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Research Article

The association between symptom burden and processing speed and executive functioning at 4 and 12 weeks following pediatric concussion

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Abstract

Objectives: Symptoms and cognition are both utilized as indicators of recovery following pediatric concussion, yet their interrelationship is not well understood. This study aimed to investigate: 1) the association of post-concussion symptom burden and cognitive outcomes (processing speed and executive functioning [EF]) at 4 and 12 weeks after pediatric concussion, and 2) the moderating effect of sex on this association. **Methods:** This prospective, multicenter cohort study included participants aged 5.00–17.99 years with acute concussion presenting to four Emergency Departments of the Pediatric Emergency Research Canada network. Five processing speed and EF tasks and the Post-Concussion Symptom Inventory (PCSI; symptom burden, defined as the difference between post-injury and retrospective [pre-injury] scores) were administered at 4 and 12 weeks post-concussion. Generalized least squares models were conducted with task performances as dependent variables and PCSI and PCSI*sex interaction as the main predictors, with important pre-injury demographic and injury characteristics as covariates. **Results:** 311 children (65.0% males; median age = 11.92 [IQR = 9.14–14.21 years]) were included in the analysis. After adjusting for covariates, higher symptom burden was associated with lower Backward Digit Span ($\chi^2 = 9.85$, $p = .043$) and Verbal Fluency scores ($\chi^2 = 10.48$, $p = .033$) across time points; these associations were not moderated by sex, $ps \geq .20$. Symptom burden was not associated with performance on the Coding, Continuous Performance Test, and Color-Word Interference scores, $ps \geq .17$. **Conclusions:** Higher symptom burden is associated with lower working memory and cognitive flexibility following pediatric concussion, yet these associations were not moderated by sex. Findings may inform concussion management by emphasizing the importance of multifaceted assessments of EF.

Keywords: Mild traumatic brain injury; cognitive functioning; neuropsychological assessment; post-concussion syndrome; youth; cognitive testing

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Introduction

Concussion, a mild subtype of traumatic brain injury (McCrory, Feddermann-Demont, et al., 2017; McCrory, Meeuwisse, et al., 2017; Silverberg et al., 2023), is common in children and adolescents. Although most children and adolescents recover within 2 weeks of injury (Ledoux et al., 2019), one-third will experience persisting symptoms after concussion lasting more than 1 month (Chadwick et al., 2022; Zemek et al., 2016). These symptoms can include ongoing physical and somatic complaints, mood disturbance, behavioral changes, and cognitive symptoms, which may be associated with impaired academic performance, school absenteeism, depressed

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mood, and lower quality of life (Howell et al., 2019; Ledoux et al., 2022; Novak et al., 2016; Russell et al., 2017, 2019). Cognitive symptoms such as difficulty concentrating and remembering, feeling like one is in a fog or slowed down, and confusion are often self-reported post-concussion (McCrory et al., 2013; Reed et al., 2021). These subjective experiences provide valuable insights into the individual's perception of their cognitive functioning and challenges. However, self-reporting alone may not provide a comprehensive understanding of the extent of cognitive changes after concussion. As such, objective evaluation of cognition through neuropsychological testing is often utilized as an indicator of recovery following pediatric concussion along with symptom ratings (Haider et al., 2018). The relation between self-reported symptoms and objective cognitive functioning is not well understood.

Processing speed refers to the ability to process information and complete cognitive tasks quickly and efficiently. While some studies have indicated alterations in processing speed in the days following concussion (Kontos et al., 2014) that tend to resolve by a few months post-injury (Hou et al., 2023; Robertson-Benta et al., 2023; Rohling et al., 2011), other studies have reported null findings across injury phases (Alsalaheen et al., 2021; Redlinger et al., 2022; Sicard et al., 2022; Sicard, Hergert, et al., 2021). Processing speed is closely linked to executive functioning (EF), which encompasses top-down cognitive processes responsible for planning, organizing, initiating, monitoring, and controlling goal-directed behavior. EF relies on efficient processing speed to analyze and integrate information in a timely manner. Accumulating evidence in pediatric and adult samples has suggested that EF is particularly susceptible to concussion, with lower performance on EF tasks in individuals within weeks to months of a concussion relative to individuals without concussion (Baillargeon et al., 2012; Chadwick et al., 2021; Halterman et al., 2006; Howell et al., 2013; Lax et al., 2015; Loher et al., 2014; Mayr et al., 2014; Moore et al., 2014, 2015, 2016, 2017, 2019; Ozen et al., 2013; Ozturk et al., 2021; Robertson-Benta et al., 2023; Sicard, Caron, et al., 2021; Sicard et al., 2018, 2019, 2020; Sicard, Harrison, et al., 2021). A recent meta-analysis indicated that athletes with a history of concussion (at least 3 months from their last concussion) perform more poorly on EF tasks when compared to controls with no history of concussion, although no such differences were observed for other cognitive domains (Redlinger et al., 2022).

To date, a limited number of studies have addressed the association between post-concussion symptom burden and cognitive functioning, especially in pediatric concussions. In children and adolescents with a concussion, neuropsychological outcomes were not solely attributable to premorbid factors but instead associated with a combination of premorbid factors and injury-related variables, including symptoms (Babcock et al., 2013; Beauchamp et al., 2018). More recently, symptom burden combined with an increased clinical risk score for persisting symptoms after concussion (Zemek et al., 2016), was found to be associated with poorer processing speed and attention within 11 days of injury, but not at 4 months (Sicard, Hergert, et al., 2021). A follow-up study showed significant group differences between symptomatic concussed adolescents and non-injured comparisons within 11 days of injury, but not at 4 months post-concussion, on an EF composite score, and no differences were observed for working memory at either time point (Robertson-Benta et al., 2023). Another study showed that symptom burden correlated with verbal learning recognition, verbal fluency, and mathematical fluency in adolescents, but not in children, within a month of their concussion (Jones et al., 2023). In youth hockey players approximately 6 days post-concussion, greater missed errors on a nonverbal working memory task were associated with greater symptom burden (Green et al., 2018). In adults, university athletes with persisting symptoms after concussion showed lower cognitive performance on a computerized working memory task relative to their asymptomatic and healthy counterparts 3 weeks to 2 months post-injury (Sicard, Harrison, et al., 2021). Moreover, in university athletes with post-concussion symptoms, headache was a significant predictor of worse attention/EF composite scores within 2 weeks of their injury (Guty et al., 2021) and attention/processing speed impairment from 6 months to 3 years post-concussion (Guty & Arnett, 2018). However, another study of children and adolescents on average 34 months post-concussion did not observe correlations between headache symptoms and EF measures included in the CNS Vital Signs battery (i.e., reaction time, complex attention, cognitive flexibility; Kwan et al., 2020). Similarly, processing speed and working memory did not significantly predict group membership (children with persisting symptoms after concussion vs. comparison) when entered into a single model (Anzalone et al., 2022).

