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Predictors of Post-concussive Symptoms in Young Children: Injury *versus* Non-injury Related Factors

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Abstract

Objectives: A notable minority of children will experience persistent post-concussive symptoms (PCS) following mild traumatic brain injury (mTBI), likely maintained by a combination of injury and non-injury related factors. Adopting a prospective longitudinal design, this study aimed to investigate the relative influence of child, family, and injury factors on both acute and persistent PCS in young children. **Methods:** Participants were 101 children aged 2–12 who presented to an Emergency Department, with either mTBI or minor bodily trauma (control). PCS were assessed at time of injury, 1 week, and 1, 2, and 3 months post-injury. Predictors included injury and demographic variables, premorbid child behavior, sleep hygiene, and parental stress. Random effects ordinal logistic regression models were used to analyze the relative influence of these predictors on PCS at early (acute – 1 week) and late (1–3 month) post-injury phases. **Results:** Presence of mTBI was a stronger predictor of PCS in the early [odds ratio (OR) = 18.2] compared with late (OR = 7.3) post-injury phase. Older age at injury and pre-existing learning difficulties were significant predictors of PCS beyond 1 month post-injury. Family factors, including higher levels of parental stress, higher socio-economic status, and being of Anglo-Saxon descent, consistently predicted greater PCS. **Conclusions:** Injury characteristics were significantly associated with PCS for 3 months following mTBI but the association weakened over time. On the other hand, pre-existing child and family factors displayed an increasingly strong association with PCS over time. Follow-up for these "at-risk" children which also addresses family stress may minimize longer-term complications. (*JINS*, 2016, *22*, 793–803)

Keywords: Mild traumatic brain injury, Concussion, Post concussive symptoms, Child, Predictors, Child, Pediatric, Behavior

INTRODUCTION

Mild traumatic brain injuries (mTBI) are extremely common during childhood, with incidence rates from Emergency Department (ED) presentations averaging around 300 per 100,000 in children aged 0–17 (Koepsell et al., 2011). These rates peak in pre-school children (421 per 100,000) where most injuries result from falls (Koepsell et al., 2011). Since the majority of children return to pre-morbid functioning relatively quickly with little intervention, routine follow up is neither feasible nor always necessary (Lloyd, Wilson, Tenovuo, & Saarijarvi, 2015). Yet for the notable minority (11–17%) who experience ongoing post-concussive symptoms (PCS) beyond 3 months post-injury (Barlow et al., 2010; Carroll, Cassidy, Peloso, et al., 2004; Ponsford et al., 1999; Zemek, Barrowman, et al., 2016), early intervention and follow-up may be pivotal in reducing long-term complications (Winkler & Taylor, 2015). Therefore, primary care clinicians need guidelines with which to discern those children at greater risk of ongoing PCS.

Few studies have prospectively examined the relative influence of injury and non-injury factors on PCS in younger children following mTBI (Kirkwood et al., 2008; Zemek, Farion, Sampson, & McGahern, 2016). PCS refer to subjective somatic, cognitive, affective, and sleep-related symptoms that are commonly, albeit not exclusively, reported by children and their parents following mTBI (Barlow et al., 2010; Mittenberg, Wittner, & Miller, 1997; Ponsford et al., 1999). The fact that PCS can be experienced by children with no evidence of neurological changes (i.e., post-traumatic amnesia, loss of consciousness (LOC), abnormal neuroimaging findings), has

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sparked ongoing debate around the etiology of PCS and the relative influence of injury and non-injury related factors.

Whereas measures of injury severity such as the Glasgow Coma Scale (GCS) and duration of post-traumatic amnesia (PTA) have been shown to be significant predictors of outcome following moderate and severe TBI, research examining their predictive utility in the mTBI population has yielded mixed findings (Carroll, Cassidy, Peloso, et al., 2004). This may be due to the heterogeneous nature of mTBI samples, poor sensitivity of the GCS in this population [i.e., 90% have a GCS of 15/15; Melo et al. (2010)], or unreliable assessment of PTA (Shores et al., 2008). However, advanced neuroimaging techniques such as diffusion tensor imaging (DTI), have demonstrated an association between pathophysiological changes following mTBI and persistent PCS (Bigler, 2008; Wilde et al., 2008).

The inclusion of trauma control groups has also been used to study the influence of other trauma-related non-brain injury factors, and is now recommended for mTBI research (Carroll, Cassidy, Holm, Kraus, & Coronado, 2004). Research in adolescents and adults has shown that mTBI consistently predicts acute PCS but shows a decreasing association with outcome over time (McNally et al., 2013; Ponsford et al., 2012). This suggests that persistent PCS are at least partially accounted for by non-injury factors such as pre-morbid demographic, child or family functioning, or post-injury reactions to the event such as stress and anxiety (Anderson, Godfrey, Rosenfeld, & Catroppa, 2012; Babikian, McArthur, & Asarnow, 2013; Ponsford et al., 2012).

