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The association between a history of concussion and variability in behavioral and neuroelectric indices of cognition

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ABSTRACT

Associations between a history of concussion and variability in behavioral and neuroelectric indices of cognition were assessed in college-aged adults with a history of concussion and a healthy control group, in response to a stimulus discrimination task and a more attentionally demanding flanker task. Greater intra-individual variability was observed only for behavioral indices of reaction time in response to the flanker task for those with a history of concussion. An association was also observed between the number of concussions resulting in a loss of consciousness and greater variability of reaction time regardless of the type of task. Relative to neuroelectric measures, a concussive history was associated with smaller P3 amplitude only in response to the flanker task; with no differences between groups observed in response to the oddball task or for intra-individual variability measures. Thus, increased variability associated with a history of concussion appears to be behavior and process specific. The behavioral metrics and functions assessed are important considerations for identifying subtle, yet persistent influences of concussion on cognitive performance. Further, factors such as loss of consciousness associated with a concussive injury may moderate the extent to which these increases in behavioral variability manifest. Thus, the identification of persistent cognitive impairment following concussive injuries necessitates the utilization of appropriate tasks and may be facilitated by going beyond behavioral measures of central tendency.

1. Introduction

Sport-related concussions represent a growing public-health threat with conservative estimates indicating that nearly 4 million concussive injuries occur annually (Langlois et al., 2006) and account for almost 9% of all high school sport-related injuries (Gessel et al., 2007). While concussion related symptoms appear to resolve within 10 to 14 days in acutely injured individuals (McCrea et al., 2009; McCrory et al., 2013), a number of concussion-related patterns of neurocognitive impairment appear to persist well beyond this time frame (Giza and Hovda, 2001; Halterman et al., 2006; Howell et al., 2013; Sozda et al., 2011). Indeed, previous research has observed persistent decrements in neurocognition for years following concussive injuries (de Beaumont et al., 2007; Moore et al., 2014). Despite such findings, the long-term influence of concussion on neurocognition remains unclear as a number of investigations have failed to observe any persistent concussion-related cognitive impairments (Broglio et al., 2006; Collie et al., 2006; Iverson et al., 2006). Such discrepancies are not altogether unexpected, given the heterogeneous nature of concussive injuries, coupled with a wide variety of performance metrics and cognitive functions evaluated within the literature (Bigler et al., 2013; Livingston et al., 2010; McKinlay, 2010). Furthermore, the vast majority of previous investigations on the cognitive ramifications of concussive injury have relied only on central tendency measures (i.e., mean) of performance.

Beyond measures of central tendency, assessment of the transient within-person fluctuation in cognitive processing during the course of a task – known as intra-individual variability (Fjell et al., 2009; Lovden et al., 2007, 2013) – may provide another index of cognitive function for the assessment of persistent concussion-related decrements. Measures of intra-individual variability such as standard deviation (SD) provide a measure of the consistency of underlying cognitive operations and have been widely used as markers of overall neurological health (Fjell et al., 2011; Lovden et al., 2007). As such, intra-individual variability may aid in the identification and prognostication of neurocognitive deficits associated with concussion. Consistent with this premise, an early investigation by Makdissi et al. (2001) observed greater standard deviation of reaction time on a simple reaction time task in a sample of six concussed athletes during the acute phase of recovery 72 h after injury, relative to seven never-concussed athletes. However, utilizing standard deviation as a measure of intra-individual variability is

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problematic when changes in reaction time also occur. That is, as mean reaction time increases there is a natural tendency for variability – as assessed using standard deviation – to also increase as a result of reducing potential bounding related to floor effects of reaction time. Accordingly a more appropriate metric of intra-individual variability is the coefficient of variation (SD of reaction time [RT]/mean RT), which attempts to adjust for such tendencies. Indeed, both Sosnoff et al. (2007) and Halterman et al. (2006) failed to find differences in intra-individual variability between previously concussed and healthy participants using a variety of tasks from the CogState battery and various components of a visuospatial attention task, respectively. Although the results of these investigations would seem to suggest that measures of variability may be ill-suited for use in identifying concussion related decrements in cognition, it is important to note that these investigations all focused on the acute-phase of injury recovery. As intra-individual variability has been found to distinguish groups more efficiently than mean RT based on a variety of clinical variables including neurodegenerative disease and age-related cognitive decline (Gamaldo et al., 2012; Lovden et al., 2007); it may be that increases in variability manifest over the long-term period following a concussive injury rather than being immediately (i.e., acutely) evident.