While these studies made important contributions to the concussion literature, their findings are limited by modest sample size (Anzalone et al., 2022; Green et al., 2018; Guty et al., 2021; Jones et al., 2023; Kwan et al., 2020; Sicard, Harrison, et al., 2021; Sicard, Hergert, et al., 2021), inclusion of transitional age youth or adult patients only (Guty et al., 2021; Guty & Arnett, 2018; Robertson-Benta et al., 2023; Sicard, Hergert, et al., 2021), inclusion of only sports-related concussions (Green et al., 2018; Guty et al., 2021; Guty & Arnett, 2018; Sicard, Harrison, et al., 2021), cross-sectional study designs (Anzalone et al., 2022; Guty et al., 2021; Guty & Arnett, 2018; Jones et al., 2023; Kwan et al., 2020; Robertson-Benta et al., 2023; Sicard, Harrison, et al., 2021), omission of specific processing speed measures (Jones et al., 2023; Sicard, Harrison, et al., 2021; Sicard, Hergert, et al., 2021), and restriction to a single EF construct (Green et al., 2018; Sicard, Harrison, et al., 2021; Sicard, Hergert, et al., 2021). Due to the limitations of existing studies, a critical knowledge gap remains regarding the association between post-concussion symptom burden and EF, following pediatric concussion.

Furthermore, these studies have not investigated the effect of sex on the interaction between symptoms and cognition. Previous research has suggested an elevated symptom burden, increased prevalence of persisting symptoms after concussion, and possibly lower cognitive functioning post-concussion in females relative to males (Alsalaheen et al., 2021; Broshek et al., 2005; Brown et al., 2015; Covassin et al., 2012, 2018; Hannah et al., 2021; Howell et al., 2018; Koerte et al., 2020; Ledoux et al., 2019; Merritt et al., 2019; Mollayeva et al., 2019; Sicard et al., 2018; Yeates et al., 2022; Zemek et al., 2016). Moreover, sex differences are observed in brain development in terms of myelination of axons, regional gray matter volumes, cortical thickness, and brain functioning (DeCasien et al., 2022; Giedd & Rapoport, 2010; Gur & Gur, 2016; Silk & Wood, 2011). Studies exploring the potential influence of sex on concussion outcomes and the relationship between symptoms and cognitive functioning are needed (Merritt et al., 2019).

The primary objective of this study was to investigate the association between symptom burden and cognition (processing speed and EF) at 4 and 12 weeks following a pediatric concussion. Higher symptom burden was hypothesized to be associated with lower processing speed and EF performance across time points.

The secondary objective was to explore the moderating effect of sex on this association.

Methods

This study was a planned secondary analysis of data from Predicting Persistent Postconcussive Problems in Pediatrics, a prospective multicenter cohort study (hereafter referred to as the 5P study). The protocol and parent study have been previously published (Zemek et al., 2013, 2016). Participants in the parent study were enrolled from the emergency departments (EDs) of nine Canadian pediatric hospitals within the Pediatric Emergency Research Canada Network (Bialy et al., 2018). Families that qualified for the study were asked to provide written consent in all cases and patient assent where applicable. Participants from four of the participating hospitals were offered participation in a neuropsychological follow-up at 4- and 12-week post-injury. The research was completed following Helsinki Declaration and included the research ethics committee at each participating institution (Alberta Children's Hospital, Children's Hospital of Eastern Ontario, Ste-Justine Hospital, Toronto Sick Kids Hospital) approved the neuropsychological component of the study.

Study setting

Recruitment

The neuropsychological study used the same inclusion and exclusion criteria as the 5P protocol. Details of patient recruitment are outlined in the published 5P protocol (Zemek et al., 2013). Briefly, children aged 5 to 18 years presenting to the ED within 48 hours of a head injury and who met concussion diagnostic criteria according to the Zurich Consensus Statement on Concussion in Sport (McCrory et al., 2013) were potentially eligible for the study. Exclusion criteria included 1) Glasgow Coma Scale ≤13, 2) absence of trauma as primary event, 3) any trauma-related abnormality on neuroimaging, 4) multisystem injury requiring hospitalization, 5) neurosurgical intervention, intubation, or intensive care unit admission, 6) intoxication at time of ED presentation, 7) severe communication difficulties (history of attention deficit hyperactivity disorder or learning disability was not exclusionary), 8) previous enrollment, 9) language barrier, 10) inability to complete the follow-up visits.

With the help of research assistants, participants answered questionnaires in electronic survey format using Research Electronic Data Capture (REDcap; Harris et al., 2009, 2019) in their first language (English or French) using a portable tablet computer. In addition to questions about patient demographics, parents completed the Acute Concussion Evaluation (Gioia et al., 2008), a 22-item dichotomous-item validated tool to objectively help diagnose concussion (as indicated by the presence of at least one symptom). Data were further collected on injury characteristics, history (prior concussion, headache, and developmental or psychiatric disorder), and both retrospective pre-injury and post-injury acute symptoms (physical, emotional, cognitive, and sleep) using the Post-Concussion Symptom Inventory (PCSI; Sady et al., 2013).

Follow-ups

The participants who consented to the neuropsychological component returned to the testing centers at 4 weeks and 12 weeks post-concussion (see Figure 1 for study endpoints). Each visit took approximately 2.5 hours, during which a comprehensive battery of neuropsychological measures was administered in their first language (English or French). In addition to the neuropsychological test battery, participants completed the PCSI at 4 and 12 weeks. To be included in the present analyses, participants must have completed at least 85% of the neuropsychological outcome measures.