With regard to demographic factors, age, gender, and history of mTBI have been associated with outcome following mTBI in previous studies. The relationship between age at injury and outcome following mTBI appears complex and the mechanisms responsible are likely multifactorial (Kolb, 1999; Kolb & Teskey, 2012; Taylor & Alden, 1997). Earlier age-at-injury has often been associated with poorer academic and intellectual outcomes following both moderate–severe (Lloyd et al., 2015; Taylor & Alden, 1997) and mild TBI (Anderson, Catroppa, Morse, Haritou, & Rosenfeld, 2001), particularly when injuries occur in the first 5–7 years of life.

There is also a suggestion that during “critical” periods of cognitive development children are more vulnerable to insult, with one study finding that early primary-aged children (i.e., 7–8 years) were more vulnerable than pre-school and older children (Crowe, Catroppa, Babl, Rosenfeld, & Anderson, 2012). A recent systematic review of PCS outcomes following mTBI, however, suggested that children older than 13 were at greater risk of persistent PCS (Zemek, Barrowman, et al., 2016a). Similarly, school-aged children describe a greater PCS burden than pre-school children, both immediately (McKinlay, Ligteringen, & Than, 2014), and several months (Barlow et al., 2010), after mTBI. The challenges of accurate PCS assessment in pre-school children must be considered when interpreting these results, however (Gioia, Schneider, Vaughan, & Isquith, 2009).

Research examining the effects of gender on outcomes following pediatric mTBI has yielded mixed results, but recent research has highlighted that females report more PCS following mTBI (Babcock et al., 2013; Taylor et al., 2010; Zemek, Barrowman, et al., 2016). Gender differences in behavioral and psychiatric outcomes have also been noted in more general TBI samples (Scott et al., 2015; Whelan-Goodinson, Ponsford, Schonberger, & Johnston, 2010). The influence of previous mTBI is unclear (Kirkwood et al., 2008), although a recent multi-center study suggested previous mTBI increases risk of persistent PCS (Zemek, Barrowman, et al., 2016). Given mixed findings, further work is needed to delineate the influence of these factors on PCS outcomes (Carroll, Cassidy Holm, et al., 2004).

Pre-injury child factors including pre-morbid learning difficulties, behavioral adjustment (Yeates et al., 2012) and pre-existing learning difficulties (Ponsford et al., 1999) have also been shown to influence PCS. There is also some preliminary evidence in adults suggesting poor pre-morbid sleep quality may be a significant predictor of poorer PCS (Theadom et al., 2015), however, this has not been explored in children.

Finally, consideration of the influence of family factors on recovery from TBI is imperative in pediatric research. The period following a child’s head injury can be extremely stressful for the child and their family, even for milder injuries (Wade et al., 2006). Lack of adequate social and medical support (Prigatano & Gray, 2007), observable changes in cognitive and behavioral functioning, often resulting in a failure of children to immediately return to social and school activities (Ganesalingam et al., 2008; Rivara et al., 1996; Taylor et al., 2001; Wade et al., 2006; Yeates, Taylor, Walz, Stancin, & Wade, 2010), and financial burden (Keenan, Runyan, & Nocera, 2006; Osberg, Baker, & Long, 1996) have been identified as contributing factors to parental distress following TBI in childhood.

This relationship may also be bi-directional, in that a stressful home environment may also impede a child’s recovery from injury (Ganesalingam et al., 2008). As such, assessment of family functioning and stress must be considered when examining the impact of childhood head injury (Anderson & Yeates, 1997; Taylor & Alden, 1997). Limited financial, social, and/or psychological family resources have shown a negative impact on recovery from TBI. They are typically measured using socio-economic status (SES) indicators or a composite measure with education and occupation. The influence of family resources may vary depending on the severity of injury, given that children who sustain more severe injuries are likely to require more intervention and rehabilitation (Stavinoha, Butcher, & Spurgin, 2012).

The current study aimed to investigate the relative influence of demographic, child, parent, and injury factors on PCS at early (acute – 1 week) and late (1–3 months) post injury phases, in young children experiencing trauma. In particular, we were interested whether children who sustained mTBI were at greater risk of early and/or late PCS than children experiencing minor bodily trauma without TBI. To assist with determining “at-risk” children during the acute stage, we also wanted to determine which pre-injury demographic (age, gender), child (pre-morbid behavior and sleep) and family factors (parental stress, SES) were associated with more persistent (i.e., late) PCS. Based on previous studies, it was hypothesized that injury factors would be strongly associated with early PCS but that the strength of that association would decline over time, and that the association of pre-morbid non-injury child and family factors with PCS would be evident early post-injury, but would increase over time post-injury.

METHOD

Participants

Participants were parents of children aged 2–12 who presented to a hospital ED from November 2012 to January 2015, with either a mild TBI (mTBI group) or minor injury not involving the head [trauma controls (TC)]. Parents were approached by nursing staff in the ED either in person while their child was under observation, or *via* telephone <48 hr after hospital presentation. Following verbal consent, parents were contacted by the primary researcher to complete eligibility screen and conduct initial interview. All data obtained were in compliance with regulations outlined in the Helsinki Declaration, and the research was approved by both the Western Health (Ref. HREC11WH90) and Monash University (Ref. 22012001523) Ethics Committees.