The ability to detect persistent, concussion-related deficits may also be dependent upon the type of cognitive tasks used. One such task that has been frequently utilized to detect concussion-related deficits in cognition is the flanker task (de Beaumont et al., 2009; Ellemberg et al., 2007; Moore et al., 2013, 2015; Pontifex et al., 2009), which requires selectively attending to a target stimulus amid an array of flanking stimuli. This task thus engages aspects of inhibitory control to attend to the appropriate stimulus while gating out task irrelevant information, and managing response interference created when the flanking stimulus are mapped to opposing action-schemas as the target stimulus (Eriksen and Eriksen, 1974). Accordingly, the nature of this task has demonstrated the requisite sensitivity to reveal concussion-related deficits persisting for months to years beyond the acute stage of injury (de Beaumont et al., 2009; Ellemberg et al., 2007; Moore et al., 2013; Pontifex et al., 2009). However, to date, the extent to which concussion-related differences in intra-individual variability manifest in response to an inhibitory control task, such as the flanker task, is as of yet unknown. As such, the current study sought to clarify previous research (Halterman et al., 2006; Makdissi et al., 2001; Sosnoff et al., 2007) by evaluating the relationship between a concussive history and response variability using intra-individual variability (i.e., CV of RT) in response to both a simple stimulus discrimination oddball task and a more demanding flanker inhibitory control task.

In addition to the assessment of behavioral variability, the present investigation sought to examine the relation of concussion history to intra-individual variability on the neuroelectric level. Within this body of literature, research has largely focused on an event-related brain potential (ERP) known as the P3 (also known as the P300 or P3b), which provides a neural index of the allocation of attentional resources during stimulus engagement (i.e., P3 amplitude; Polich, 2007) and stimulus classification and processing speed (i.e., P3 latency; Verleger, 1997). This ERP component has considerable utility for revealing persistent concussion-related deficits in brain function (Moore et al., 2014). Indeed, previous ERP research indicates that individuals with a history of concussion exhibit reductions in the allocation of attentional resources as indexed by decreased P3 amplitude (Broglio et al., 2009; Gosselin et al., 2012; Moore et al., 2014; Theriault et al., 2009) and delays in stimulus classification and processing speed as indexed by P3 latency, relative to their healthy counterparts (de Beaumont et al., 2009; Gaetz et al., 2000). Further, similar to behavioral measures, these concussion-related influences on the P3-ERP component appear to be disproportionately larger in response to tasks requiring greater amounts of cognitive engagement. However, despite the growth of research in this area, we have little understanding of how a history of concussive injury may relate to greater trial-by-trial variability in these neural indices of attention. Such information is particularly important given the utilization of signal averaging in the ERP approach, wherein the event-related signal is averaged across multiple trials. As such, greater intra-individual variability in this signal would – as a function of signal averaging – manifest as reductions in the amplitude of the ERP signal, which could also impact latency measures. Thus, it may be that previous findings of concussion-related impairments in the allocation of attentional resources and processing speed may instead simply be reflective of greater variability in these neural processes. Accordingly, the final purpose of the present study was to examine the association between a history of concussion and neuroelectric indices of stimulus engagement in response to two commonly employed tasks (i.e., a simple stimulus-discrimination task and an inhibitory control task) to better understand how a history of concussion may differentially manifest across neuroelectric and behavioral indices of performance as a function of the aspect of cognition assessed.

Based on previous findings, it was hypothesized that in response to a relatively simple oddball task, neither mean nor intra-individual variability of behavioral performance would demonstrate persistent concussion-related impairments in cognition. By contrast, a more demanding flanker task would yield reduced mean level performance and exhibit greater intra-individual variability in concussed relative to non-concussed athletes. Relative to the examination of neuroelectric indices of attention, it was hypothesized that athletes with a previous concussive history would demonstrate reductions in the allocation of attention (as indexed by smaller P3 amplitude) and delays in stimulus classification and processing speed (as indexed by longer P3 latency) regardless of the aspect of cognition assessed. However, the magnitude of the concussion-related deficits was hypothesized to be larger in response to the modified flanker task owing to its more demanding nature of the task characteristics. Given growing interest in this area of research, the investigation of how best to characterize metrics of cognitive performance and the potential interplay of the aspect of cognition assessed may provide insight into accurate detection and tracking of potential concussion-related cognitive impairments that persist well beyond the acute and sub-acute phases of injury.