Outcome measures

Neuropsychological testing

A comprehensive battery of neuropsychological measures was administered to participants in this component of the study ($n = 311$). The battery included measures of intelligence, language, visual-spatial/motor functions, memory, processing speed, EF, and academic achievement (see Beauchamp et al., 2018 for a description of the neuropsychological test battery). The selection of the neuropsychological tests was grounded in the availability of standardized French and English versions across our study's age range, inclusion in the Common Data Elements (CDE) for concussion for cross-study comparisons and data sharing (Broglio et al., 2018), their utility for concussion assessment, and their capacity for a multifaceted assessment of higher order cognitive functioning. Selected measures for the present study include the Coding and Digit Span subtests of the Weschler Intelligence Scale for Children Fourth Edition (WISC-IV; Wechsler, 2014) or the Weschler Adult Intelligence Scale Fourth Edition (WAIS-IV; Wechsler, 2008), the Conners' Continuous Performance Test (CPT-II; Conners & Staff, 2000), and the Color-Word Interference Test and the Verbal Fluency subtests of the Delis-Kaplan Executive Functioning System (D-KEFS; Delis et al., 2001). The Medical Symptom Validity Test (MSVT) allowed for the assessment of performance validity and effort in a subset of participants at each visit (4 weeks $n = 72$; 12 weeks $n = 58$; Green, 2004). The MSVT was added to the neuropsychological test battery a year into the study, See Supplementary Material 1 for details. Specific outcome variables used in the current analysis are presented in Table 1. Psychometric characteristics for the neuropsychological measures are presented in Supplementary Material 2.

Post-concussion symptom inventory (PCSI)

The PCSI was used to measure symptom burden. The PCSI is a postconcussion symptom rating scale specifically adapted for children, adolescents, and their parents, with items that are developmentally appropriate and assist in differentiating concussed from non-concussed children and adolescents (Gioia et al., 2009; Sady et al., 2013). The PCSI has three self-rated symptom scales for children aged to 7 years (PCSI-SR5; 13 items on a three-point scale), 8 to 12 years (PCSI-SR8; 17 items on a three-point scale), and 13 to 18 years (PCSI-SR13; 20 items on a seven-point scale). The PCSI measures physical (e.g., visual problems, numbness or tingling, headache, balance problems, sensitivity to light or sound), cognitive (e.g., difficulty remembering, difficulty concentrating, feeling slowed down or thinking slowly, feeling mentally foggy), emotional (e.g., irritability, sadness, nervousness, feeling more emotional), and sleep-related symptoms (e.g., drowsiness, trouble falling asleep, sleeping more than usual).

Internal consistency was strong for the total PCSI symptom score for PCSI-SR8 and PCSI-SR13 in a concussed sample within 30 days of injury ($\alpha = .90$–$.94$; Sady et al., 2013). Test–retest reliability (3–14 days retest interval) coefficients for PCSI-SR8 and PCSI-SR13 in non-concussed children were moderate to strong (ICCs = .65–.89; Sady et al., 2013).

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Table 1. Neuropsychological outcomes measured at 4 and 12 weeks following concussion

Neuropsychological Task	Outcomes Measure	Cognitive Domain(s) Measured
WISC-IV/WAIS-IV Coding	Scaled score	Processing speed and visual-motor coordination
WAIS-IV/WISC-IV Digit Span backward condition	Scaled score	Working memory
Conner's CPT-II	Omission t-score	Sustained attention, vigilance, and response inhibition
D-KEFS Color-Word Interference Test	Inhibition versus Color Naming contrast scaled score	Response inhibition and selective attention
D-KEFS Verbal Fluency, letter fluency condition	Scaled score	Phonemic fluency and cognitive flexibility

Note: CPT-II = Continuous Performance Test II; D-KEFS = Delis-Kaplan Executive Function System; WAIS-IV = Wechsler's Adult Intelligence Test Fourth Edition; WISC-IV = Wechsler's Intelligence Scale for Children Fourth Edition.

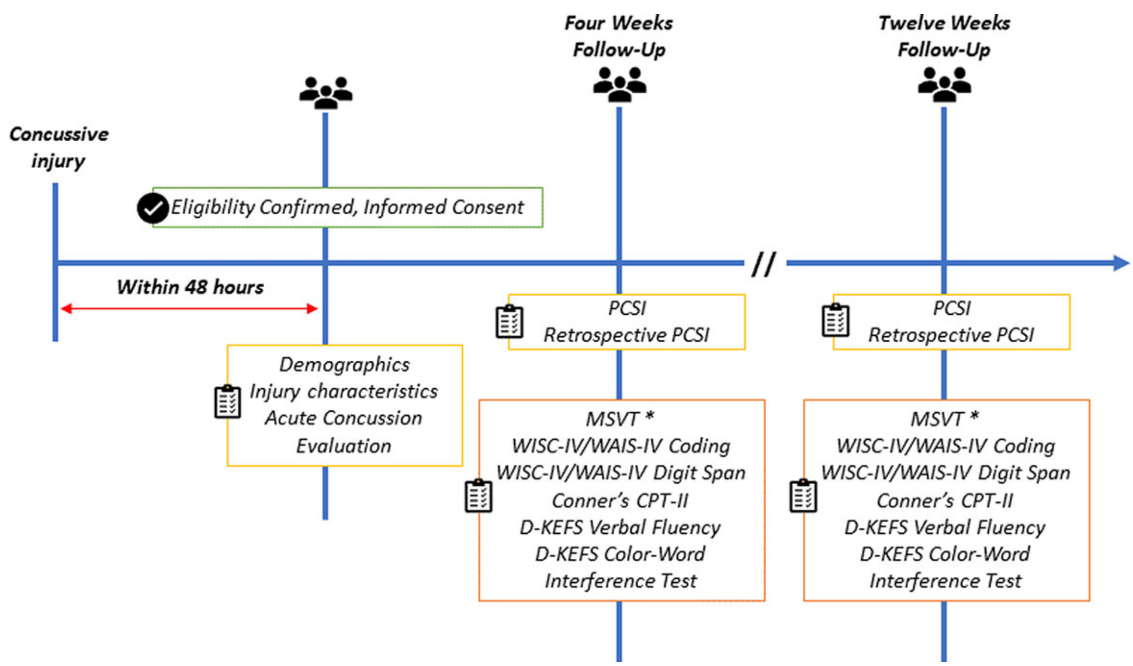

Figure 1. Study flow diagram. *Note*. CPT-II = Continuous Performance Test II; D-KEFS = Delis-Kaplan Executive Function System; MSVT = Medical Symptom Validity Test; PCSI = Post-Concussion Symptom Inventory children version; WAIS-IV = Wechsler Adult Intelligence Scale Fourth Edition; WISC-IV = Wechsler Intelligence Scale for Children Fourth Edition. * MSVT was completed by a subset of participants.

In the present study, the age-specific retrospective (pre-injury rating of symptoms) and current PCSI (yesterday and today's rating of symptoms) were administered at 4 and 12 weeks. Similar to previous studies (Gagnon et al., 2020; Ledoux et al., 2019; Lumba-Brown et al., 2020), symptom burden was defined as the absolute difference between current ratings and retrospective ratings (delta score).