Inclusion criteria for the mTBI group included: (1) recent (<48 hr) history of trauma to the head, resulting in LOC <30 min and a GCS score of 13–15 on presentation to ED, and/or >2 transient neurological symptoms (nausea, vomiting, dizziness, headache, confusion/disorientation, or sensitivity to noise/light; (2) age between 2 years 0 months and 12 years 11 months; (3) English-speaking or presence of a family member suitable to interpret. Participants were excluded if they (1) were intubated or required general anesthesia following injury; (2) had focal neurological signs, seizures, or intracerebral abnormality on computed tomography (CT); (3) had a history of neurological or psychiatric illness; (4) injury resulted from child abuse; or (5) they had a history of moderate-severe TBI.

Inclusion in the control (TC) group required (1) recent (<48 hr) history of minor injury (e.g., laceration, soft tissue injury fracture, or dislocation) to parts of the body other than skull and/or spinal cord, including lacerations to the face and scalp, with no disturbance of consciousness. Other inclusion criteria were the same as for the mTBI group. The inclusion of an injury-control comparison group is now recognized as an important methodological control for the effects of general trauma and pre-morbid behavioral differences (Satz et al., 1997). Both mTBI and control groups were further divided by age into preschool and school-aged children, based on whether the child had commenced school at time of injury.

Materials and Procedure

Participants were recruited by nursing staff by one of two methods: (1) face-to-face during post-injury observation period, or (2) through retrospective searching of recent medical admissions (<48 hr). There was no known systematic bias as to who was approached by the hospital staff. Following verbal consent, the primary researcher then contacted participants to complete final screen and obtain written consent. With the exception of two cases that required an interpreter, all interviews were conducted *via* telephone.

Post-concussive symptoms. Given the lack of PCS scales validated for use in this age group, a decision was made to generate a comprehensive list of items (symptoms) from the most commonly used and available PCS scales where parental report available [Rivermead Post-concussive Questionnaire (Gagnon, Swaine, Friedman, & Forget, 2005), Post-injury Symptom checklist (Yeates et al., 2001), the Acute Concussion Evaluation (Gioia, Collins, & Isquith, 2008), from review by Gioia et al. (2009)], with the aim to capture the widest range of symptoms possible. That is, the physical/somatic, cognitive, behavioral, affective, and sleep-related symptoms from the different scales were cross-checked, with equivalent items matched up (e.g., "was sensitive to noise" and "noise sensitivity") and additional or unique items all included. This resulted in a 28-item PCS scale, which measured both presence and severity [5-point severity scale ranging from "0" (not experienced at all) to "4" (a severe problem)] of symptoms in the acute phase (within 72 hr of injury), 1 week, 1 month, 2 months, and 3 months post-injury. Preliminary reliability analysis of the scale revealed good internal consistency across follow up time points [Cronbach's α mean = 0.86 (SD = 0.02; Range = 0.83–0.89), with no single items reducing the α value below 0.84. if deleted], providing justification for inclusion of all 28 items (Cronbach, 1951).

Items included on the scale measuring retrospective parent ratings of premorbid PCS were also collected during the first interview, and thus PCS scores reflected a change from this pre-morbid level. Given the inherent difficulties in eliciting symptom presence in younger children (Anderson & Yeates, 1997), a semi-structured interview was used, whereby concrete behavioral exemplars were supplied for each symptom to assist parents with identification of symptoms in their children and avoid misinterpretation of terminology (e.g., 'More emotional': "has your child become more 'teary' or 'sooky', perhaps crying over things they wouldn't have before, or to over-reacting to situations or throwing tantrums unnecessarily?"; or for 'Anxiety': "has your child become more 'clingy' or more nervous about leaving you when you drop them off at school/kindergarten/daycare?".

Demographic factors

These included age, gender, reported history of mild TBI, pre-existing learning difficulties (score on Learning Disability sub-scale on the Clinical Assessment of Behavior) and SES. SES score was calculated by residential postcode using the Socio-economic Indexes data [values range one (most disadvantaged) to 10 (most advantaged) area (Australian Bureau of Statistics, 2013)].

Injury related factors

Mechanism of injury and whether a child sustained an mTBI or TC were collected. Measures of injury severity included the Glasgow Coma Scale (GCS) and parental report of LOC (when witnessed). PTA was not routinely recorded in the ED.

Child factors

Premorbid ratings of children's behavior were collected during initial interview using the Clinical Assessment of Behavior-Parent version (Bracken & Keith, 2004) and re-administered at 1 and 3 months post-injury to document behavioral changes across that period. The CAB produces an overall Behavioral Index (CBI) and two clinical scales (Internalizing Behavior and Externalizing behavior).

