



Acute and protracted disruptions to inhibitory control following sports-related concussion

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ABSTRACT

Extant evidence demonstrates disruptions to inhibitory control from as little as six months to as long as several years following sports-related concussion. However, the sensitivity of tasks requiring inhibitory control for detecting disruptions to cognition during the acute, subacute, and protracted phases of recovery remains in question. Accordingly, the purpose of this study was to examine concussion-related disruptions to inhibitory control across recovery. Athletes with sports-related concussion ($n = 55$; 22 female) completed an inhibitory control task within 72 h of injury, after returning to play, and within one month following return to play. Matched control athletes ($n = 55$; 22 female) were tested at similar intervals. Behavioral indices of performance were analyzed using univariate multi-level modeling. Findings indicated that the concussion group exhibited decrements to inhibitory control immediately after injury and up to one month following return to play, with no such observable differences at the return to play period. In addition to being sensitive to detecting chronic cognitive deficits resulting from sports-related concussion, these findings suggest that inhibitory control measures have the requisite sensitivity to identify the immediate and protracted signs of neurocognitive dysfunction following sports-related concussion. Accordingly, integrating assessments of inhibitory control into baseline, post-injury, and post-season measurement of cognitive function may prove useful for tracking the acute and persistent effects of sports-related concussion across an athlete's career. Athletes exhibiting impaired inhibitory control across the phases of recovery may be at greater risk of reinjury, thereby suggesting that integrating inhibitory control assessments into existing clinical measures may be of interest for informing concussion management and return-to-play decisions.

1. Introduction

Although compelling evidence exists to support the immediate (Belanger and Vanderploeg, 2005) and persistent neurocognitive deficits following sports-related concussion (De Beaumont et al., 2009), the sensitivity of neuropsychological tests to detect concussion-related impairments may depend upon the cognitive domain being measured and the sensitivity of the test to distinguish concussion-related disruptions across recovery (Guskiewicz et al., 2001; McGowan et al., 2018). Whereas some neurocognitive deficits appear during the first few days following sports-related concussion (Catena et al., 2009; Halterman et al., 2006; Howell et al., 2013; McGowan et al., 2018; van Donkelaar et al., 2005), others exhibit a more protracted time course following injury (Pontifex, O'Connor, Broglio and Hillman, 2009; Schatz et al., 2006). Nonetheless, immediately following sports-related concussion, disruptions to a number of cognitive processes have been observed,

including impairments in orientation, attention, mental set shifting, memory, and information processing speed (Collins et al., 1999; Delaney et al., 2002; Erlanger et al., 1999; Guskiewicz et al., 2001; Johnston et al., 2001; Matser et al., 2001). Although many of these cognitive impairments appear to recover to near baseline levels within five to seven days (Belanger and Vanderploeg, 2005), persistent deficits in inhibitory control have been observed (Moore et al., 2014; Moore et al., 2016; Parks et al., 2015; Pontifex et al., 2012, 2009), with decrements demonstrated up to several years after sustaining a sports-related concussion (Moore et al., 2014). Given that concussion-related impairments in inhibition appear to persist long after traditional recovery periods, it is vital to understand whether such disruptions might be detected immediately following the concussive injury — providing a potential index for those athletes who require a more protracted recovery period — or whether such impairments only manifest months to years following the injury. However, a critical barrier to understanding

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this relationship is the lack of evidence elucidating concussion-related deficits in inhibition across recovery (i.e., immediately following injury, at return to play, and one month following return to play).

Inhibitory control, a subclass of cognitive control functions, refers to the ability to selectively attend to and respond to task-relevant information while resisting interference from distracting information or pre-potent responses (Diamond, 2013). In other words, inhibitory control describes our capacity for impulse control or interference suppression and has a ubiquitous influence on physical health (Moffitt et al., 2011). For example, deficits in inhibition have been found to relate to substance abuse disorders (Ivanov et al., 2008), delinquent behaviors (Morgan and Lilienfeld, 2000), and poorer social-emotional competence (Rhoades et al., 2009). Within the extant literature, a growing number of investigations have examined the long-term impacts of sports-related concussion on cognition, highlighting impairments in inhibition months to years following the acute stages of injury (De Beaumont et al., 2009; Ellemberg et al., 2007; Moore et al., 2014, 2015; Ornstein et al., 2004; Parks et al., 2015; Pontifex et al., 2012, 2009; Wall et al., 2006). Specifically, in one such investigation Parks et al. (2015) examined concussion-related decrements in inhibitory control between individuals with a history of concussion and individuals with no history of concussion during performance of a flanker task. The flanker task (Eriksen and Eriksen, 1974) is conceptually simplistic in that it requires participants discriminate a centrally presented target stimulus amid laterally flanking stimuli that either indicate the same response (congruent; i.e., < < < <) or indicate the opposite response (incongruent; i.e., > > < <) as the central stimulus. Thus, the flanking stimuli must be inhibited in order to reduce the potential for perceptually-induced response interference while the dominant perceptual cues activate the action-schema. In the case of the incongruent array, there is greater response interference elicited between the correct and incorrect responses as the target and flanking stimuli are mapped to opposing action-schemas, thus requiring greater inhibition to suppress this perceptually-induced response interference. This interference increases the potential for an incorrect response, thereby slowing mean reaction time. Using this task, Parks et al. (2015) observed that not only did individuals with a history of concussion demonstrate poorer response accuracy—relative to individuals with no history of concussion—but they also demonstrated greater reaction time variability, suggesting a compromised capacity to manage inhibitory control demands. Because these measures are affected by the amount of competing information presented at the same time as the task-relevant information, an additional means of gaining insight into these relationships while at the same time accounting for differences in cognitive processes unrelated to the aspect of cognition of interest—such as motor speed—is to examine the cost associated with the additional task demands. In the flanker task, the interference cost provides an index of the additional inhibitory control and interference suppression requirements induced by the incongruent stimuli over and above that induced by the congruent stimuli (e.g., interference cost reaction time = incongruent trials reaction time – congruent trials mean reaction time). Thus, despite exhibiting generally poorer overall performance on the flanker task, concussed individuals have also demonstrated a compromised capacity to handle this competing information—exhibiting a greater interference cost relative to matched control individuals (De Beaumont et al., 2009; Moore et al., 2015; Pontifex et al., 2009).