2. Methods

2.1. Participants

The concussion group was comprised of 48 (10 female) college-aged students recruited from the University of Illinois at Urbana-Champaign based on self-report of previous concussion diagnosis by a medical practitioner (26 with one past self-reported concussion, 22 with two or more past self-reported concussions). Participants in the concussion group were screened to ensure that they were symptom free at the time of testing and that their injury occurred within the context of sport and/or recreation participation. The mean time elapsed since their last concussive injury was reported as approximately 4.2 ± 3.4 years prior. A healthy control group comprised of 50 (25 female) college-aged students with a similar history of athletic participation was also recruited; no significant differences for any demographic variables were observed between groups (t's (96) ≤ 1.9, p's ≥ 0.06, d's ≤ 0.39). To reduce the likelihood that an individual with an undocumented concussion was placed in the control group, individuals in this group were also asked if "following a blow to the head, have you experienced any concussion like symptoms," with a list of clinical diagnostic symptoms provided (McCrory et al., 2009). Only participants free of clinical diagnostic symptoms, a concussive history, and any prior cerebral injury were placed in the control group. All participants provided written informed consent that was approved by the Institutional Review Board of the University of Illinois at Urbana-Champaign and reported being free of any neurological disorder, cardiovascular disease, medication that influence central nervous system function, and had (corrected to)

Table 1
Demographic characteristics, mean task performance and neuroelectric measures (±SD) as a function of group.

Measure	Concussion	Healthy control
Sample characteristics		
N	48 (10 females)	50 (25 females)
Age (years)	20.5 ± 2.2	19.7 ± 1.6
IQ (K-BIT composite)	106.5 ± 7.7	108.1 ± 7.7
Education (years)	14.2 ± 1.2	13.8 ± 1.6
Number of concussions	1.7 ± 1.1	–
Concussions resulting in loss of consciousness (%)	43.8	–
Time since last concussion (years)	4.2 ± 3.4	–
Oddball behavior		
Nontarget response accuracy (% correct)	99.2 ± 0.8	99.5 ± 0.6
Target response accuracy (% correct)	98.2 ± 2.5	97.5 ± 3.2
Target reaction time (ms)	373.3 ± 36.2	380.3 ± 39.5
Target CV of RT (ms)	0.189 ± 0.048	0.185 ± 0.045
Oddball neuroelectric measures		
Nontarget amplitude (μV)	4.7 ± 3.5	5.8 ± 3.8
Nontarget CV of amplitude (μV)	0.917 ± 1.375	0.681 ± 2.665
Nontarget latency (ms)	388.8 ± 36.7	393.2 ± 34.1
Nontarget CV of latency (ms)	0.189 ± 0.014	0.186 ± 0.015
Target amplitude (μV)	14.5 ± 6.9	15.7 ± 7.3
Target CV of amplitude (μV)	0.644 ± 0.326	0.61 ± 0.316
Target latency (ms)	393.1 ± 42.2	385.2 ± 40
Target CV of latency (ms)	0.157 ± 0.032	0.166 ± 0.035
Flanker behavior		
Congruent response accuracy (% correct)	90.7 ± 7.6	94.1 ± 5.5
Congruent reaction time (ms)	402.7 ± 50	392.7 ± 46.5
Congruent CV of RT (ms)	0.203 ± 0.049	0.182 ± 0.045
Incongruent response accuracy (% correct)	79.9 ± 10.8	82.6 ± 10.4
Incongruent reaction time (ms)	461.9 ± 60.1	454 ± 56.9
Incongruent CV of RT (ms)	0.188 ± 0.037	0.172 ± 0.039
Flanker neuroelectric measures		
Congruent amplitude (μV)	9.2 ± 5.1	11.5 ± 5.1
Congruent CV of amplitude (μV)	0.718 ± 0.282	0.712 ± 0.295
Congruent latency (ms)	399.6 ± 40.3	391.7 ± 24.9
Congruent CV of latency (ms)	0.165 ± 0.035	0.162 ± 0.021
Incongruent amplitude (μV)	9.3 ± 5.5	11.1 ± 4.9
Incongruent CV of amplitude (μV)	0.815 ± 0.458	0.745 ± 0.38
Incongruent latency (ms)	434.9 ± 41.8	428.5 ± 32.5
Incongruent CV of latency (ms)	0.159 ± 0.027	0.152 ± 0.024

normal vision. Table 1 summarizes the demographic data for all participants.