A baseline of children's sleep habits was obtained during initial interview using the Owen's Children's Sleep Habits Questionnaire (CSHQ; Owens, Spirito, & McGuinn, 2000) (CSHQ) and re-administered at 1 and 3 months post-injury. The CSHQ is a 36-item parental-report screening measure designed to assess behaviorally and medically based sleep problems in school children. It has been validated in toddlers and pre-school children (Goodlin-Jones, Sitnick, Tang, Liu, & Anders, 2008).

Family factors

The Parenting Stress Index/Short Form (PSI/SF) is a 36-item self-report questionnaire which is a derivative of the Parenting Stress Index full-length test. It aims to identify parent-child problem areas in parents of children ages 1 month to 12 years, and was used as a pre-injury measure in this study (Abidin, 1983). Statistical factor analysis of the PSI/SF yields three constructs or scales, namely Parental Distress, Parent-Child Dysfunctional Interaction, and Difficult Child. It also generates a Total Stress Score, which reflects overall stresses reported in the areas of personal parental distress, stresses derived from the parent's interaction with the child, and stresses that result from the child's behavioral characteristics.

Data Analysis

Univariate outliers with Z score >3.29 ($p < .001$, two-tailed test) were identified [five cases on Sleep Index, four cases on Behavior (CBI) index, four cases on PCS Scale] and assigned a score one unit larger than the next most extreme score (Tabachnick & Fidell, 2013). There were no negative PCS change scores (premorbid to follow-up). Group differences (mTBI, TC) at baseline were evaluated using t tests (normally distributed data) and chi-square (categorical data) analysis. Unless otherwise specified, statistical significance was set at 0.05. Analysis was conducted using Stata Statistical Software Version 14 (Stata Corporation, College Station, TX).

The main outcome variable (total PCS) was re-coded as an ordinal categorical variable (whereby 0 = no PCS, 1 = 1–2 PCS, 2 = 3–5 PCS, and 3 = >6 PCS) and analyzed using random effects ordinal logistic regression (Hosmer, Lemeshow, & Sturdivant, 2013). Important when dealing with ordinal outomes, the proportional odds assumption of ordinal logistic regression was upheld. Proportional odds assumes that the relationship between each pair of (in this case, PCS) outcome groups is the same (i.e., that the coefficients that describe the relationship between the lowest *versus* all higher categories of the response variable, are the same as those that describe the relationship between the next lowest category and all higher categories). This assumption was tested by running a series of binary logistic regressions on the different levels of PCS.

To examine PCS over time, time was dichotomized into early (acute to 1 week) and late (1 to 3 months) post-injury phases, to simplify interpretation, and because such separation of acute *versus* persistent PCS was believed to be clinically meaningful.

The advantages of using random effects regression modelling are that it: (1) estimates both individual and injury group trend lines over multiple time points; (2) is less restrictive regarding missing data and uses data from all individuals, and, therefore, does not rely on endpoint analysis, and (3) allows time-invariant variables (e.g., gender) to be absorbed by the intercept (Gibbons et al., 1993).

To identify key variables and reduce the number of variables relative to sample size, initial separate ordinal logistic regression analyses were run to examine the predictive utility of each of the individual 15 predictor variables on PCS3. An interaction term between each variable and time was also included, as this allowed assessment of whether a variables' influence on PCS varied across time (early *vs*. late). As recommended by Hosmer and colleagues, a p value of .2 was applied to determine which variables, and/or their interactions with time, would be included in the final model (2013). The use of the more liberal p value was to capture variables which showed weak associations by themselves, but exhibited stronger associations with the outcome variable when combined with other variables.

Based on these criteria, the following variables were included in the final model; age, SES, history of mTBI, learning disorder, reporter education, reporter ethnicity, pre-morbid stress, injury group, and LOC. The following variables were not included; gender, reporter gender, premorbid PCS, pre-morbid child sleep, and pre-morbid behavior.

Two separate random effects ordinal logistic regression models were run to examine the influence of the predictor variables selected in the initial analyses described above, on early and late PCS, respectively. Then, to determine whether each variable's relationship with PCS was statistically different at early *versus* late post-injury stages, the same ordered logistic regression models were examined longitudinally using a time variable. Interaction terms that were statistically significant in the preliminary analyses (Table 3) were included; that is, if a variable had a statistically significant interaction ($p < .05$) with time (early, late) on PCS, then this suggested that variable's relationship with PCS differed between the early and late post-injury phases. As displayed in Table 4, these variables included age and a history of learning disorder. Given the inter-correlation between age and injury group, injury group was no longer statistically significant when all variables were entered together. It should be noted, however, that if age was removed from the model there was a statistically significant interaction between injury group and time on PCS.

RESULTS

Recruitment ran consecutively for 26 months during which time 322 potential mTBI and 3650 TC were admitted to the ED. Of these, 101 participants were successfully recruited into the study (47 mTBI, 55 TC), all of which remained in the study at 3 months post-injury. Table 1 outlines participant demographics, children's injury details and child/parent pre-injury factors.