For each item, both a current (post-injury) rating and a pre-injury rating are obtained, with the difference constituting the item "delta score." To ensure that participants of all age groups (5–7, 8–12, and 13–18) could be included in the same analyses, adjustments were made to account for the difference in scaling between age groups. We achieved this by uniformly rescaling all item mean delta scores to be consistent with the 7-point symptom rating scale used by the 13–18 years age group (i.e., rescaled to a range from 0 to 6). A higher symptom burden may indicate that an individual has more severe symptoms or a greater number of symptoms on post-injury assessments relative to pre-injury assessments.

Statistical analysis

Descriptive statistics were used to summarize the data. To examine the relationship between symptom burden and cognition, generalized least squares models (Harrell, 2015b) were fitted with each of the five neuropsychological outcomes specified as dependent variables in separate models. Data were structured in a "long" format such that information from both time points could be concurrently assessed within the same statistical model, and a "week" variable (i.e., 4 or 12) was included to differentiate between study time points. Independent variables retained in these models include symptom burden, continuous age, sex, and the interaction between symptom burden and sex. The interaction between symptom burden and week was tested but was not significant and was not retained in any model. The following covariates were added to the five models: week (4 vs. 12 weeks), maximum symptom duration from previous concussions (no previous concussion; 1–2 weeks, 3–4 weeks; 5–8 weeks; more than 8 weeks), history of migraine, learning disability, attention deficit (hyperactivity) disorder, other developmental disorders, anxiety, depression, and sleep disorder; and mechanism of injury (sports/recreation; non-sport/fall; motor vehicle collision; assault).

Given repeated measurements and the clustered nature of the study data (i.e., subjects recruited from multiple study sites), compound symmetry covariance structure was applied to "week," with site specified as a grouping factor to correct for within-subject

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correlation (i.e., participant nested within site). To allow for nonlinearity, restricted cubic splines (Harrell, 2015a) with four knots (placed at 5th, 35th, 65th, 95th quantiles) were specifically used for symptom burden; due to technical constraints, only three knots (placed at 10th, 50th, 90th quantiles) were applied for the models for inhibition and cognitive flexibility. A complete case analysis approach was conducted where observations with missing values on any covariate or outcome were excluded. After model fitting, multiple degrees-of-freedom Wald chi-square tests (inclusive of all linear and nonlinear components and any interaction terms) and associated *p*-values (two-sided) were obtained for all predictors to evaluate their association with each model outcome. A $p < .05$ was considered statistically significant. Where symptom burden was found to be associated with an EF measure, this relationship was further examined by graphical means (e.g., partial effect plots). Weighted contrasts based on sex and sex-specific contrasts were specified for 75th versus 25th quantiles, and for 90th versus 10th quantiles to provide estimates of effect size associated with symptom burden (high vs. low scores).

Sensitivity analyses were conducted to determine whether the main findings would significantly change if participants with invalid effort based on the MSVT (scores ≥85% on the Immediate Recall, Delayed Recall, and Consistency metrics; (Green, 2004) were removed from the analyses. Details are presented in Supplementary Material 1. Briefly, crude analyses (i.e., with symptom burden as the only independent variable and week as the only covariate due to degrees of freedom constraints) were conducted for the full sample ($N = 311$) and parallel sensitivity analyses were conducted using only those with MSVT data ($N = 95$).

All analyses were performed using *R* version 4.0.3 (R Core Team, 2022), and statistical modeling was conducted with functions from the *rms* package (Harrell, 2023).

Results

Participants

311 children (202 males, 109 females) with a median age of 11.92 years (interquartile range, 9.14–14.21) were enrolled in the neuropsychological component of the study. Of those, 172 completed both follow-up assessments, 115 completed only the 4-week assessment, and 24 completed only the 12-week assessment (see Figure 2).

Table 2 presents participants' demographic and injury characteristics. Most children did not have a history of concussion before the eligible injury (71.9%) and most concussions were sport- or recreation-related (63.7%).

Only 103 (33.1%) participants completed the MSVT at either time point. Demographic and injury characteristics stratified by those who completed the MSVT and those who did not are presented in Supplementary Table 1. Participants who completed the MSVT had a higher prevalence of history of anxiety (12.7%) than those who did not complete the MSVT (5.8%), $p = .03$.

Association of symptom burden and cognitive functioning

Descriptive values for outcome measures at the 4- and 12-week follow-ups are presented in Table 3. Full results (i.e., all five Wald chi-square and five covariate effect tables) are presented in Supplementary Material 2.

Higher symptom burden was significantly associated with lower scores on the Backward Digit Span, $\chi^2(\mathrm{df} = 4) = 9.85$, $p = .04$

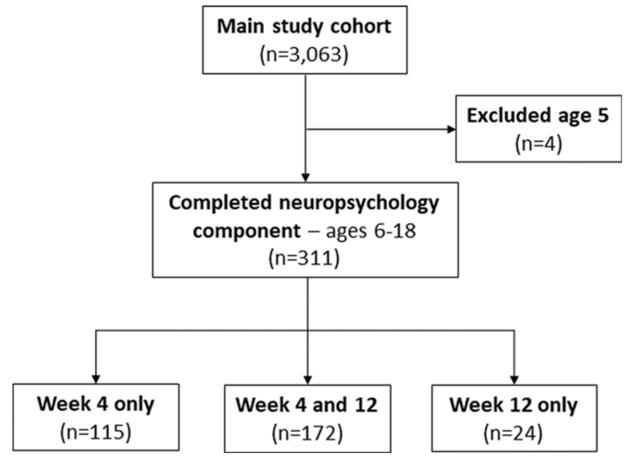

Figure 2. Flowchart of recruitment for the main study and those enrolled in the neuropsychological component in four of the study sites.

[75th vs. 25th quantiles: Estimate = −0.59 (95%CI = −1.15, −0.03); 90th vs. 10th quantiles: Estimate = −0.82 (95%CI = −1.48, −0.16)]. The interaction of symptom burden and sex was not significant, $ps \geq .32$, see Figure 3. Because sex was not significant, sex-specific contrasts are presented in Supplementary Material 2. Moreover, older age (nonlinear) and history of learning disability were associated with lower scores on Backward Digit Span, $ps \leq .02$.

Similarly, higher symptom burden was significantly associated with lower scores on Verbal Fluency, $\chi^2(\mathrm{df} = 4) = 10.48$, $p = .03$ [75th vs. 25th quantiles: Estimate = −0.29 (95%CI = −0.95, 0.36); 90th vs. 10th quantiles: Estimate = −0.57 (95%CI = −1.27, 0.14)]. The interaction of symptom burden and sex was not significant, $ps \geq .20$, see Figure 4. Because sex was not significant, sex-specific contrasts are presented in Supplementary Material 2. Moreover, week 4 (vs. 12) assessment and history of Learning Disability were associated with lower scores on Verbal Fluency, $ps \leq .01$.

