International Journal of Psychophysiology xxx (xxxx) xxx–xxx

Contents lists available at ScienceDirect

International Journal of Psychophysiology

journal homepage: www.elsevier.com/locate/ijpsycho

Registered Reports

Cortical thickness in pediatric mild traumatic brain injury including sports-related concussion

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ARTICLE INFO

Keywords:
Mild traumatic brain injury (mTBI)
Concussion
Cortical thickness
Brain development
Free-surfer
Post-concussion symptoms

ABSTRACT

This investigation explored whether differences in cortical thickness could be detected in children who sustained a mild traumatic brain injury (mTBI) compared to those with orthopedic injury (OI) and whether cortical thickness related parental reporting of symptoms. To achieve this objective, FreeSurfer®-based cortical thickness measures were obtained in 330 children, 8 to 15 years of age, with either a history of mTBI or OI. Imaging was performed in all participants with the same 3 Tesla MRI scanner at six-months post-injury, where a parent-rated Post-Concussion Symptom Inventory (PCSI) was also obtained. Robust age-mediated reductions in cortical thickness were observed, but no consistent group-based differences between the mTBI and OI groups were observed. Also, the relation between mechanism of injury (i.e., sports-related, recreational, fall, motor vehicle accident or other) and cortical thickness was examined. Injuries associated with any type of abuse were excluded and children with OI could not have experienced a MVA. Mechanism of injury did not differentially relate to cortical thickness, although in the fall group, parental rating using the PCSI showed increased symptom reporting to be associated with reduced cortical thickness in the left interior frontal, temporal pole and lateral temporal lobe as well as in the right temporal pole. Results from these preliminary findings are discussed in terms of injury variables and developmental factors associated with mTBI in childhood.

In the developing brain, cortical thickness dynamically relates to age. After initial thickening of the cortical mantle in infancy and early childhood, there is a thinning of cortical gray matter that progresses throughout adolescence, even into early adulthood (E. L. Dennis and Thompson, 2013; Giedd et al., 2010; Moeskops et al., 2015). The dynamics of cortical gray matter thickness is thought to reflect maturational effects of both synaptogenesis as well as synaptic pruning (Khundrakpam et al., 2016). First established in post-mortem and animal studies (see review by Epstein, 1986), contemporary methods of image analysis now employ a variety of neuroimaging techniques that non-invasively assess human cortical development, including in vivo cortical thickness (Brown and Jernigan, 2012; Helms, 2016; Mills and Tamnes, 2014; Silk and Wood, 2011).

Aberrations in cortical development may set the stage for adverse outcomes in cognition, emotion and behavior (Cannon, 2016; M. Dennis et al., 2013; Selemon and Zecevic, 2015; Thomas et al., 2016), where a single event may alter development (Squier and Jansen, 2010). In particular, as argued by Shapiro et al. (2016) the late effects of frontotemporal maturation coincide with either the onset of or predisposition to a variety of neuropsychiatric disorders. As such, anything that might disrupt this trajectory has the potential to influence outcome, including traumatic brain injury (TBI) during childhood. A variety of factors associated with skull and brain anatomy render the frontal and temporal lobes particularly vulnerable to trauma-induced deformation; regionally these areas are where pathological changes in brain morphology most likely occur (Bigler, 2007), including pediatric TBI (Bigler et al., 2016b; Levan et al., 2015; McCauley et al., 2010; Merkley et al., 2008; Wilde et al., 2012).

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https://doi.org/10.1016/j.ijpsycho.2018.07.474
Received 21 September 2017; Received in revised form 7 July 2018; Accepted 18 July 2018

Studies that have examined frontotemporal pathologies associated with TBI in children, have shown that these relate to injury severity; more severe injuries particularly at the moderate-to-severe end of the spectrum, are associated with greater pathological changes within the frontal and temporal lobes, including thinning of the cortical mantel (Levan et al., 2015; Merkley et al., 2008; Wilde et al., 2012). However, whether mild TBI (mTBI) alters the trajectory of cortical brain development and cortical thickness in children has not been established. Importantly, since sports or recreational activities are common sources for mTBI in children (Bryan et al., 2016; Cohen et al., 2009), it is important to know if milder forms of brain injury alter developmental trajectories of cortical thickness.

Studies in adults have been mixed where some have shown altered cortical gray matter to be associated with mTBI while others have not (Churchill et al., 2017; Espana et al., 2017; Goddeyne et al., 2015; Govindarajan et al., 2016; King et al., 2016; List et al., 2015; Mayer et al., 2015; Meier et al., 2016; Sussman et al., 2017). Inconsistencies in findings have been assumed to relate to heterogeneity of injury mechanisms, injury severity even within the mild spectrum and individual differences, among other things (Bigler, 2017; Kamins et al., 2017; McCrea et al., 2017). Accordingly, using a cross-sectional design, this investigation explored cortical thickness as measured using the semi-automated FreeSurfer® (http://surfer.nmr.mgh.harvard.edu/) software suite for processing and analyzing magnetic resonance imaging (MRI) scans from children 8 to 15 years of age who had sustained a mTBI. For comparison, a group of children of comparable age and sex with orthopedic injury (OI) were identified, recruited, and assessed within the same emergency department (ED) of a Level 1 Trauma Center at a regional children's hospital. Children diagnosed with mTBI met American Congress of Rehabilitation Medicine (ACRM, 1993) criteria for mTBI. In contrast, those who experienced OI involving limb fracture could not have experienced trauma to the head nor meet any ACRM criteria for mTBI. All children underwent a 3.0 Tesla MRI at approximately 6-months post-injury on the same scanner.