Moreover, concussed individuals have exhibited a slowing of reaction time across diverse tasks immediately (Kontos et al., 2012; Sosnoff et al., 2007) and up to two months following sports-related concussion (Howell et al., 2013). Although this slowing of reaction time might allow for the greater variability in reaction time (as assessed through standard deviation of reaction time) manifested by concussed individuals (Makdissi et al., 2001; Parks et al., 2015), greater reaction time variability has still been observed from as early as eight months up to 10 years following a concussive injury (Hetherington et al., 1996;

Parks et al., 2015) even after accounting for differences in mean reaction time through the calculation of the intraindividual coefficient of variation of reaction time [(standard deviation/mean)*100] (Abdi, 2010). Thus, while a history of concussive injury clearly appears to relate to compromised inhibitory control, within the acute and subacute stages of injury, the extent to which concussive injuries manifest with impairments in inhibition may be obfuscated by the tasks employed to assess inhibition.

Within the widely popular Immediate Post-Concussion Assessment and Cognitive Testing (ImPACT) tool, the impulse control composite score—as an index of inhibitory control—has not been found to differentiate between concussed and matched control individuals during the acute stages of injury unless combined with visual memory and processing speed performance scores (Schatz et al., 2006). However, this impulse control composite score is computed based upon the total number of incorrect responses (i.e., number of incorrect distractors) during the interference phase of the X's and O's visual spatial memory task in which individuals are asked to complete a speeded two-choice reaction time task with no inhibitory control demands and the number of incorrect responses on the Color Match task, which is effectively a modification of the Stroop task (Schatz et al., 2006). In the classic Stroop task (1935), individuals are asked to indicate the color of ink in which a string of letters are presented (i.e., 'XXX' presented in GREEN ink). Given the pre-potent tendency to read, when the string of letters form a color word (i.e., 'RED' presented in GREEN ink) the participants must inhibit the tendency to read in order to respond to the color of the ink. Thus, inhibitory demands are quantified by the extra processing time/accuracy required to suppress the prepotent and dominant reading response for incongruent color words relative to when responding to the generic string of letters or color words presented in a congruent color (i.e., the difference in performance between 'RED' presented in GREEN ink and 'GREEN' presented in GREEN ink). In the ImPACT Color Match task however, individuals are instructed to respond when the word is presented in a congruent color (i.e., respond when the word 'GREEN' is presented in GREEN ink) and to not respond when the word is presented in an incongruent color (i.e., do not respond when the word 'RED' is presented in GREEN ink). Thus, the Color Match task operates as a Go/No-go task without the benefit of first developing a pre-potent response that needs to be suppressed. Because the impulse control composite score is based upon metrics that place relatively minimal demands upon inhibitory control, it is perhaps unsurprising that it has not shown to be particularly effective in differentiating concussed and matched control individuals.

Alternatively, impairments in inhibition have been observed within three days following sports-related concussion when assessed using the Attentional Networks Task (Fan et al., 2002). The Attentional Networks Task combines cued reaction time and flanker task paradigms, thereby requiring participants to determine the direction (i.e., left or right) of a central target stimulus arrow. Presentation of the target stimulus occurs above or below a central fixation point and may or may not be preceded by a cue to shift visuospatial attention or be accompanied by flanking stimuli (Fan et al., 2002). Accordingly, the nature of this task conflates multiple aspects of cognition including inhibition and the shifting of visuospatial attention (Fan et al., 2002; Nigg, 2000). Recent evidence has suggested that concussion-related cognitive dysfunction is particularly evident in response to tasks requiring shifts of visuospatial attention (McGowan et al., 2018). Therefore, the Attentional Networks Task may observe concussion-related decrements simply as a function of the demands placed upon reorienting attention rather than upon the inhibitory demands of the task. Thus, the degree to which decrements in inhibitory control manifest within these acute stages of injury remains an open question. Accordingly, the purpose of the present investigation was to determine how sports-related concussion influences inhibitory control across the acute, subacute, and protracted stages of recovery to better inform approaches for individualized concussion management.