Injury groups (mTBI, TC) did not differ significantly in gender, socio-economic status, level of parental education or history of previous head injury. Injury groups did differ significantly on age and this was considered a limitation, as discussed below. The majority of injuries were due to falls, as expected in younger mTBI populations. Based on GCS scores, the mTBI group's injuries were very mild, with 95% scoring the maximum 15 of 15. Baseline assessment of behavior and sleep habits revealed no statistically significant differences in scores between mTBI and TC children (Table 1). Further examination using classification cutoffs also revealed that the percentage of children classified as showing clinically "at risk" behavioral problems also did not differ on the overall behavioral index (13% of mTBI and 11% of TC, χ^2 (1) = 0.11; p = .74), or on externalizing (24% mTBI and 12% TC, χ^2 (1) = 2.14; p = .14) and internalizing (9% mTBI and 11% of TC, χ^2 (1) = 0.14; p = .71) behavior scales. Ratings of parental stress were comparable between injury groups at baseline.

Parental report of PCS by mTBI and TC groups across the post-injury period are displayed in in Table 2. In brief, PCS peaked in the acute post-injury phase for both groups but mTBI children experienced significantly more PCS (i.e., more than half the group reporting at least six PCS). Over the first week post-injury, there was a significant drop in

Table 1. Demographics, injury factors, and pre-morbid clinical characteristics

	mTBI n = 46	TC n = 55	p	ES
Demographics				
Gender (male), n (%)	29 (63)	39 (71)	.40	.08
Age (months), mean (*SD*)	7.5 (2.9)	5.1 (3.1)	<.001	.80
Pre-school group	3.7 (1.1)	2.8 (1.0)	.02	.85
School group	8.9 (1.9)	8.1 (2.2)	.14	.39
SES[a], mean (*SD*)	5.0 (2.6)	5.2 (2.4)	.43	.08
Learning difficulties[b]	50.8 (9.4)	48.2 (7.8)	.15	.30
Reporter education			.10	.21
< HS Grad	18 (39.1)	14 (25.5)		
HS Grad	17 (37.0)	18 (32.7)		
> HS Grad	11 (23.9)	23 (41.8)		
Injury characteristics				
Mechanism of injury			.25	.17
Fall	36 (78.3)	49 (89.1)		
Collision	3 (6.5)	3 (5.5)		
Sports-related	7 (15.2)	3 (5.5)		
Glasgow Coma Scale				
14	2 (4.3)	—		
15	44 (95.6)	—		
LOC[c], *n* (%)	8 (17.4)	0 (0.0)	<.01	.32
Witnessed, *n* (%)	17 (37.0)	13 (23.6)	.15	.15
History of mTBI				
Yes (w LOC)	1 (2.2)	1 (1.8)	.29	.16
Yes (no LOC)	8 (17.4)	4 (7.3)		
Pre-morbid child factors				
Behaviour (CAB-CBI), mean (*SD*)	50.6 (8.26)	49.5 (8.30)	.51	.13
Sleep Habits (OCSHQ), mean (SD)	42.1 (5.6)	40.4 (4.4)	.10	.34
Pre-morbid family factors				
Parental Stress (PSI-SF), mean (SD)	72.0 (19.6)	67.4 (16.0)	.20	.26

Note. mTBI, mild traumatic brain injury group; TC, trauma control group; ES = effect size (phi (2x2) and Cramer's V (2x3) reported for categorical variables and Cohen's d used for continuous variables); SES, socio-economic status; HS, high-school graduate; LOC, loss of consciousness; CAB, Clinical Assessment of Behaviour; CBI; Clinical Behavioural Index; OCSHQ, Owen's Children's Sleep Habits Questionnaire; PSI-SF, Parental Stress Index-Short Form;
[a]Value represents a decile value determined by postcode (ranging 0 – 10), lower decile value = lower SES. Mann-Whitney test applied to compare this ordinal variable across groups;
[b]Determined by children who scored in the clinically significant range on the Learning Disorder sub-scale of the CAB;
[c]All reported LOC was suspected to be less than 10 s.

Table 2. Percentage of children with PCS within each group (mTBI, TC), across the post-injury period

	Time post-injury											
			Early				Late					
	Premorbid		Acute		1 Week		1 Month		2 Month		3 Months	
No. of PCS	mTBI $n = 46$	TC $n = 55$	mTBI $n = 46$	TC $n = 55$	mTBI $n = 46$	TC $n = 55$	mTBI $n = 46$	TC $n = 55$	mTBI $n = 46$	TC $n = 55$	mTBI $n = 46$	TC $N = 55$
None	56.5	65.5	0.0	45.5	26.1	80.0	45.7	81.8	58.7	89.1	60.9	89.1
1–2	32.6	25.5	4.3	45.5	34.8	16.3	37.0	14.5	19.6	10.9	13.0	5.5
3–5	6.5	3.6	34.8	9.1	32.6	3.6	4.3	3.6	6.5	0.0	17.4	5.5
6+	4.3	5.5	60.9	0.0	6.5	0.0	13.0	0.0	15.2	0.0	8.7	0.0

Note. PCS = post-concussive symptoms mTBI = mild traumatic brain injury group; TC = trauma control group.