Neither symptom burden nor the interaction of symptom burden and sex were significant predictors of scores on the Coding, CPT-II, and Color Word Interference tests, $ps \geq .17$. However, other covariates in these three models were significant. History of migraine, history of learning disability, and symptom duration from previous concussion(s) of 3−4 weeks, 5−8 weeks or >8 weeks were associated with lower scores on the Coding task, $ps \leq .05$. Female sex, week 12 (vs. 4) assessment, history of sleep disorder, and symptom duration from previous concussion(s) of <1 week or 1−2 week were associated with higher scores on the Coding task, $ps \leq .05$. Older age was associated with lower scores on the CPT-II, $ps < .001$, while history of learning disability was associated with higher scores on the CPT-II, $p = .005$. Finally, history of developmental disorders was associated with lower scores on the Color-Word Interference test, $p = .05$.

Sensitivity analyses Detailed results are presented in Supplementary Material 1. At 4 weeks, 68 (21.9%) participants had a valid performance on the MSVT, 3 (1.0%) had an invalid performance, and 240 (77.2%) had no MSVT scores. At 12 weeks, 53 (17.0%) participants had a valid performance, 5 (1.6%) had an invalid performance, and 253 (81.4%) had no MSVT scores. Importantly, scores on the five neuropsychological tasks did not differ between those with valid performance on the MSVT/no MSVT and those with invalid MSVT at both time points, $ps \geq .16$.

95 participants were included in the sensitivity analyses. For WISC-IV/WAIS-IV Backward Digit Span, the crude analysis of the

Table 2. Participant demographic information

Variable	*n*	Value
Sex, freq (%)	311	
Female		109 (35.0)
Male		202 (65.0)
Age, median [IQR]	311	11.92 [9.14, 14.21]
Time between head injury and triage (hours), median [IQR]	309	3.25 [1.65, 17.15]
Previous number of concussion(s), freq (%)	310	
0		223 (71.9)
1		59 (19.0)
2		18 (5.8)
3		7 (2.3)
4		3 (1.0)
Maximum symptom duration from previous concussion(s) (weeks), freq (%)	308	
Never had a concussion		223 (72.4)
<1 week		33 (10.7)
1–2 weeks		23 (7.5)
3–4 weeks		12 (3.9)
5–8 weeks		7 (2.3)
>8 weeks		10 (3.2)
History of migraine, freq (%)	309	39 (12.6)
History of learning disability, freq (%)	310	29 (9.4)
History of attention deficit disorder, freq (%)	310	24 (7.7)
History of developmental disorder, freq (%)	308	11 (3.6)
History of anxiety, freq (%)	310	25 (8.1)
History of depression, freq (%)	311	9 (2.9)
History of sleep disorder, freq (%)	311	10 (3.2)
Mechanism of injury, freq (%)	311	
Sports/Recreation		198 (63.7)
Non-sport/Fall		102 (32.8)
Motor vehicle collision		7 (2.3)
Assault		4 (1.3)
Loss of consciousness, freq (%)	311	
No		244 (78.5)
Yes		33 (10.6)
Unknown		34 (10.9)
Duration of loss consciousness, median [IQR]	31	0.50 [0.15, 1.00]
Seizure following injury, freq (%)	311	8 (2.6)
Symptom burden at initial ED visit, median [IQR]	302	1.76 [1.06, 2.47]
Academic achievement prior to concussion, freq (%)	308	
Straight A student		83 (26.9)
A & B grades		122 (39.6)
Straight B student		55 (17.9)
B & C grades		39 (12.7)
Below C grades		9 (2.9)

Note: ED = Emergency Department. Symptom burden is operationalized as the average item delta score (post-injury minus retrospective pre-injury, rescaled 0–6) on the Post-Concussion Symptom Inventory self-report, age-appropriate version.

Table 3. Outcome variables at 4 weeks and 12 weeks post-concussion

Measures	4 weeks				12 weeks			
	N	Median [IQR]	Min	Max	N	Median [IQR]	Min	Max
Symptom burden	284	0.20 [0.00, 0.88]	0.00	3.88	273	0.05 [0.00, 0.53]	0.00	3.88
WISC-IV/WAIS-IV Coding	287	10.00 [8.00, 11.00]	1.00	17.00	196	10.00 [8.00, 13.00]	1.00	18.00
WISC-IV/WAIS-IV Backward Digit Span	287	10.00 [9.00, 12.00]	3.00	17.00	196	10.50 [8.75, 12.00]	3.00	18.00
Conner's CPT-II	271	46.96 [43.76, 53.02]	40.06	161.44	183	46.96 [44.04, 52.82]	40.06	130.41
D-KEFS Color-Word Interference Test	236	10.00 [9.00, 11.00]	3.00	17.00	163	10.00 [9.00, 12.00]	4.00	17.00
D-KEFS Verbal Fluency	245	9.00 [7.00, 12.00]	2.00	19.00	172	11.00 [8.00, 12.00]	2.00	19.00

Note: CPT-II = Continuous Performance Test II; D-KEFS = Delis-Kaplan Executive Function System; WAIS-IV = Wechsler Adult Intelligence Scale Fourth Edition; WISC-IV = Wechsler Intelligence Scale for Children Fourth Edition. Symptom burden is operationalized as the average item delta score (post-injury minus retrospective pre-injury, rescaled 0–6) on the Post-Concussion Symptom Inventory self-report, age-appropriate version.

full sample revealed symptom burden as a significant predictor ($p = .02$), while in the sensitivity analysis, only week of assessment was significant ($p = .003$). For the D-KEFS Color Word Interference Test, the sensitivity analysis revealed that symptom burden was a significant predictor ($p = 0.04$), while no predictors were significant in the crude analysis. For D-KEFS Verbal Fluency, symptom burden and week of assessment were significant ($ps \leq .03$) in the crude analysis, while the sensitivity analysis showed only week as a significant predictor ($p < .001$). For both the WISC-IV/WAIS-IV Coding and Conner's CPT-II Omission, the results were similar between crude and sensitivity analyses.