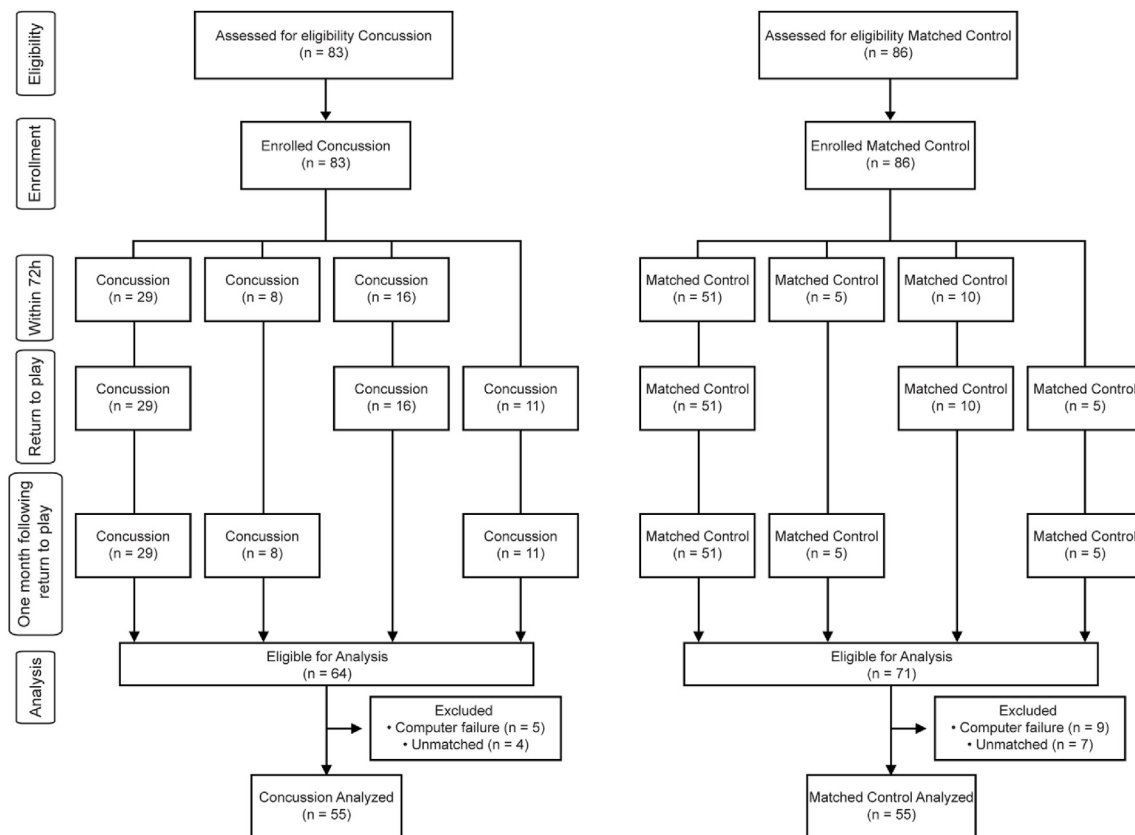


Fig. 1. CONSORT flow diagram of the retention of participants in each group through each testing period. Participants identified as still eligible had at least two of the three testing points. Missing testing points are denoted by the absence of a box within a column. Participants without an age- and sex-matched control or in which there was an equipment error were excluded from analysis.

2. Method

2.1. Participants

The concussed group comprised 55 varsity and collegiate club athletes (22 female, mean age = 18.0 ± 2.2 years) with a sports-related concussion identified by a specialized health professional (certified athletic trainer/physician). Concussion was defined as altered mental status resulting in short-term impairments caused by a blow to the head or body, leading to one or more of the following symptoms: headache, nausea, vomiting, dizziness/balance problems, fatigue, trouble sleeping, drowsiness, sensitivity to noise or light, blurred vision, difficulty remembering, or difficulty concentrating (McCrory et al., 2017). A group of 55 athletes (22 female, mean age = 18.1 ± 2.3 years) with similar athletic participation (i.e., varsity or collegiate club athletes) served as matched controls. See Fig. 1 for a CONSORT flow diagram of enrollment. These groups were obtained by recruiting a total of 169 athletes (83 concussed, 86 matched control) from the mid-Michigan area. Athletes with sports-related concussion participated in testing within 72 h of their sports-related concussion, following return to full athletic participation, and then at one month following return to play. Athletes with concussion were cleared for return to full athletic competition by independent specialized healthcare professionals (certified athletic trainer/physician) unaffiliated with the research team following each school's respective concussion protocol, which followed a stepwise progression after athletes become asymptomatic. Athletes with concussion were tested within ± 1 day of the date at which they returned to full athletic participation. Following initial enrollment, each concussed participant was matched with a control participant by sex and age; matched controls were asked to participate in congruent periods of testing. For instance, if the time lag between the initial

assessment (within 72 h of injury) and the return to play assessment sessions for a concussed athlete was 10 days, the respective matched control athlete was tested at the same interval between the initial assessment and return to play assessment. All participants were free of neurological disease or physical disabilities, indicated normal or corrected-to-normal vision, and provided written informed consent in accordance with the Institutional Review Board at Michigan State University before testing. No participants in the present study reported a loss of consciousness associated with their concussive injury or a history of more severe traumatic brain injury, evidence of abnormality visible on Computerized Tomography (CT) of the head related to the traumatic event (neuroimaging not required for enrollment), or hospital admission due to either head injury or collateral injuries for > 24 h.

2.2. Procedure

A repeated-measures design was used in which each athlete in the concussion group was tested at three time points: within 72 h of injury (2.1 ± 0.8 days following injury), at return to play (16.3 ± 7.9 days following injury), and at one month after return to play (55.5 ± 15.5 days following injury). Control athletes were matched with athletes in the concussion group with regard to the interval between testing periods and were brought in for initial testing, testing aligning with the concussed athlete's return to play (18.3 ± 14.0 days following initial testing), and testing aligning within one month following the concussed athlete's injury (60.4 ± 23.1 days following initial testing). The duration between testing periods did not differ between the concussed and matched control groups, $t's (105) \leq 1.2$, $p's \geq 0.2$, $d's \leq 0.24$ [95% CI: -0.21 to 0.64]. Prior to the initial testing (within 72 h of injury), a trained experimenter administered the Conley Evaluation (DeRenzo et al., 1998) to assess the capacity of individuals older than 18 years to