PCS and a steady tapering of symptoms up to 1 month post-injury. PCS persisted in a notable minority of children from 1 to 3 months post-injury, with 18% of mTBI and 5% of TC children remaining symptomatic 3 months post-injury.

Results from the preliminary ordinal logistic regression analyses examining the association of individual variables with PCS are outlined in Table 3. LOC, history of mTBI, parent cultural background, and pre-morbid parental stress levels, were all significantly associated with PCS overall. Pre-existing learning difficulties and injury type (mTBI, TC) had varying associations with PCS across time as evidenced by significant interactions of these variables with time.

Results from the two separate random effects ordinal regression analysis are outlined in Table 4, showing the association of predictor variables with early PCS (left column) and late PCS (right column). The strongest predictor of early PCS was having sustained an mTBI. These children were 16 times more likely to experience a greater number of PCS than those who sustained a mild bodily injury. Having sustained an mTBI was a statistically significant predictor of both early and late PCS (main effects in Table 4).

A range of non-injury factors were also significantly associated with PCS. Higher SES and greater levels of pre-morbid stress were statistically significant predictors of early PCS, whilst being of Anglo-Saxon decent was a statistically significant predictor of late PCS. Significant interactions were also found between time and age at injury, $\beta = -0.02$ (SE(β) = .01, 95% confidence interval (CI) [–0.03, –0.01], $p < .01$, and time and pre-existing learning difficulties, $\beta = -0.07$ (SE(β) = .03, 95% CI [0.02, 0.12], $p < .01$, indicating that children with pre-existing learning difficulties and those older in age were more likely to have reported symptoms in the late post-injury phase (i.e., beyond 1 month).

DISCUSSION

This study aimed to identify injury and non-injury predictors of PCS at both early (acute to 1 week) and late (1 to 3 months) post-injury stages following trauma in young children. Consistent with research in older children and adults, children who had sustained mTBI were much more likely to experience PCS during both the acute and non-acute post-injury phase, than demographically similar children with mild trauma to their body (Ponsford et al., 2012; Yeates et al., 2012). This result lends support to the presence of

Table 3. Preliminary regression analyses examining predictors individually on PCS, and as an interaction with time

	OR	95% CI	*p*-Value
Age (months)*	1.01	1.00, 1.02	<.01
Gender	1.32	0.78, 2.22	.30
SES	1.09	0.96, 1.19	.20
History mTBI[a]	1.95	0.92, 4.13	.08
Learning disorder**	1.03	1.00, 1.06	.09
Reporter education			
<HS *vs* HS	1.26	0.68, 2.33	.45
<HS *vs* >HS	0.51	0.27, 0.95	.03*
HS *vs* >HS	0.64	0.35, 1.17	.15
Reporter ethnicity[b]	0.35	0.19, 0.63	<.01
Reporter gender	0.99	0.48, 2.02	.96
Pre-morbid PCS			
1–2 PCS	1.26	0.71, 2.26	.43
3–5 PCS	0.93	0.27, 3.25	.91
6+ PCS	1.02	0.31, 3.31	.98
Pre-morbid PCS (any)	1.19	0.70, 2.01	.86
Injury group (mTBI/TC)**	13.62	7.71, 24.07	<.001
LOC	5.03	2.05, 12.35	<.001
Pre-morbid sleep	1.02	0.98, 1.07	.31
Pre-morbid behaviour	1.01	0.99, 1.04	.37
Pre-morbid stress	1.02	1.01, 1.04	<.01

Note. PCS = post-concussive symptoms; SES, socio-economic status; mTBI, mild traumatic brain injury group; TC, trauma control group; HS, high-school graduate; LOC, loss of consciousness; Gender (male coded 0; female coded 1).
**p*-Value for interaction term was <.2 so was included in final model (age * time, $\beta = 0.01$ (SE (β) = .01, 95% CI [–0.02, 0.00], $p = .09$).
***p*-Value for interaction term (predictor variable * time) statistically significant at $p < .05$. This included the following interactions; Learning Disorder * Time, OR = 1.05, 95% CI [1.00, 1.10], $p = .039$; Injury Group (mTBI/TC) * Time, OR = 0.44, 95% CI [0.20, 0.97], $p = .04$).
[a]Parental report of history of mTBI which included suspected mTBI.
[b]Reporter Ethnicity coded 0 for Anglo-Saxon and coded 1 for ‘other’ (Asian, African, other).