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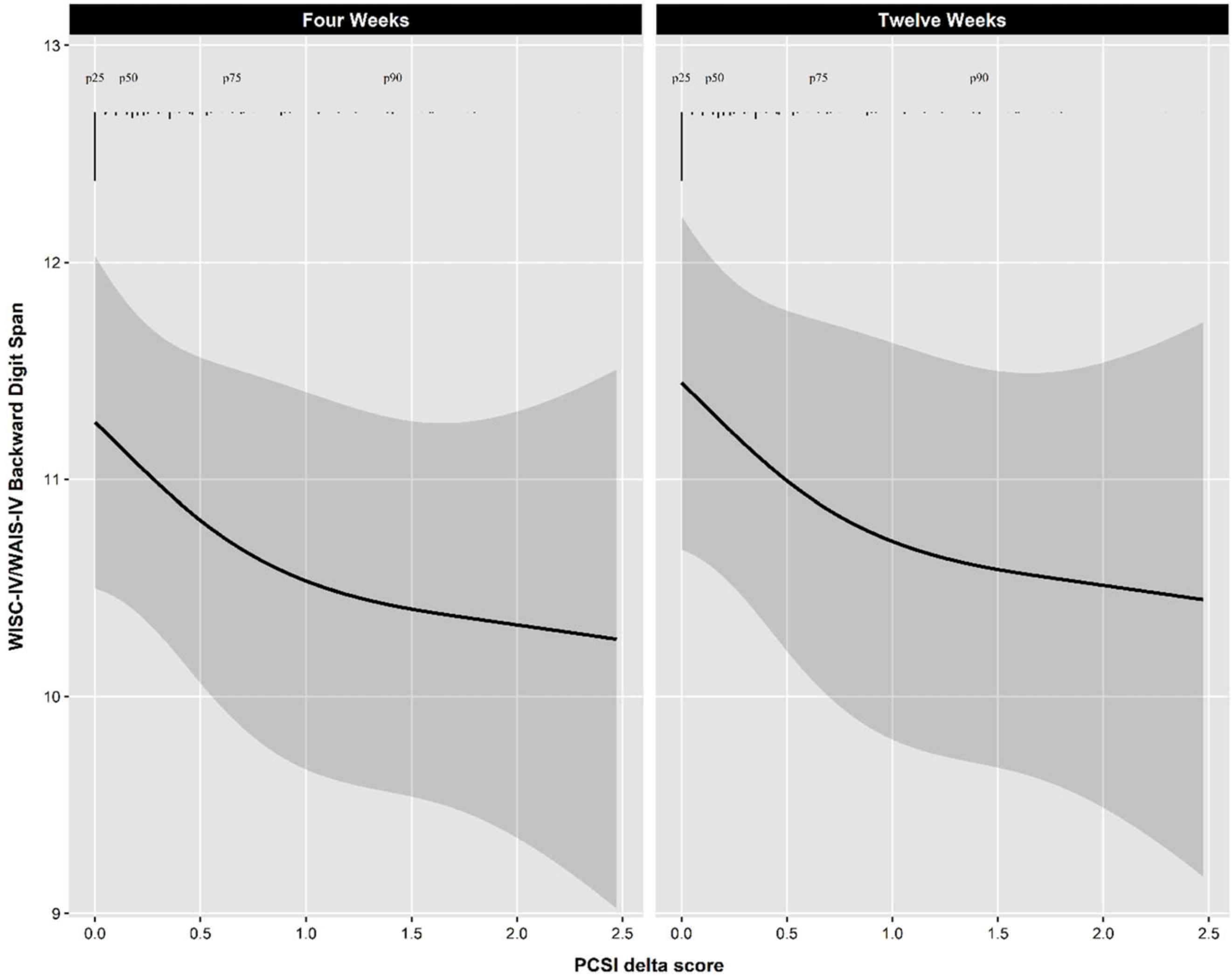

Figure 3. Graphical representation of the negative association between the symptom burden measured by the Post-Concussion Symptom Inventory (PCSI) the t-score on the Backward Digit Span subtest of the Wechsler's Intelligence Scale for Children Fourth Edition/Wechsler's Adult Intelligence Scale Fourth Edition (WISC-IV/WAIS-IV) at 4 weeks and 12 weeks following pediatric concussion. *Note*. Adjusted to: age = 11.92, maximum symptom duration from previous concussion(s) (weeks) = never had concussion, history of learning disabilities = no, history of attention deficit disorder = no, history of depression = no, history of anxiety = no, history of developmental disorders = no, history of sleep disorder = no, personal history of migraine = no, mechanism of Injury = sports/recreation.

Discussion

In this large prospective cohort pediatric concussion study, greater symptom burden was associated with lower scores on the WISC-IV/WAIS-IV Backward Digit Span and D-KEFS Verbal Fluency neuropsychological tests at 4- and 12-week post-concussion, after adjusting for several characteristics known to be associated with symptom reporting and cognitive functioning. These associations remained consistent over time and were not moderated by sex. Symptom burden was not associated with performance on the WISC-IV/WAIS-IV Coding, CPT-II, and D-KEFS Color-Word Interference tasks.

The WISC-IV/WAIS-IV Backward Digit Span is a measure of working memory, which refers to the ability to temporarily store and manipulate information that is no longer perceptually present (Baddeley & Hitch, 1994). The D-KEFS Verbal Fluency is considered a measure of cognitive flexibility, which involves the ability to switch between mental sets, tasks, or strategies, and our ability to adapt to the constantly changing environment (Diamond, 2013; Miyake & Friedman, 2012). Previous studies have demonstrated that performance on both the Digit Span Backwards and Verbal Fluency tests are affected by pediatric concussion. Specifically, children and adolescents with a concussion scored lower on the Verbal Fluency subtest and the Digit Span Backwards condition in the subacute (i.e., within 11 days post-injury) and early chronic phase (i.e., approximately 4 months) of injury when compared to a typically developing comparison group (Sicard et al., 2022). However, in the later study, group comparisons were not stratified based on post-concussion symptoms, and the association between symptom burden and cognitive function was not investigated. While the cognitive differences between concussion and comparison groups are subtle, exploring whether these differences are associated with symptom burden can contribute to a more comprehensive understanding of pediatric concussion and inform approaches to management and intervention.

