobayashi and colleagues (Kobayashi, Glover, & Temple, 2007) found that when comparing children and adults on ToM tasks, the bilateral TPJ and the right inferior parietal lobule are areas that are important for ToM during both childhood and adulthood. However, in the child group, there was more activity in the right superior temporal gyrus (STG), the right temporal poles, the cuneus, and the right ventromedial PFC. In contrast, in the adult group, there was more activity in the left amygdala compared to the child group. The authors suggest that the regions that were more activated in the child group may represent areas that are recruited by the cognitive precursors of ToM during development. Furthermore, the same study examined whether the performance of both groups could be affected by the modality in which the ToM task was presented. The findings indicate that children's ToM seems to be more tied to the visual modality than adults' ToM, which is more tied to the verbal modality. These developmental differences may hint at the fact that the language and cognitive capabilities adults rely on when confronted with ToM tasks are different from the strategies available to and employed by children. Given that the children in the study were eight years old and that the major ToM milestones in childhood occur between the ages of three and seven, future studies looking at children in that age range will help to further elucidate developmental aspects in the neural substrates of ToM. In a similar context, studies have been conducted in blind individuals in order to examine if being deprived of a modality (i.e. vision) affects brain regions recruited for ToM tasks. Bedny et al. (Bedny, Pascual-Leone, & Saxe, 2009) found that the regions solicited during ToM tasks for congenitally blind adults are the same as those recruited by sighted adults. Namely, the blind individuals showed activations in the biltateral TPJ, the mPFC, the PC, and the anterior STS. The authors conclude that in congenitally blind and sighted adults, inferring mental states based on seeing is an akin process. That is, visual experience is not a requisite for being able to neurally represent another person's experiences. In blind individuals, the same brain regions are recruited for ToM tasks, regardless of the modality solicited. Their findings further suggest that at least some aspects of ToM development are based on inborn influences and on more abstractly-represented experiences, independent of modality in which the information was acquired.

Gender differences have been studied extensively in relation to discrepancies in performance on ToM tasks. Behavioural studies have provided evidence that women perform better on ToM tasks than do men, regardless of age, and these gender differences are apparent even in children (Carrington & Bailey, 2009). As with developmental aspects of ToM, the literature on neuroimaging and gender differences for ToM is scant and constitutes a rich area for future research endeavours. One of the few imaging studies on this topic was conducted by Krach and colleagues (Krach et al., 2009), who found that women elicit more activity in the mPFC than men during ToM tasks. The scientific community has also studied blind individuals in order to see if being deprived of a modality affected brain regions being recruited for ToM tasks.

Proponents of cultural neuroscience have started to delve into the question of the impact of culture (and language) on socio-cognitive functions. Lack of consideration of these external factors may influence interpretations of both behavioural and neurofunctional aspects of social cognition. Many studies fail to control for these variables, and this may introduce significant methodological bias, as noted by Kobayashi and colleagues (Kobayashi et al., 2007). The authors studied a group of bilingual Japanese-English speaking children and compared them to a group of monolingual English children on a ToM task. They found that only bilingual children tested with Japanese stories showed activation in one of the typical four ToM areas (mPFC). Surprisingly, even monolingual English children did not show any activation in the TPJ. Based on these results, Perner and Aichhorn (Perner & Aichhorn, 2008) speculate that when presented with a ToM task, the activation seen in the TPJ could be influenced by environmental factors such as culture or language. However, how each of these factors possibly contributes to these differences in activation is still unknown. Their argument is founded on previous studies that have shown that bilingual children perform better on false-belief tasks than monolingual children; that performance on false-belief tasks is related to verbal intelligence; and that deaf children with language delays also exhibit delays in performance on false-belief tasks (Perner & Aichhorn, 2008). Of note, generalization across ToM tasks is still premature because no studies have examined other types of ToM tasks. In interpreting these results, researchers and clinicians should also bear in mind that there may be important inter-individual differences in performance on ToM tasks regardless of external factors. As Carrington and Bailey (Carrington & Bailey, 2009) state: "some individuals consistently show insight into mental states and adapt their behavior accordingly, whereas others show less awareness" (p. 2330). Therefore, 'normal' individual differences may in part explain the lack of consistency across neuroimaging studies. Otsuka et al. (Otsuka, Osaka, Ikeda, & Osaka, 2009) provide evidence in favour of this argument, demonstrating a correlation between performance on a ToM task and activation in the anterior STS, and thus suggesting that the anterior STS might reflect individual differences in ToM. However, given the correlational nature of their study, future studies need to be conducted to establish the cause-and-effect relation between these two elements.