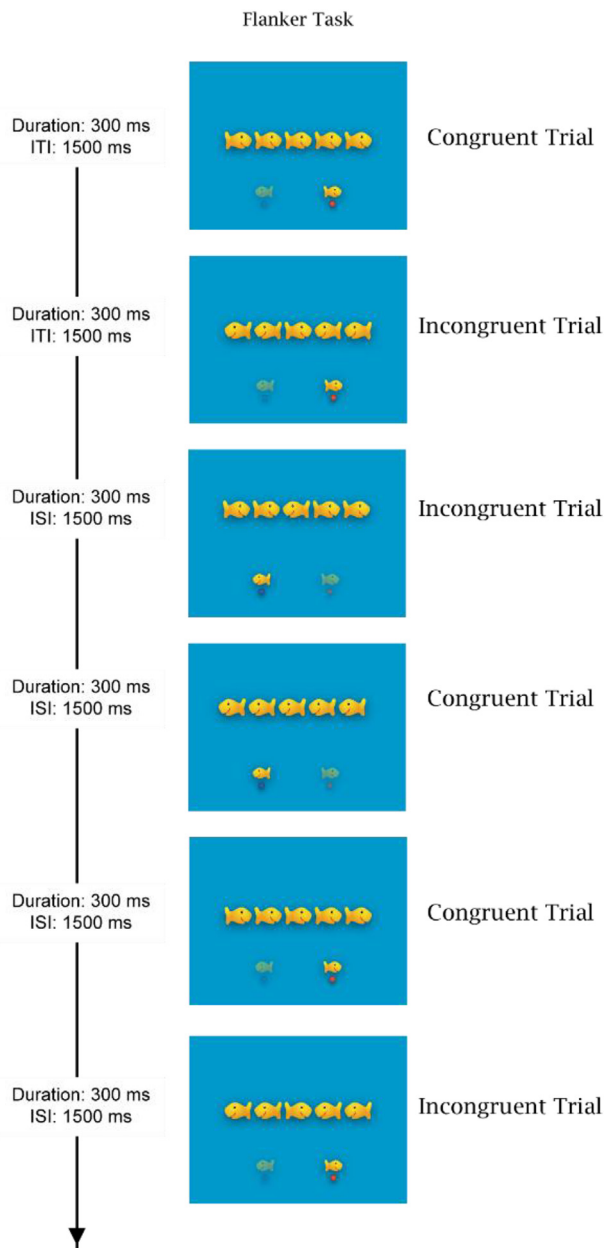


Fig. 2. Illustration of the modified flanker task. For reference, the correct response to each stimulus is depicted. Response mapping cues remained on the screen during task completion to alleviate working memory load and to maintain consistency with current clinically-relevant neuropsychological test batteries.

provide informed consent; guardians provided informed consent for participants younger than 18 years old. Participants were asked to complete a health and demographics screening questionnaire and then were asked to complete the inhibitory control task on a laptop.

2.3. Inhibitory control task

A flanker task (Eriksen and Eriksen, 1974; Pontifex et al., 2013; see Fig. 2) was used to determine how inhibitory control may be impaired across the phases of recovery following sports-related concussion. All testing occurred in a quiet setting (e.g., empty classroom, laboratory, or medical office) in which the athlete was seated in front of the laptop and completed the task individually with only the experimenter present. In this task, participants were instructed to make a left index finger button press on a laptop keyboard when the target stimulus

pointed left and a right index finger button press when the target stimulus pointed right. Participants were instructed to respond as accurately as possible to the direction of the centrally presented target fish amid either congruous (target facing the same direction) or incongruous (target facing the opposite direction) flanking fish. Trials were presented with equal probable congruency and directionality such that no more than four of the same trial type occurred sequentially and responses were equally distributed across left- and right-handed responses. Participants completed 40 practice trials while trained experimenters closely monitored the participants to ensure they were performing the task in a manner that demonstrated comprehension as indicated by overall performance above 50% correct (98% of athletes demonstrated performance on these practice trials $\geq 60\%$). Following the practice trials, participants completed 120 experimental trials. The stimuli were orange fish presented focally for 300 ms on a blue background with a response window of 1450 ms and an inter-trial interval of 1500 ms (see Fig. 2). Participants were provided with task instructions prior to the start of each condition. Additionally, the button-response mapping cues (i.e., left and right) were visible on the participant's screen during the task to maintain consistency with existing clinically-relevant neurocognitive assessment batteries.

3. Statistical analysis

Data were analyzed using multi-level modeling as this approach is robust to unbalanced data (i.e., missing observations) and accounts for a number of sources of variability (Goldstein, 2011; Volpert-Esmund et al., 2018). Analyses were conducted with $\alpha = 0.05$ and Benjamini-Hochberg false discovery rate control = 0.05 for post-hoc decompositions. All analyses were performed using the lme4 (Bates et al., 2015), lmerTest (Kuznetsova et al., 2017), and emmeans (Lenth et al., 2017) packages in R version 3.4.0 (R Core Team, 2013) with Kenward-Roger degrees of freedom approximations. The experimental protocol required that all participants be tested within ± 1 day of the return to play period and within ± 5 days of the one month following return to play period. Participants who did not adhere to the protocol or in which there was an equipment failure resulting in missing data from two sessions were excluded from analyses (see Fig. 1). For each athlete with sports-related concussion, a matched control athlete was identified based upon age and sex. Participants without an age- and sex-matched control were excluded from analysis. This approach resulted in a final analysis of 110 participants (55 concussed, 55 matched control).

For each inferential finding, Cohen's d with 95% confidence intervals were computed as standardized measures of effect size, using appropriate variance corrections for between-subjects (d_b) and repeated-measures comparisons (d_{rm} ; Lakens, 2013). Given a sample size of 110 participants and beta of 0.20 (i.e., 80% power), the present research design theoretically had sufficient sensitivity to detect t -test differences between concussed and matched control groups exceeding $d = 0.54$ (with a two-sided alpha) as computed using G*Power 3.1.2 (Faul et al., 2007). Mean reaction time (ms), response accuracy (% correct), standard deviation of reaction time, and intraindividual coefficient of variation of reaction time data were analyzed using a 2 (Group: concussed, matched control) \times 2 (Sex: female, male) \times 3 (Time: within 72 h, return to play, and one month following return to play) \times 2 (Trial Type: congruent, incongruent) univariate multi-level model modeling the random intercept associated with Participant, Participant \times Time, Participant \times Congruency, and Participant \times Time \times Congruency. Additional analyses for the interference cost of each variable (i.e., reaction time, response accuracy, standard deviation of reaction time, and intraindividual coefficient of variation of reaction time) were performed separately to determine if a sports-related concussion differentially impacted upon the interference cost using a 2 (Group: concussed, matched control) \times 3 (Time: within 72 h, return to play, and one month following return to play) univariate multi-level model modeling for the random intercept associated with Participant and Participant \times Time.

Table 1
Demographic characteristics as a function of group (± SD).

Measure	Concussion	Matched Control	<i>p</i>
N	55	55	
Female	40%	40%	1.0
Age	18.0 ± 2.2 years	18.1 ± 2.3 years	0.87
Race	27% nonwhite	29% nonwhite	1.0
Contact Sport	78%	29%	< 0.001
			*
Incurred a Prior Concussion	47%	18%	0.002 *
Number of Prior Concussions	0.8 ± 1.2	0.3 ± 0.8	0.009 *
Time Since Last Concussion	2.0 ± 0.8 years	2.3 ± 0.9 years	0.33
Left handed (<i>n</i>)	8	5	0.50

Note: Race was unreported by 4 participants from the concussion group and 2 participants from the matched control group. Handedness was unreported by 1 participant in the concussion group. * denotes the *t*-test or chi-square test was significant at $p < 0.05$. Contact sport indicates the percentage of athletes in each group that reported playing a contact sport during the present season (i.e., not an indication of a history of contact sport participation).