Because the mTBI mechanism of injury has the potential to differentially affect brain structure (Bayly et al., 2005; Ghajari et al., 2017; Ommaya et al., 2002), another objective of this investigation was to explore whether any differences in cortical development could be ascribed to mechanism of injury. For example, in contact sports-related injury, the child athlete has some awareness of potential and impending impact while participating in collision sports. Furthermore, in some sports, protective headgear is worn. In non-vehicular recreational injuries, like skateboarding, there is typically no helmet, although there may be some anticipation of injury. In contrast, falls and motor vehicle accident (MVA) related mTBIs often occur without warning or anticipation of an adverse event. Furthermore, impact dynamics with head injuries from certain types of falls as well as MVAs likely have greater force than that which may occur in sports-related head injuries. As such, mechanism of injury is an important variable to consider, which previously, has not been examined in cortical thickness studies of pediatric mTBI.

In the current study, five different types of mechanism of injury were examined: sports-related concussion (SRC), recreational injuries, falls, motor vehicle accidents and other categories, which included those with incomplete information to determine mechanism of injury or overlapping injuries. Brain injuries associated with physical abuse or assault were excluded. Interestingly, the sports, recreational, and fall categories apply to both mTBI as well as OI participants as identical mechanisms of injury, except that in the OI subjects, the trauma could not involve the head or neck.

For this investigation, the relations of cortical thickness to age and mechanism of injury were explored along with the degree to which post-concussive symptoms (PCS) related to cortical thickness, assessed at six months post-injury using the Post-Concussion Symptom Inventory (PCSI; see Gioia et al., 2008).

1. Methods

Within the same Level 1 trauma center ED, 330 children aged 8 to 15 years were prospectively recruited to participate (N = 330; 143 males with mTBI +79 with OI and 76 females with mTBI +32 with OI). The average mTBI participant age was 12.06 years of age (S.D. = 1.82) and 12.35 (2.16) for OI participants, a difference that was not significant ($t = 0.6$, $p = 0.50$). All mTBI children had a GCS score ≥ 13 and met ACRM (ACRM, 1993) criteria for mTBI. Since this investigation focused on the mildest of injuries, the majority of the children with TBI had a GCS = 15. Only seven had a GCS of 14 (two had sustained their injuries from a MVA, two from recreational injuries, three from slip and fall injuries). No child with sports-related mTBI had a GCS score other than 15. OI children could not have sustained any trauma to the head nor have any alteration in level of consciousness associated with their OI and did not meet ACRM criteria for mTBI. All OI cases associated with an MVA were excluded, because of the potential for occult mTBI.

All children consecutively presented to the ED for examination and were recruited for the study between 2012 and 2016. Initial behavioral, neuropsychiatric and symptom reporting was established in the acute, sub-acute and chronic post-injury periods, with the research MRI performed at approximately 6 months' post-injury. For the purposes of this investigation, we examined only the parent rating of concussion symptoms observed in their child at 6-months post injury, when MRI scanning was obtained. As stated in the Introduction, in terms of mechanism of injury, there was a natural delineation of four general categories: 1) sports-related, 2) recreation, 3) falls, and 4) vehicular accidents.

Operationally, these divisions were defined as follows: (1) sports-related mTBI injuries occurred as a result of some type of school- or community- organized sport, including practice (n = 96 diagnosed with mTBI; n = 38 with OI), (2) recreation involved injury while engaged in leisure activities including roller blading, skate boarding, surfing, riding a bicycle (non-motorized), rock climbing, etc. (n = 51 with mTBI; n = 37 with OI (3); falls occurred during unstructured indoor or outdoor activities at home, school, neighborhoods, stores or other environments (n = 59 with mTBI; n = 34 with OI) and (4) motor vehicle accidents occurred where some motorized vehicle was the cause of the head injury including car/truck accidents, motorcycle and scooter accidents, auto-pedestrian and all-terrain vehicle accidents (n = 13 with mTBI). There was also a fifth 'Other Category'; however, only three subjects were included that category, where information about injury mechanism was insufficient to specifically determine mechanism of injury, or where the injury involved more than one of the categories listed above. The sample size in the fifth category precluded any meaningful analysis.

1.1. Neuropsychological Testing

1.1.1. Wechsler abbreviated scale of intelligence – second edition (WASI-II; Wechsler, 2011)

Intellectual testing was obtained to provide a descriptive statement about the overall cognitive ability of the children participating in this study but was not a focus of this investigation.

1.1.2. Post-Concussion Symptom Inventory (PCSI)

The Post-Concussion Symptom Inventory (PCSI; see Gioia et al., 2008), specifically the parent assessment form (PCSI-P), was administered, where parents rated symptoms at 6 months post-injury, at the time when scanning was performed. The PCSI covers basic post-concussive symptom reporting on a 6-point scale from 0 = Not a problem, 3 = Moderate problem and 6 = Severe problem. This study examined only parental rating, as the parent may be in the best observational role to rate symptoms/problems following injury (Bernard et al., 2017).