Clinical insights into the neural substrates of theory of mind

A discussion of the neuroanatomical and functional bases of social cognition would be incomplete without consideration of clinical conditions in which ToM deficits are common occurrences. As such, developmental, neurological, and psychiatric conditions that affect socio-cognitive functioning provide a rich source for understanding the link between neurological processes and socio-emotional function (see summary Table 1). One neurological condition in which important ToM deficits have been observed is acquired brain injury (ABI). In their review, Martín-Rodríguez and León-Carrión (Martin-Rodriguez & Leon-Carrion, 2010) found that ToM deficits in adults with frontal lobe lesions due to ABI followed a particular task-related hierarchy. Deficits were most severe on ToM tasks in which an understanding of indirect speech (i.e. sarcasm, metaphors, irony) was required. Less severe, but nonetheless important deficits were found on social faux-pas tasks, followed by second-order belief and first-order belief ToM tasks. However, this descending order of severity does not fit the “hierarchy of ToM tasks hypothesis” [21]. According to the hypothesis, in some disorders skills that develop later in life should be most impaired by neural disruption (Baron-Cohen, O'Riordan, Stone, Jones, & Plaisted, 1999; Brune, 2003; Stone, Baron-Cohen, & Knight, 1998). However, the review suggests that individuals with ABI show fewer deficits on faux-pas tasks than on tasks requiring an understanding of indirect speech even though one’s understanding of faux-pas develops later in life. In addition, the review found that frontal lobe lesions affect the performance on faux pas tasks while right hemisphere damage has an impact on the understanding of indirect speech and faux pas. However, recent neuroimaging studies question this link between right-hemisphere damage and ToM deficits in ABI and emphasize the importance of the left-hemisphere as well as the connection between the two hemispheres (Tesink et al., 2009). Neuroimaging studies on this topic would be greatly aided by behavioural studies looking at whether ToM abilities are independent of other general cognitive capacities (language, executive functions). The specific impact of severe traumatic brain injury on ToM skills has also been explored in children. Findings indicate that children between the ages of 5 and 7 years with severe TBI show developmental lag on tasks of first- and second-order mental states comparable to their peers, suggesting stagnation or even regression of existing ToM skills (Walz et al., 2009). Additionally, Walz and colleagues (Walz, Yeates, Taylor, Stancin, & Wade, 2010b) found that even when strong predictors of ToM abilities, such as age, task-specific cognitive demands, and verbal skills were taken into account, children who sustained severe TBI still performed more poorly than typically developing peers and children suffering from orthopedic injuries. Another study conducted by the same group corroborates the aforementioned findings in that they found the same results in a younger group (3 years old) of children having sustained severe TBI [22]. Parkinson's Disease (PD) is also the focus of scientific scrutiny in relation to ToM abilities. In order to understand the ToM deficits in PD, Bodden et al. (Bodden, Dodel, & Kalbe, 2010) propose that a distinction be made between 'cognitive ToM', in which one intellectually understands mental states, and 'affective ToM' which provides an appreciation of others' emotions. Of note, ToM deficits are primarily observed in individuals with advanced PD, with cognitive ToM deficits appearing first, followed by deficits in affective ToM once the disease has progressed further. Neuroanatomically, early emerging deficits in cognitive ToM appear to be attributed to early atrophy of the dorsolateral prefrontal-striatal circuitry whereas later deficits in affective ToM seem to be related to the protracted degeneration of the frontostriatal-limbic circuitry. In this regard different PD etiologies may result in different ToM deficits.