4. Results

4.1. Demographics

Analysis of demographic variables (see Table 1) revealed no significant differences between groups for age or in the time since last concussion, t 's (35) ≤ 1.0 , $p \geq 0.3$, $d_s \leq 0.36$ [95% CI: −0.34 to 1.06]. Similarly, no differences between groups were observed with regard to the proportion of the sample identifying as female, as nonwhite, or as left handed, X^2 's ≤ 0.4 , p 's ≥ 0.50 . However, a larger proportion of the concussed group identified as participating in contact sport during the season in which data collection occurred, $X^2 = 24.7$, $p \leq 0.001$ and having incurred a prior concussion, $X^2 = 9.3$, $p = 0.002$. Contact sport athletes reported participation in football, basketball, rugby, wrestling, ice hockey, cheerleading, soccer, and lacrosse. Noncontact athletes reported participation in swimming, rowing, cross-country running, track and field, and baseball.

4.2. Reaction time

Table 2 presents all task performance measures for athletes with concussion and matched control athletes collapsed across congruency. Analysis of flanker mean reaction time revealed a main effect of Congruency, such that faster reaction time was observed for congruent (310.2 ± 61.3 ms) relative to incongruent (356.8 ± 65.7 ms) trials, see Fig. 3: t (108) = 20.7, $p < 0.001$, $d_{rm} = 0.79$ [95% CI: 0.66 to

0.91].

4.3. Interference cost reaction time

Analysis of interference cost reaction time (incongruent trials reaction time – congruent trials reaction time) revealed a main effect of Group such that athletes with concussion demonstrated greater cost associated with the difficulty in resolving the additional interference induced by incongruent trials (51.5 ± 31.8 ms) relative to matched controls (42.5 ± 26.5 ms), see Fig. 3: t (107) = 2.0, $p = 0.05$, $d_s = 0.37$ [95% CI: 0.00 to 0.75].

4.4. Response accuracy

Analysis of flanker response accuracy revealed a Group × Time interaction, F (2, 170) = 11.0, $p < 0.001$, $f^2 = 0.10$ [95% CI: 0.00 to 0.23]. Post-hoc decomposition of the Group × Time interaction revealed that athletes with concussion exhibited decreased accuracy within 72 h of injury (75.5 ± 20.8%) relative to matched controls (88.0 ± 14.1%), see Fig. 3: t (143) = 4.6, $p < 0.001$, $d_s = 0.94$ [95% CI: 0.52 to 1.35]. However, no such differences were observed at return to play or at one month following return to play, see Fig. 3: t 's (141) ≤ 2.0 , p 's ≥ 0.05 , d_s 's ≤ 0.42 [95% CI: −0.06 to 0.84]. Additionally, findings revealed a main effect of Congruency such that congruent (91.2 ± 10.7%) trials were more accurate than incongruent (76.1 ± 18.4%) trials, see Fig. 3: t (107) = 13.5, $p < 0.001$, $d_{rm} = 0.84$ [95% CI: 0.67 to 1.01].

4.5. Interference cost response accuracy

Analysis of flanker interference cost response accuracy (incongruent trials % correct – congruent trials % correct) revealed no main effects or interactions, see Fig. 3: F 's (1, 107) ≤ 3.7 , p 's ≥ 0.058 , f^2 's ≤ 0.62 [95% CI: 0.00 to 1.09].

4.6. Standard deviation of reaction time

Analysis of standard deviation of reaction time revealed a Group × Time interaction. Post-hoc breakdown revealed greater variability for athletes with concussion (102.8 ± 51.7 ms) relative to matched controls (71.7 ± 29.1 ms) within 72 h, see Fig. 3: t (186) = 4.8, $p < 0.001$, $d_s = 0.99$ [95% CI: 0.57 to 1.40]. At one month following return to play, athletes with concussion continued to have greater variability (89.6 ± 36.2 ms) than matched controls (67.2 ± 26.1 ms), see Fig. 3: t (206) ≥ 3.3 , p 's ≤ 0.001 , $d_s = 0.71$ [95% CI: 0.28 to 1.13]. However, no such group differences were

Table 2
Task performance measures as a function of group collapsed across congruency (± SD).

Measure	Concussion (<i>n</i> = 55)			Matched Control (<i>n</i> = 55)		
	Within 72 h	Return to play (RTP)	One month following RTP	Within 72 h	Return to play (RTP)	One month following RTP
Reaction Time (ms)						
Collapsed	336.9 ± 94.9	334.8 ± 65.2	325.2 ± 64.0	340.0 ± 63.2	335.7 ± 56.7	333.7 ± 58.0
Interference Cost	56.6 ± 35.1	48.9 ± 30.0	48.9 ± 30.4	43.0 ± 25.4	41.1 ± 26.7	43.2 ± 28.0
Response Accuracy (%)						
Collapsed	76.0 ± 20.8	83.2 ± 18.3	80.9 ± 16.3	88.0 ± 14.1	87.7 ± 14.7	86.4 ± 12.3
Interference Cost	−18.6 ± 12.8	−16.7 ± 13.5	−16.5 ± 13.1	−12.7 ± 13.0	−13.0 ± 13.9	−13.1 ± 9.9
Standard Deviation of Reaction Time (ms)						
Collapsed	102.8 ± 51.7	81.3 ± 38.2	89.6 ± 36.2	71.7 ± 29.1	68.2 ± 25.8	67.2 ± 26.1
Interference Cost	4.1 ± 47.4	−4.3 ± 38.4	−5.7 ± 28.2	−2.1 ± 19.9	−6.7 ± 22.5	−6.4 ± 20.7
Intraindividual Coefficient of Variation Reaction Time (ms)						
Collapsed	0.34 ± 0.24	0.27 ± 0.20	0.31 ± 0.15	0.22 ± 0.14	0.21 ± 0.13	0.21 ± 0.13
Interference Cost	−0.004 ± 0.013	−0.005 ± 0.013	−0.006 ± 0.008	−0.003 ± 0.008	−0.005 ± 0.010	−0.005 ± 0.007

Note: Mean performance was collapsed across congruent and incongruent trials of the flanker task, whereas the interference cost represents the additional cost associated with the greater interference of the incongruent trial relative to the congruent trial.