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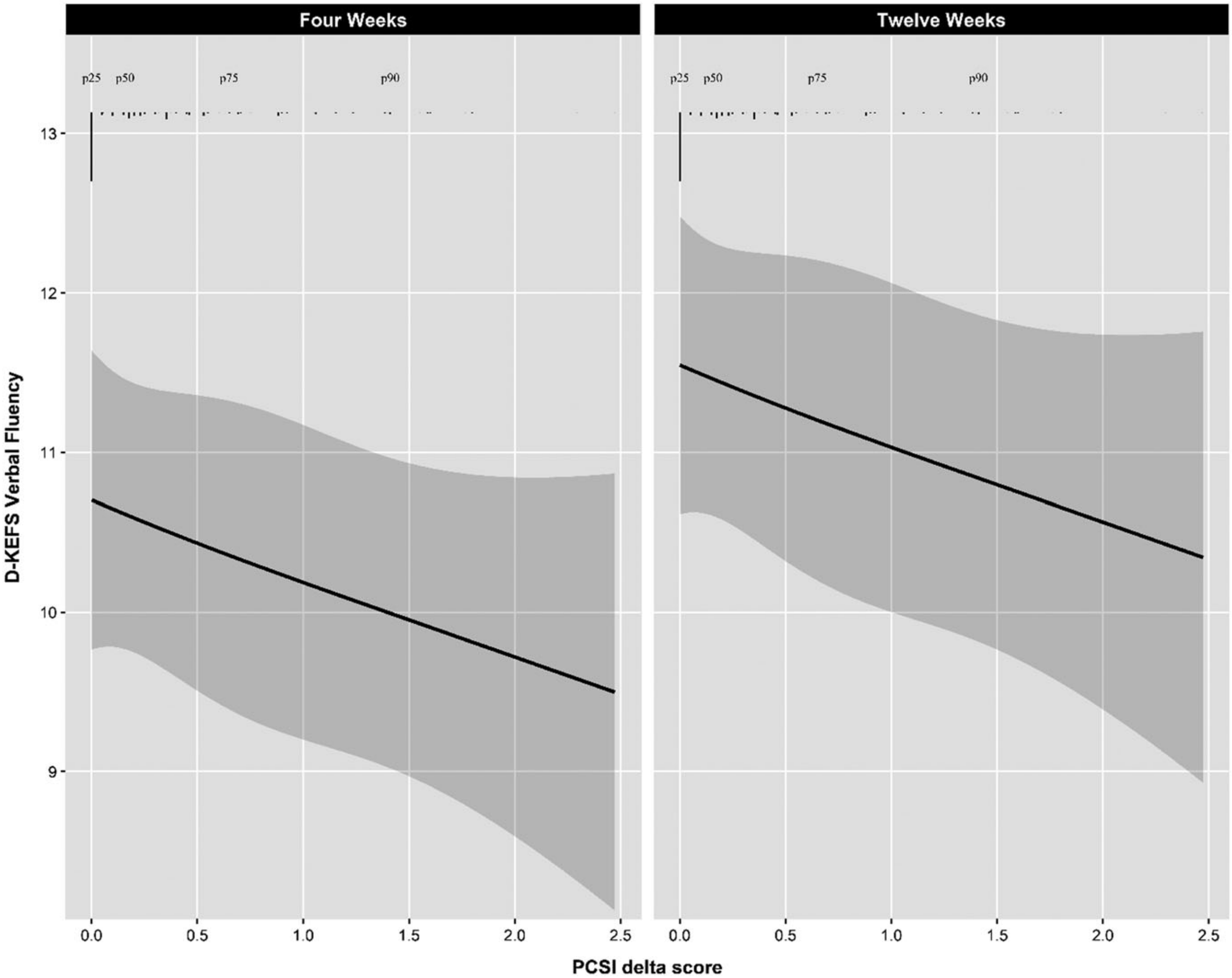

Figure 4. Graphical representation of the negative association between the symptom burden measured by the Post-Concussion Symptom Inventory (PCSI) and the scaled score on the Verbal Letter Fluency subtest of the Delis-Kaplan Executive Function System battery (D-KEFS) at 4 weeks and 12 weeks following pediatric concussion. *Note*. Adjusted to: age = 11.92, maximum symptom duration from previous concussion(s) (weeks) = never had concussion, history of learning disabilities = no, history of attention deficit disorder = no, history of depression = no, history of anxiety = no, history of developmental disorders = no, history of sleep disorder = no, personal history of migraine = no, mechanism of Injury = sports/recreation.

Previous studies found that greater symptom burden was associated with lower cognitive performance on a computerized nonverbal working memory task on average 6 days following pediatric concussion (Green et al., 2018), on a computerized task assessing processing speed and attention within 11 days post-injury (Sicard, Hergert, et al., 2021), and on paper-and-pencil tasks of verbal learning, verbal fluency, and mathematical fluency within a month post-injury (Jones et al., 2023). While the present study employed paper-and-pencil neuropsychological tests measuring different constructs, used delta scores rather than post-concussion scores alone, and examined time points further removed from the concussive event, our findings align with these previous studies in finding significant associations between symptom burden and EF measures.

In the current study, we opted to utilize symptom burden as the independent variable in our models and cognitive test performance as the dependent variable, aligning with the approach employed in previous research. By doing so, we aimed to maintain consistency and facilitate comparisons with existing research in pediatric concussion. However, the associations observed in the current study do not imply causation and further studies are required to fully understand the relationship between symptoms and cognitive outcomes after a pediatric concussion. The associations may be bidirectional, implying a reciprocal relationship between the two types of outcomes. On one hand, symptoms may have a detrimental impact on cognitive performance. The presence of physical discomfort, headaches and pain, or emotional distress associated with the symptoms can serve as distractions, making it more challenging to concentrate, remember information, or engage in complex cognitive tasks. Moreover, symptoms such as sleep disturbances and mood changes can directly affect cognitive efficiency. On the other hand, lower EF can contribute to the experience of symptoms. Difficulties in working memory and cognitive flexibility can impede the ability to effectively regulate cognitive and behavioral processes, potentially leading to the emergence or exacerbation of symptoms commonly associated

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with concussion, such as headaches, fatigue, difficulties concentrating/remembering, and mood changes. Thus, cognitive difficulties and symptom burden may reinforce each other in a feedback loop, potentially leading to a cycle of worsening symptoms and declining EF if not effectively managed. By recognizing that lower cognitive functioning can contribute to symptom burden, and vice versa, healthcare providers and researchers can better address the complex interplay between symptoms and cognitive performance. Future studies using cross-lagged panel designs can help investigate the direction of causality between cognitive functioning and symptomatology, shedding light on potential causal relationships and providing valuable insights for targeted interventions.

Novel to this study was the exploration of the effect of sex on the association of symptoms and cognitive functioning following pediatric concussion. The significant associations between symptom burden and EF measures observed were not moderated by sex. This finding challenges previous observations that males and females may experience different symptom burden or cognitive outcomes following concussion (Alsalaheen et al., 2021; Broshek et al., 2005; Brown et al., 2015; Covassin et al., 2012, 2018; Hannah et al., 2021; Howell et al., 2018; Koerte et al., 2020; Merritt et al., 2019; Mollayeva et al., 2019; Sicard et al., 2018; Yeates et al., 2022; Zemek et al., 2016). The present null findings could indicate that a combination of various factors, including but not limited to symptom burden, may interact, and associate with cognitive outcomes following concussion. Including factors such as age, history of psychological and neurodevelopmental comorbidities, and migraines might have reduced the influence of sex on the association between symptom burden and cognitive functioning in the present study. While including these factors in the model can reduce the influence of sex on the association between symptom burden and cognitive functioning, it does not necessarily mean that sex is not a relevant factor. Given the limited available data, more research is needed to understand how biological sex, as well as gender identity, and other personal characteristics, may moderate the interaction between symptoms and EF following pediatric concussion.