Table 4. Results from random effects ordinal regression analyses, predicting PCS at both early (acute – 1 week) and late (1 – 3 months) post-injury stages

	Early		Late	
Predictors	OR	95% CI	OR	95% CI
Age (months)#	1.00	0.99, 1.00	0.98**	0.97, 1.00
SES	1.19**	1.07, 1.38	1.12	0.99, 1.26
History of mTBI	1.13	0.41, 2.40	0.88	0.40, 1.92
Learning disorder (CAB)#	1.02	0.96, 1.07	1.08**	1.03, 1.14
Reporter education	1.08	0.52, 2.19	0.62	0.30, 1.27
Reporter ethnicity	0.57	0.25, 1.11	0.36*	0.15, 0.85
Pre-morbid stress	1.02*	1.00, 1.05	1.02*	1.00, 1.04
Group (mTBI, TC)	16.24**	7.58, 34.79	6.61**	3.26, 13.36
LOC	1.56	0.49, 4.89	1.55	0.651, 3.94

Note. OR = odds ratios; # indicates significant interaction with time (early, late) in model, indicating the difference in coefficients between early and late is statistically significant at $p < .05$, e.g., the coefficient for learning disorder (1.02) at the early stage is statistically significant from the coefficient for learning disorder (1.08) at the late stage.
*$p < .05$.
**$p < .01$.

neurophysiological changes occurring in the days to weeks following mTBI, and for some children over extended periods of time (Giza & Hovda, 2014). Given PTA was not routinely assessed, and 95% of our sample had GCS scores of 15/15, the influence of injury severity within the mTBI group was difficult to determine. An alternative indicator of severity, LOC, also did not predict persistent PCS, however. The failure of traditional TBI severity measures to accurately predict outcome following mTBI may reflect the relatively variable or retrospective application of such measures in mTBI cases, or simply that they lack sensitivity in this group. However, given that presence of an mTBI was such a significant predictor of PCS in this study, attempts to identify reliable injury severity markers and have these consistently collected in adults and children with mTBI should continue.

As hypothesized, a combination of injury, child, and family factors were the strongest predictors of PCS beyond 1 month post-injury. Children who had sustained mTBI, who were older in age, and who had pre-existing learning difficulties were at increased risk of persistent PCS. The predictive utility of these variables increased over the post-injury period. This finding supported our hypothesis that non-injury factors would make an increasing contribution to outcome over time.

This effect of age is in disagreement with findings in moderate to severe TBI samples which support an "early vulnerability hypothesis" that the immature brain is more vulnerable to the deleterious effects of TBI (Lloyd et al., 2015; Taylor & Alden, 1997), but is consistent with other mTBI studies highlighting greater PCS in older children (Barlow et al., 2010; Zemek, Barrowman, et al., 2016). This might suggest that below a certain severity threshold the negative outcomes associated with age diminishes. Alternatively, the effect of age on outcomes following mTBI may be better represented through "critical periods." For example, our results were somewhat consistent with Crowe and colleagues (2012), who identified that early primary-school aged child (i.e., 7 to 8 year olds), may be at greater risk than pre-school and perhaps older children.

This forces consideration of the varying environmental demands placed on children of different ages; although school-aged children must attend school where they are expected to learn and acquire new skills, it could be argued that pre-school children return to a more supportive and familiar environment with less cognitively demanding daily routines. In support of this, there is evidence to suggest that the effects of early brain injury may worsen over time as they interact with developmental processes and impede the acquisition of new skills (Gronwall, Wrightson, & McGinn, 1997; McKinlay, Dalrymple-Alford, Norwood, & Fergusson, 2002; Oddy, 1993; Taylor & Alden, 1997). Thus the greater reporting of PCS in older children in this study may reflect the fact that greater demands are placed on these children. It may also be that younger children are less able to self-report such symptoms and their parents may be less aware of them. Taken together, these findings further highlight the complex relationship between age at injury and recovery (Kolb & Teskey, 2012).

The influence of pre-existing learning difficulties or conversely, of "brain reserve" on outcomes following mTBI has been relatively well documented (Babikian et al., 2013; Ponsford et al., 1999; Satz et al., 1997) and was supported in this study of younger children. This adds further weight to the theory of "brain reserve capacity" theory which purports that children with pre-existing learning difficulties have a reduced capacity to cope with cerebral insult (Satz, 1993). Research in adults has documented a relationship between pre-existing sleep disturbance and outcomes following mTBI (Chan & Feinstein, 2015; Kraus et al., 2009; Theadom et al., 2015); therefore, this was also examined in our study. Our results did not support this relationship in children; however, we used only a brief subjective measure of sleep. Thus, future research should include more detailed measures of sleep, incorporating both objective (i.e., physiological) and subjective sleep measures on which to base more sounds conclusions.

The hypothesis that injury factors (i.e., having sustained an mTBI) would have a decreasing strength of association with PCS over time was also supported. Despite this decline, however, mTBI remained the strongest predictor of persistent PCS, even after controlling for age, and pre-existing child and family characteristics. This appears to be in conflict with previous research which demonstrates demographic, child, and family factors as stronger determinants of PCS beyond 1 month post-injury (McNally et al., 2013; Olsson et al., 2013), and may reflect the heterogeneous nature of mTBI injuries (i.e., varying levels of injury severity). The possibility that our results support the presence of more lasting neuro-metabolic changes (i.e., dysfunctional excitatory neurotransmission) following mTBI, must also be considered (Giza & Hovda, 2001, 2014; MacFarlane & Glenn, 2015).