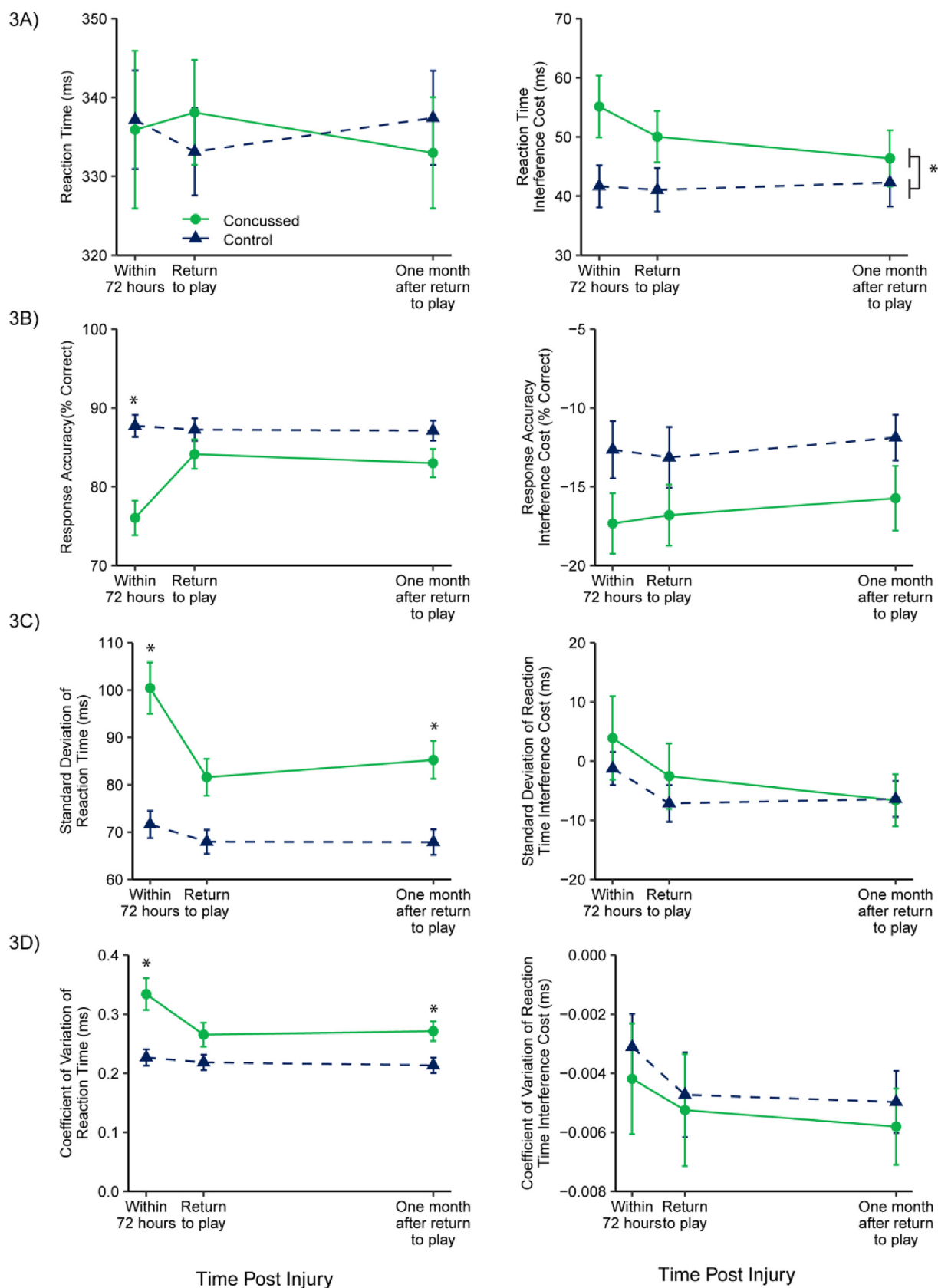


Fig. 3. Mean values (\pm SE) for each group and testing period collapsed across congruency for (3A) mean reaction time and interference cost reaction time, (3B) response accuracy and interference cost response accuracy, (3C) standard deviation of reaction time and interference cost of standard deviation of reaction time, and (3D) intraindividual coefficient of variation and interference cost of intraindividual coefficient of variation. * denotes the *t*-test was significant at $p < 0.05$.

observed at return to play, see Fig. 3: $t(183) = 2.0$, $p = 0.043$, $d_s = 0.41$ [95% CI: 0.01 to 0.80] after correction for false discovery rate (Benjamini-Hochberg critical alpha = 0.038).

4.7. Interference cost standard deviation of reaction time

Analysis of interference cost of standard deviation of reaction time (incongruent trials standard deviation of reaction time – congruent trials standard deviation of reaction time) revealed no main effects or interactions, see Fig. 3: $F_s(1, 105) \leq 1.9$, $p_s \geq 0.2$, $f^2_s \leq 0.65$ [95% CI: 0.00 to 1.14].

4.8. Intraindividual coefficient of variation of reaction time

Analysis of intraindividual coefficient of variation of reaction time revealed a Group \times Time interaction, see Fig. 3: $F(2, 169) = 4.3$, $p = 0.015$, $f^2 = 0.10$ [95% CI: 0.00 to 0.23]. Post-hoc breakdown of this interaction revealed greater variability within 72h for athletes with concussion (0.34 ± 0.26 ms) relative to matched controls (0.22 ± 1.4 ms). At one month following return to play, athletes with concussion continued to have greater variability (0.31 ± 0.15 ms) than matched controls (0.21 ± 0.2 ms), see Fig. 3: $t_s(152) \geq 2.9$, $p_s \leq 0.005$, $d_s \leq 0.71$ [95% CI: 0.19 to 1.12]. However, no such group differences were observed at return to play, see Fig. 3: $t(139) = 1.6$, $p = 0.1$, $d_s = 0.33$ [95% CI: -0.07 to 0.72].