Psychiatric illnesses have also received attention in relation to ToM deficits. In particular, such deficits are well documented in individuals with schizophrenia and have been investigated via neuroimaging. Brunet-Gouet and Decety (Brunet-Gouet & Decety, 2006) found abnormal prefrontal and amygdala activation in individuals with schizophrenia, which translated behaviourally into general deficits in mental state inference. Furthermore, abnormal activity in the inferior parietal lobule was identified and this resulted in abnormal source monitoring. That is, individuals with schizophrenia are impaired in monitoring their actions and when making self-other distinctions. Additionally, erroneous processing of contextual information in individuals with schizophrenia performing ToM tasks has been attributed to general impairment of dopamine transmission in the brain. Brunet-Gouet and Decety (Brunet-Gouet & Decety, 2006) conclude that “the inability to maintain a stable and relevant social context for the processing of one’s own or other people’s mental representations and the impairment of the ability to modify this type of context may arise from acute neurotransmitter disturbances” (p. 86). A positron emission tomography study conducted by Andreasen and colleagues (Andreasen, Calarge, & O'Leary, 2008) supports previous studies which have found that individuals with schizophrenia have a deficit in soliciting the cortico-cerebellar-thalamic-cortical circuit. Similarly, the areas of increased brain activity (as observed through blood flow) found in their study suggest that these individuals may need to utilize resources in the right hemisphere to compensate for impairments in the left hemisphere. These finding beg the question: is this a problem in brain lateralization or use of different strategies? Individuals with schizophrenia might be using a more “logical” process rather than a “social” process for ToM tasks. Walter and colleagues’ fMRI study examining the relation between ToM and paranoid schizophrenia yielded similar results; there was a general dysfunction of the ToM circuitry in the brain of individuals with paranoid schizophrenia (Walter et al., 2009). The authors argue that as soon as a social element is present, the difference in neural activation in individuals suffering from schizophrenia versus their healthy counterparts becomes obvious, especially in the mPFC and the TPJ, the structures that have most consistently been associated with ToM. Given that the mPFC and the TPJ have been respectively attributed the roles of distinguishing between one’s mental states and those of others as well as communicating intentions, Walter and colleagues (Walter et al., 2009) posit that individuals with schizophrenia are not able to differentiate between their own mental states and those of others, leading to “hyper-ToM”. As stated by the authors: “schizophrenic patients perceive agency where others see none (…) the ToM module in paranoid schizophrenia might malfunction because it is overactive from the start and thus isn’t well suited to distinguish properly between mental and physical states” (p 175). Benedetti and colleagues’ (Benedetti et al., 2009) results corroborate the aforementioned statements in that individuals with schizophrenia present abnormal neural activations in mPFC and temporal structures while performing ToM tasks. Furthermore, these differences in activation in the mPFC are present early on in the evolution of the disease, leading the authors to suggest that they might have identified a biological basis for the socio-cognitive problems affecting this psychiatric population.

Bipolar disorder also constitutes a psychiatric condition of interest in terms of the neural substrates of ToM. Malhi and colleagues (Malhi et al., 2008) found that individuals suffering from euthymic bipolar disorder do not show the same consistent, widespread activation that is seen in healthy individuals performing ToM tasks. In fact, even within the bipolar group, only the left anterior cingulate, the precuneus, and the cuneus bilaterally showed some consistency in activation. Of note, the activations found in the patient group do not include structures that are typically activated during ToM tasks in healthy individuals, such as the mPFC and the TPJ. Although individuals suffering from bipolar disorder seem capable of solving ToM tasks, they may not have the level of understanding and appreciation that is seen in healthy peers; they seem to lack cognitive flexibility in that they do not seem capable of changing their cognitive perspective to suit particular social situations.

Given that socio-cognitive deficits are the hallmark of autism spectrum disorder (ASD), researchers have focused on the neural correlates of ToM deficits in this population. In particular, Di Martino and colleagues (Di Martino et al., 2009) published a meta-analysis of the ASD neuroimaging literature in relation to socio-cognitive tasks (not restricted to ToM tasks). These researchers found that there is a consistent pattern of hypoactivation and abnormal activity in regions typically involved in ToM, such as the mPFC, the amygdala and the anterior cingulate cortex. Likewise, there seems to be inappropriate soliciting of lower-order processing regions such as the supplementary motor area (SMA) in lieu of higher-order processing regions such as the anterior cingulate and pre-SMA. Additionally, Brieber and colleagues (Brieber et al., 2007) identified gray matter abnormalities close to the right TPJ, which may explain the ToM deficits individuals with ASD exhibit. Further abnormalities were found in the medial temporal and inferior parietal lobe.