The present analysis is not only novel, but also builds upon our previously published research, which found that 10.3% of children in the current sample exhibited cognitive impairments (i.e., 2 or more subtests on a battery of 10 tasks having a score of 1.5 SD below the mean) at 4 weeks, and 4.5% by 12 weeks (Beauchamp et al., 2018). The observed association between symptoms and EF has important clinical implications, suggesting that children who experience symptoms may also have difficulties with working memory and cognitive flexibility. Intervention strategies aiming at simultaneously decreasing symptoms and improving cognitive functioning, such as active rehabilitation and psychosocial intervention, may help promote recovery and improve the ability to return to school, to learning, and sports. In cases where children are athletes, the association between symptom burden and EF may have implications for return-to-play decisions, as alterations of EF may increase the risk of re-injury (Bertozzi et al., 2023; McPherson et al., 2019; Wilke & Groneberg, 2022). Overall, the association between symptoms and cognitive functioning highlights the importance of considering cognitive outcomes, even if subtle, in the management of concussion, and emphasizes the need for multidisciplinary approaches to promote optimal recovery and functional outcomes.

The present study is characterized by numerous strengths, including the longitudinal assessment of symptom burden and cognition, multifaceted assessment of EF (i.e., multiple domains), inclusion of primary school-age children and non-sport-related concussions, and relatively large sample size. Methodological limitations should also be acknowledged. First, participants were recruited from an ED setting, so the findings may not generalize to those seeking care outside of the ED (e.g., specialty care clinic or sports medicine clinic), those not seeking medical care, or those with delayed symptom presentation (48 to 72 hours post-injury). Second, the lack of pre-injury data and the absence of a comparison group does not allow us to definitively attribute symptoms and lower cognitive performance to the concussion. The absence of true pre-injury symptom ratings may be seen as a limitation. The retrospective nature of symptom reporting introduces the possibility of "good old day bias," wherein participants might inadvertently recall their pre-injury symptoms as less severe than their actual experiences, potentially influencing the study's outcomes. However, a large prospective study indicated that children and adolescents recall their retrospective pre-injury symptom ratings with good-to-perfect stability over the first 3 months following their concussion (Teel et al., 2019).

Third, the use of delta scores, though common, might introduce technical constraints and limitations that warrant acknowledgment. Delta scores may not precisely capture the true magnitude of change, particularly in our specific context where rescaling the delta score was necessary, thereby adding a layer of complexity to interpretation. Nevertheless, the approach used ensures comparable scoring of symptom burden across different age groups and allows for comparison with previous studies (Gagnon et al., 2020; Ledoux et al., 2021; Lumba-Brown et al., 2020). However, prior research suggests that employing standardized change algorithms, such as reliable change indices, is more suitable than simple change scores for assessing the prevalence of persisting symptoms after concussion (Mayer et al., 2020). As such, future investigations should validate reliable change indices for the PCSI across age groups and injury phases, akin to the approach applied to another frequently used symptom scale in pediatric concussion research (O'Brien et al., 2021). Fourth, performance validity during was not assessed for all participants in this study, as validity testing was added to the assessment battery after the first year of enrollment. Nevertheless, the sensitivity analysis suggests that the outcomes are unlikely to be significantly influenced by validity considerations. Future studies should incorporate measures of test and symptom validity in their neuropsychological battery, similar to a recently published paper that investigated IQ after pediatric concussion (Ware et al., 2023). Fifth, whether specific symptoms or symptom subtypes were associated with lower cognitive functioning was not investigated, although previous adult studies found an association between headaches and cognitive functioning within 1 month (on average 6 days) and longer (range = 6–36 months) post-concussion. Herein, we anticipated a significant portion of our participants would have already experienced symptom resolution by the time of assessment, as the proportion of children identified with persisting symptoms after concussion was 35.1% in a recent meta-analysis (Chadwick et al., 2022). The limited number of individuals presenting with specific symptoms at the 4-week and 12-week time points combined with the heterogeneous nature of post-concussion symptoms would not have been sufficient to conduct a comprehensive analysis of the association between these symptoms and cognitive functioning. By assessing overall symptom burden, we captured a broader spectrum of symptoms and their collective association with cognitive functioning. Finally, the present dataset does not allow for causality assessment, for

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which alternative analytic approaches would be required, such as cross-lagged panel models or structural equation modeling, which are not feasible with our dataset. Nevertheless, our analytical approach leveraged the longitudinal nature of the data by treating symptom burden as a time-varying covariate. This allowed us to examine how symptoms are associated with changes in cognition, providing insights into the dynamics of the relationship over time.

Conclusions

The current study shows modest negative associations of symptom burden with both working memory and cognitive flexibility several weeks following a pediatric concussion. More research on cognition and persisting symptoms after concussion is warranted to provide an improved standard of care, targeted management strategies, and optimize recovery and functional outcomes, as suggested by the recent systematic review of the Concussion in Sports Group (Yeates et al., 2023).

Supplementary material. The supplementary material for this article can be found at https://doi.org/10.1017/S1355617724000043.

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Competing interests. VS received royalties for the sales of a concussion book (Commotions Cérébrales) by Flammarion Québec.

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BB receives royalties for the sales of three pediatric neuropsychological measures (ChAMP, MEMRY, and MVP) and royalties for the sale of a textbook (Pediatric Forensic Neuropsychology). He has a private practice where he provides assessments for people with concussion, he is a paid consultant with the NHL Concussion program, and he has received grant funding to study concussion.

MB receives royalties for the sales of a textbook (Pediatric Neuropsychology). She receives grants and philanthropic funding to study pediatric concussion. She has received travel support and honorarium for presentations to multiple organizations.

MK received grants and philanthropic funding to study pediatric concussion. She has received travel support and honorarium for presentations to multiple organizations. She has provided assessment for children, youth, and adults with concussion in a private practice setting and as a medical legal assessor. MK is currently a contractor at FIREFLY, a Northwestern Ontario FASD Diagnostic Clinic and Autism Diagnostic Hub, and at Mackenzie Health, Centre for Behaviour and Health Sciences.

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