4.9. Interference cost coefficient of variation of reaction time

Analysis of interference cost of intraindividual coefficient of variation of reaction time (incongruent trials intraindividual coefficient of variation of reaction time – congruent trials intraindividual coefficient of variation of reaction time) revealed no main effects or interactions, see Fig. 3: $F_s(1, 105) \leq 0.8$, $p_s \geq 0.4$, $f^2_s \leq 0.26$ [95% CI: 0.00 to 0.50].

5. Discussion

The present investigation examined the effects of sports-related concussion on inhibitory control within 72 h following injury, at return to play, and at one month following return to play. Overall, findings indicated that concussion-related decrements in inhibition are apparent during the acute period following sports-related concussion and persist up to one month following return to play. Namely, athletes with concussion exhibited greater reaction time cost associated with compromised interference suppression across all time periods, decreased response accuracy within 72h of injury, and greater variability in reaction time (as indexed by heightened standard deviation of reaction time and intraindividual coefficient of variation of reaction time) within 72h of injury and at one month following return to play. Collectively, these findings suggest that disruptions to inhibitory control exhibit a trajectory of recovery such that concussion-related impairments manifest across the acute and protracted phases of recovery, with a failure to observe concussion-related dysfunction during the subacute period. These findings provide compelling preliminary evidence that inhibitory control assessments do have the requisite sensitivity to detect concussion-related decrements during the acute period following injury in addition to persistent impairments beyond the return-to-play period.

The current findings corroborate previous investigations suggesting that acute impairments in inhibitory control following sports-related concussion exist in a relatively large sample (Bruce and Echemendia, 2003; Catena et al., 2009; Echemendia et al., 2001; Howell et al., 2013; van Donkelaar et al., 2005). Specifically, consistent with studies suggesting impaired inhibitory control as assessed using the Attentional Networks task (Haltermann et al., 2006; Howell et al., 2013; van Donkelaar et al., 2005), these concussion-related decrements are

observed in the greater cost associated with interference suppression and poorer response accuracy. Accordingly, the present findings would appear to suggest that the concussion-related deficits observed using the Attentional Networks Task occur not just as a result of the required shifts in visuospatial attention but also as a result of inhibitory impairments. Further, the present findings replicated previous investigations observing more persistent concussion-related decrements in reaction time, response accuracy, and interference control on the flanker task over the course of months and years following injury. The present investigation extends previous research by demonstrating that concussion-related inhibitory control deficits are present during relatively shorter time frames: within 72 h of injury and up to one month following concussive injury than demonstrated in the extant literature (De Beaumont et al., 2009; Moore et al., 2014, 2015; Parks et al., 2015; Pontifex et al., 2012, 2009). Accordingly, as the present investigation only assessed participants through a period one month following return to play, future research is necessary to determine whether these concussion-related decrements in inhibition are persistent in a trait-like fashion throughout an athlete's life or rather if they serve as an index of those individuals with more severe concussive injuries who require more prolonged return-to-play protocols.

Consequently, the present findings demonstrate the efficacy of inhibitory control tasks in detecting cognitive impairments following concussive injury, suggesting that such tasks may prove useful for tracking the acute and cumulative effects of sports-related concussion immediately following injury and across an athlete's career. Accordingly, neurocognitive assessments oriented towards concussive injuries should seek to integrate task components that place demands upon inhibitory control to increase the sensitivity of the assessment in detecting these immediate and delayed impairments in cognition. Further, the present findings provide additional support for going beyond measures of mean reaction time, thereby also examining the variability of performance using standard deviation of reaction time and coefficient of variation of reaction time (MacDonald et al., 2006; Parks et al., 2015; Stuss et al., 1994).

Specifically, greater reaction time variability was observed in athletes with sports-related concussion during the acute and protracted periods. While the conservative false discovery rate approach ultimately rejected the statistical finding at the return to play period, it is important to note that variability in performance was not statistically different between the subacute and protracted assessments within the concussion group ($p = 0.2$, $d_{rm} = 0.15$ [95% CI: -0.10 to 0.41]) suggesting consistency of the variability findings. Accordingly, although differences between groups for mean level performance were ameliorated following return to athletic participation, persistent impairments in variability of reaction time remain apparent well beyond this period. These measures of reaction time variability thus may be more useful in tracking concussion-related decrements across recovery. However, the growing body of evidence demonstrating cognitive disruptions induced by subconcussive impacts (Broglio et al., 2012; Dashnaw et al., 2012; Gysland et al., 2012) is of interest when interpreting the present findings. Because a larger proportion of athletes in the concussion group participated in contact sports during the season in which data collection occurred, the influence of greater exposure to subconcussive impacts in this group on the present findings cannot be ruled out and further research is warranted to elucidate the influence of subconcussive impacts and concussion history on disruptions to inhibitory control across recovery.

Although the present investigation was not designed to elucidate the mechanisms underlying these concussion-related impairments in inhibitory control, speculatively prior research has suggested perturbations to the neural network subserving cognitive control operations – of which inhibitory control is a subdomain. Indeed, concussive injuries have been associated with axonal injury and compromised white-matter integrity (Gennarelli and Graham, 1998; Medana and Esiri, 2003; Povlishock and Katz, 2005), particularly in areas subserving

cognitive control (Niogi et al., 2008). Accordingly, incorporating findings across animal models and neuroimaging in humans, it is thought that a concussive injury results in an initial ionic flux accompanied by altered neuronal cell metabolism and cytoskeletal damage, which contribute to axonal injury and impaired neuronal transmission (Giza and Hovda, 2014). Given the robust nature of cognitive operations, such acute neurophysiological perturbations may not necessarily manifest unless the neural system is sufficiently taxed. The resource-intensive nature of cognitive control tasks thus enhances the likelihood of detecting impairments given the combination of cognitive load and integration of information across various neural systems. Indeed, concussion-related impairments have been detected across aspects of cognitive control, including working memory (Stulemeijer et al., 2010; Tay et al., 2010), cognitive flexibility (Howell et al., 2013; Mayr et al., 2014; McGowan et al., 2018), and inhibitory control (Moore et al., 2014; Parks et al., 2015; Pontifex et al., 2009). Although evidence to support disruptions to inhibitory control within the acute periods of recovery remains scarce, converging evidence has demonstrated persistent impairments in inhibitory control six months to 41 years following sports-related concussion (De Beaumont et al., 2009; Ellemberg et al., 2007; Moore et al., 2014, 2015; Parks et al., 2015; Pontifex et al., 2012, 2009), thereby providing evidence that concussive injuries may result in chronic impairments to neural networks underlying aspects of cognitive control.