Conclusions

The investigation of the neural correlates of socio-cognitive abilities is still in its infancy given that the technology permitting this endeavor is relatively recent. However, substantive literature in relation to the neuroanatomical and functional bases of social cognition is now emerging, with a specific focus on ToM. The brain regions involved in ToM abilities have received particular attention and studies have yielded relatively consistent results; the mPFC and the TPJ seem to be the key players in ToM abilities, with several other brain regions assigned "peripheral" roles. To further knowledge of the neural underpinnings of ToM, researchers have also examined neurological and psychiatric populations in which socio-cognitive deficits were common clinical symptoms of the illness. Although this investigation has been fruitful, much research is still needed to further elaborate the brain abnormalities observed in relation to the presenting behavioural deficits. Clinically, research into the neural substrates of social cognition is beneficial to medical practice, such as neurosurgery, given that the goal of a surgery is to maximize the removal of unhealthy tissue while minimizing the cognitive deficits and impact on patients' quality of life. Although ToM is an ability that is more abstract and more difficult to evaluate during surgery than other abilities (such as language) that neurosurgeons aim to preserve, it is of critical importance because it underlies social competence. Disruption of ToM and its related socio-cognitive skills may lead to social isolation, psychological distress, and socially maladaptive behaviours. Neuroanatomical and functional knowledge of underlying circuitry may guide neurosurgeons so that they may preserve fundamental social abilities.

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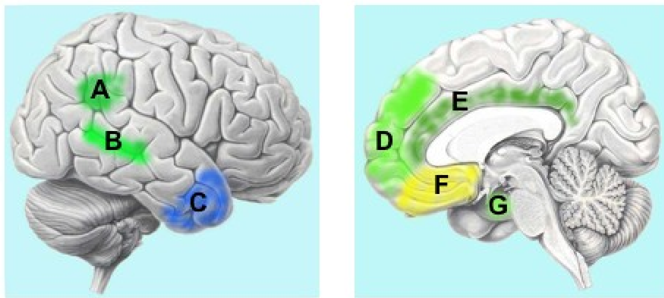
Table 1. Clinical manifestations of ToM deficits and brain circuits involved in specific pathologies

Pathology	Brain circuitry involved	Problem	ToM deficits
Acquired Brain Injury	Frontal lobes	Lesion	Indirect speech, faux pas, second-order beliefs, first-order beliefs
Parkinson's Disease	Dorso-lateral prefrontal-striatal circuitry	Early atrophy	Cognitive ToM deficits
	Fronto-striatal-limbic circuitry	Protracted degeneration	Affective ToM deficits
Schizophrenia	Medial prefrontal cortex, amygdala, temporoparietal junction	Abnormal activation	General deficits in mental state inference; "hyper-ToM"
	Inferior parietal lobule	Abnormal activation	Abnormal source monitoring
	Dopamine circuitry	General transmission impairment	Erroneous contextual information
	Cortico-cerebellar-thalamic-cortical circuit	Inappropriate recruitment	General ToM deficits
Bipolar Disorder	Left anterior cingulate, precuneus, cuneus bilaterally	High individual variability; consistent activations do not include regions typically recruited for ToM	Restricted ability to mentalize; decreased cognitive flexibility
Autism Spectrum Disorders	Medial prefrontal cortex, amygdala, anterior cingulate cortex, medial temporal lobe, inferior parietal lobe	Abnormal activation	General ToM deficits
	Supplementary motor area	Inappropriate recruitment of lower order processing brain areas	Difficulty with perception of specific social stimuli
	Right temporoparietal junction	Grey matter abnormalities	General ToM deficits

Figure 1. Brain areas commonly reported to be activated in theory of mind and moral reasoning



Overlap (green) between areas commonly reported to be activated in studies of theory of mind (blue) and moral reasoning (yellow). (A) Temporo-parietal junction; (B) Superior temporal sulcus; (C) Temporal pole; (D) Medial prefrontal cortex; (E) Cingulate cortex; (F) Orbitofrontal cortex; (G) Amygdala.