2.2. Experimental tasks

2.2.1. Oddball task

We assessed simple stimulus discrimination using a visual oddball task. Participants viewed a series of shapes consisting of predominately 5-cm tall white triangles and were instructed to respond with a right hand thumb press only when a randomly occurring 5-cm tall white inverted triangle appeared (Hagen et al., 2006). Target stimuli occurred with a probability between 0.12 and 0.2 resulting in approximately 40 to 48 target trials. All stimuli were presented focally on a computer monitor at a distance of 1 m for 100 ms, with a 950 ms response window and a 2000 ms inter-trial interval. Mean level performance was characterized for response accuracy and latency; while intra-individual variability was quantified as the intra-individual coefficient of variation (CV of RT [SD/mean]) to the target stimulus.

2.2.2. Flanker task

We assessed inhibitory control using a modified flanker task (Eriksen and Eriksen, 1974; Pontifex et al., 2011). Participants were instructed to respond as quickly and accurately as possible to the direction of a centrally presented target arrow, which was flanked by an array of lateral congruous (e.g. <<<<< or >>>>>) or incongruous (e.g. <<><< or >><>>) arrows. The target–flanker stimulus array occurred with equal probability resulting in 200 congruent and 200 incongruent trials. The stimuli were 3 cm tall white arrows presented focally for 80 ms on a black background with a response window of 1000 ms and a variable inter-stimulus interval of either 1100, 1300, or 1500 ms. Mean level performance was characterized for response accuracy and latency; while intra-individual variability was quantified as the intra-individual coefficient of variation (CV of RT [SD/mean]) for the congruent and incongruent trials separately.

2.3. ERP recording

Electroencephalographic (EEG) activity was recorded from 64 electrode sites arranged in an extended montage based on the International 10-10 system (Chatrian et al., 1985) using a Neuroscan Quik-cap (Compumedics Neuroscan, 2003). Recordings were referenced to averaged mastoids (M1, M2), with AFz serving as the ground electrode, and impedance less than 10 kΩ. Additional electrodes were placed above and below the left orbit and on the outer canthus of each eye to monitor electro-oculographic (EOG) activity with a bipolar recording. Continuous data were digitized at a sampling rate of 500 Hz, amplified 500 times with a DC to 70 Hz filter, and a 60 Hz notch filter using a Neuroscan Synamps 2 amplifier. Continuous data were corrected offline for EOG artifacts using a spatial filter (Compumedics Neuroscan, 2003). This ocular-artifact reduction procedure performs a principle component analysis (PCA) to determine the major components that characterize the EOG artifact between all channels, and then reconstructs all of the original channels without the artifact components. Stimulus-locked epochs were created for correct trials from −100 to 1000 ms around the stimulus, baseline corrected using the −100 to 0 ms pre-stimulus period, and filtered using a zero phase shift low-pass filter at 30 Hz (24 dB/octave). Trials in which an amplitude excursion of ±75 μV occurred were identified as artifact and excluded. The P3 component was evaluated as the mean amplitude within a 50 ms interval surrounding the largest positive going peak within a 300–600 ms latency window (Gamer and Berti, 2010; Sass et al., 2010). Based on the topographic maxima of the P3 (Polich, 2007), data were then averaged across a 9-electrode site region of interest over the central-parietal and parietal regions (C1/Z/2, CP1/Z/2, P1/Z/2).[1] Amplitude was measured as the difference between the mean pre-stimulus baseline and mean peak-interval amplitude; while peak latency was defined as the time point corresponding to the maximum peak amplitude.

2.4. Procedures

Participants completed an informed consent, a health history/demographics questionnaire, and a concussion screening questionnaire. The Kaufman Brief Intelligence Test (K-BIT; Kaufman and Kaufman, 1990) was administered by a trained experimenter to screen intelligence quotient. Upon the completion of the above, participants were fitted with a 64-channel Quik-cap (Neuro, Inc., Charlotte, NC). Participants were then seated in a sound attenuated testing chamber where they were administered the oddball task followed by the flanker task, with task instructions and 20 practice trials administered before each task.