The present finding that inhibitory control exhibits a trajectory of recovery following sports-related concussion such that disruptions are observed within 72 h and at one month following return to play, with no such decrements during the return to play period may be speculatively explained by recent evidence from animal models observing similar patterns of recovery in myelin disruption and degradation following mTBI (mild traumatic brain injury; Armstrong et al., 2016; Wright et al., 2016). Namely, these disruptions have been implicated in traumatic axonal damage leading to white matter degradation (Yeh et al., 2014), which may result in long-term neurodegeneration and cognitive impairments. Demyelination following mTBI may lead to reduced white matter integrity and slowed neural conduction speed, which are pathologic features often observed following concussive injury (Bigler and Maxwell, 2012). Indeed, mice receiving an impact to the closed skull—modeling mTBI—have exhibited demyelinated axons at 2 days and at 6 weeks following injury, with no such differences at 1 week post-injury (Wright et al., 2016). This pattern of recovery parallels the present findings: inhibitory control decrements were observed at acute and protracted periods, with no such disruptions during the subacute phase. Moreover, demyelination at 3 days post-injury returns to pre-injury levels by 1 week (Wright et al., 2016), suggesting remyelination is carried out during this subacute period by oligodendrocytes. As early as 3 days following injury, an increase in newly generated oligodendrocytes has been observed, thereby supporting the subsequent remyelination during the 3 days to 1 week period following injury (Wright et al., 2016). Because remyelination is an integral component of the recovery process following mTBI—underlying the recovery of nerve conduction speed—return-to-play decrements in inhibitory control may be obscured during the subacute recovery phase due to rapid remyelination during this period—thereby attenuating potential impairments in information processing speed. Therefore, remyelination appears to not only coincide with the resolution of symptoms typically observed within 1–2 weeks following concussive injury, but also with the recovery of information processing speed. Furthermore, evidence suggests that in milder forms of traumatic brain injury myelin degradation as a consequence of the neurometabolic cascade may take longer to occur (Wright et al., 2016); thus, decrements in inhibitory control may again become apparent at more chronic time points. Taken together, the evidence speculatively suggests that axonal damage and demyelination may explain the observed impairments to inhibitory control during the acute and protracted periods whereas remyelination during the 1 week following injury may support the lack

of decrements observed at the return-to-play period.

While the present study provides preliminary evidence that disruptions to inhibitory control manifest within the acute and protracted periods of recovery following sports-related concussion, the findings are not without limitations that should be addressed by future investigations. Although both the concussion group and the matched control group consisted of athletes with a history of incurring previous concussive injuries, this inclusionary approach enhances the generalizability of the findings to typical athletic populations and presents as a bias against finding any effects if residual impairments persisted in the matched control group. Future studies should use pre-concussion baseline assessments to ensure that the observed findings do indeed reflect the effects of sports-related concussion rather than individual differences in baseline performance. Although all participants were subject to the same testing parameters during the study protocol—as a part of the clinical management of the concussive injury by the site or athletes' medical care provider—concussed athletes could have been exposed to additional assessments that could have altered cognitive performance (i.e., by inducing a cognitively-fatigued state leading to reduced performance or alternatively by incurring practice effects leading to enhanced performance). While all testing for the present study was administered at least 3h following any such assessments—mitigating their impact—and the findings of prolonged impairments beyond the return to play period when the athletes would no longer be undergoing such additional assessments speak against this potential confound; future research should attempt to minimize such potential differences between groups. Additionally, it is important to emphasize that the observed findings are reflective of athletes with sports-related concussion, thus further research is necessary to determine the extent to which these findings might generalize to populations with severe traumatic brain injury.

Collectively, findings from the present investigation indicate that concussion-related disruptions to inhibition are observable within 72 h following injury and up to one month following return to play. Thus, these findings provide compelling preliminary evidence to suggest that inhibitory-control dysfunction following sports-related concussion manifests during the acute periods of recovery, suggesting that tasks requiring inhibitory control may be useful additions to immediate post-concussion clinical assessments. Further research is necessary to determine the clinical relevance of these immediate concussion-related decrements in inhibition—that is, the degree to which these acute disruptions are indicative of more severe concussive injuries, warranting prolonged clinical management. Because interference suppression is critical for attending to task-relevant information during competitive play, returning athletes to play while exhibiting persistent inhibitory control dysfunction may increase their risk of incurring additional injury.

Author disclosure statement

No conflicting financial interests exist.

CRediT authorship contribution statement

Amanda L. McGowan: Methodology, Software, Validation, Formal analysis, Investigation, Data curation, Writing - original draft, Writing - review & editing, Visualization, Project administration. **Abigail C. Bretzin:** Investigation, Data curation, Writing - review & editing, Project administration. **Jennifer L. Savage:** Investigation, Writing - review & editing, Project administration. **Kyle M. Petit:** Investigation, Writing - review & editing, Project administration. **Tracey Covassin:** Methodology, Validation, Resources, Writing - review & editing, Supervision, Project administration, Funding acquisition. **Matthew B. Pontifex:** Methodology, Software, Validation, Formal analysis, Resources, Writing - original draft, Writing - review & editing, Visualization, Supervision, Project administration, Funding acquisition.

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