Higher levels of parental stress were consistently associated with greater PCS across both acute and late post-injury periods. This may suggest that either parental stress leads to greater endorsement of PCS by parents, or alternatively, that environmental stress somehow influences the development or expression of PCS within the child (Ganesalingam et al., 2008; Yeates et al., 2010). The impact of family burden on mTBI outcomes has received relatively less attention than in moderate and severe TBI groups, perhaps given the majority of children return to pre-morbid functioning relatively quickly following mTBI. Yet the perceived stress that parents experience following their child's injury may not necessarily be correlated with the severity of injury and thus should be considered as equally important in this population (Wade et al., 2011). Even for children who are discharged quickly after injury, families remain the major long-term source of support and thus play a critical role in a child's recovery from a TBI (Taylor et al., 1995). This is especially the case for younger children who remain extremely dependent on their parents and carers in everyday life.

Lower SES and limited family resources have often been associated with poorer outcomes following pediatric TBI, particularly following more severe TBI (Yeates et al., 2010). Contrary to expectations, results from this study revealed that higher SES was a statistically significant predictor of parental reporting of PCS. This may reflect methodological differences in SES indicators used. Studies which adopt composite measures of SES value which incorporate parental education level, occupation, and family income, have shown that SES consistently predicts outcome (particularly in moderate and severe TBI populations), whilst those examining one component of SES such as our study, show less consistent findings (Stavinoha et al., 2012). An alternative explanation may be that the influence of SES on outcome is not well-defined in the mild compared with more severe TBIs. In fact, one previous mTBI study has revealed a similar relationship between higher SES and greater PCS (Yeates et al., 2012).

With regard to other socio-cultural influences, parents from Anglo-Saxon backgrounds reported more PCS in their children. Whereas the research in adults has suggested that ethnic minorities have worse functional outcomes, the evidence in children is less substantiated (Saltapidas & Ponsford, 2007; Stavinoha et al., 2012). There is some evidence that socio-cultural factors may moderate the effects of pediatric TBI on parents and families, but more research on this is needed to better inform primary care clinicians (Yeates et al., 2002). Given pediatric studies often rely on parental report of outcomes, it is also important for researchers to consider the potential influence of cultural factors on parents' willingness or openness to report the effect of pediatric TBI or attribution of symptoms to the injury.

An alternative explanation is that observed influence of SES and cultural factors may reflect variations in awareness of mTBI and/or symptoms attributed to mTBI. More educated parents may be more aware of public information/ media around mTBI or "concussion," and as a result may be more either more sensitive to symptoms or more likely to misattribute/over-interpret symptoms in the context of a suspected mTBI.

Limitations of this study must be acknowledged and should be considered when reviewing these results. PCS measures were administered solely to parents of children. This may have resulted in reporting bias whereby more observable or externalizing symptoms were over-endorsed and internalizing symptoms were missed (Ayr, Yeates, Taylor, & Browne, 2009; Gioia et al., 2009; Hajek et al., 2011). Whereas inter-rater agreement between children and their parents on symptom report has been moderate, it can be quite variable (Gioia et al., 2009; Sady, Vaughan, & Gioia, 2014). Nevertheless, this highlights the significant challenges of PCS assessment in younger children and the lack of scales valid for use in this population (Gioia et al., 2009). It should also be noted that pre-morbid ratings of child (i.e., behavior, sleep) and family (i.e., stress) factors were collected retrospectively. As such, parents' perception of their child's pre-morbid characteristics may have been influenced by trauma (Brooks et al., 2014).

The potential for sampling bias must also be considered. Given the majority of children's injuries were very mild, it could be argued the final sample was composed of parents who were more sensitive or cautious, as they made the decision to admit their child to ED. Furthermore, parents with this tendency may also be more likely to agree to participate in research. Additionally, there were several pre-morbid variables which have been shown to be associated with persistent PCS that were not measured in this study. These include pre-morbid somatization (Grubenhoff et al., 2016; Nelson et al., 2016), post-injury child coping (Woodrome et al., 2011), post-injury symptom exaggeration (Araujo et al., 2014; Kirkwood, Peterson, Connery, Baker, & Grubenhoff, 2014), and post-injury family litigation (Connery, Peterson, Baker, & Kirkwood, 2016). Finally, given our groups differed on age it proved difficult to tease out the effects of age. Future studies need larger samples sizes to allow for matching methods such as propensity scores (Guo & Fraser, 2015).

In conclusion, recovery from mTBI depends on a complex interplay of injury-related factors, pre-existing child factors, and the environmental context in which the child recovers from injury. Prolonged symptoms following mTBI can be frustrating for children and challenging for parents, and given most children are discharged home with little or no follow-up, greater emphasis needs to be placed on identifying these "at risk" children upon presentation to primary care facilities. Such identification would allow for early interventions such as provision of education, and outpatient follow up where required, both of which have been shown to be effective in reducing persistent PCS (Winkler & Taylor, 2015).

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