2.5. Statistical analysis

Table 1 provides demographic characteristics, mean task performance, and neuroelectric measures as a function of group. Analysis of

[1] Analyses were also conducted on a 6-electrode site region of interest over the frontal and fronto-central regions (F1/Z/2, FC1/Z/2) where the P3 ERP component does not exhibit its topographic maxima (Polich, 2007). No significant main effects of Group or interactions involving Group were observed in response to the oddball task, F's(1,96) ≤ 3.1, p's ≥ .08, η_p^2's ≤ .03, or the flanker task, Fs(1,96) ≤ 2.5, p's ≥ .12, η_p^2's ≤ .025.

performance at the mean level (response accuracy, mean RT, P3 amplitude, and P3 latency) and individual trial level (CV of RT, individual trial CV of P3 amplitude, and individual trial CV of P3 latency) were conducted separately for each dependent variable. Analysis of the oddball task was conducted using 2 (group: control, concussion) × 2 (stimulus: target, non-target) multivariate repeated measures ANOVAs to assess for group differences in all variables with the exception of mean RT and CV of RT. Analysis of reaction time measures of the oddball task were conducted using one-way ANOVAs (group: control, concussion) as no responses were required in response to the non-target stimulus. Analysis of the flanker task was conducted using 2 (group: control, concussion) × 2 (congruency: congruent, incongruent) multivariate repeated measures ANOVAs. To address limitations resulting from the fixed administration order – the oddball task was administered first followed by the flanker task – which may relate to fatigue, follow-up analysis were also conducted by splitting the trials into early and late blocks. Analyses of behavioral measures were then repeated with the addition of this factor (time: early, late). Analysis of early vs late trials were not performed for neuroelectric measures due to insufficient number of trials for both halves of the tasks. Post hoc comparisons were conducted using Bonferroni corrected *t* tests. The family wise alpha level for all tests was set at $p = .05$ prior to Bonferroni correction. In addition, nonparametric bivariate correlations were conducted to examine the relationship between injury variables (i.e., time from injury, number of injuries, loss of consciousness) and behavioral/ERP indices of performance (see Table 2). The data analysis was performed in PASW Statistics, 19.0.

3. Results

3.1. Oddball task group differences in behavioral performance

Analysis of response accuracy revealed a main effect of stimulus type, $F(1,96) = 28.2$, $p < .001$, $\eta_p^2 = .23$, with greater accuracy for non-target (99.4 ± 0.7% correct) stimuli relative to target (97.8 ± 2.9% correct) stimuli. No main effects, $F(1,96) = .48$, $p = .49$, $\eta_p^2 = .005$, or interactions, $F(1,96) = 2.5$, $p = .11$, $\eta_p^2 = .03$, with group were observed for response accuracy. Follow up analysis of early vs late trials for response accuracy revealed a main effect of Time, $F(1,96) = 5.3$, $p = .024$, $\eta_p^2 = .05$, with greater response accuracy for later trials (98.9 ± 2.1% correct) relative to early trials (98.3 ± 2.1% correct). No interactions with Time were observed, F's$(1,96) \leq 2.6$, p's $\geq .11$, η_p^2's $\leq .03$.

Analysis of reaction time revealed no significant differences between groups, $F(1,96) = .84$, $p = .36$, $\eta_p^2 = .009$; with follow up analysis observing a main effect of Time, $F(1,96) = 20.8$, $p < .001$, $\eta_p^2 = .18$, with longer RT observed for later trials (383.6 ± 41.7 ms) relative to early trials (370.4 ± 39.4 ms). No interactions with Time were observed, F's$(1,96) \leq 1.4$, $p \geq .23$, η_p^2's $\leq .02$. Similarly, analysis of intra-individual coefficient of variation of RT revealed no significant differences between groups, $F(1,96) = .18$, $p = .67$, $\eta_p^2 = .002$; with follow up analysis observing a main effect of Time, $F(1,96) = 12.4$, $p = .001$, $\eta_p^2 = .11$, with decreased variability for later trials (0.169 ± 0.053 ms) relative to early trials (0.193 ± 0.058 ms). No interactions with Time were observed for intra-individual coefficient of variation of RT, F's$(1,96) \leq .3$, p's $\geq .56$, η_p^2's $\leq .004$.

Table 2
Nonparametric bivariate correlations between injury variables, task performance, and neuroelectric measures.

Measure	Time since last concussion	Number of concussions	Concussions resulting in loss of consciousness
Oddball behavior			
Nontarget response accuracy (% correct)	0.065	−0.177	−0.148
Target response accuracy (% correct)	0.14	−0.088	−0.281*
Target reaction time (ms)	0.022	−0.206	−0.062
Target CV of RT (ms)	−0.133	0.038	0.307*
Oddball neuroelectric measures			
Nontarget amplitude (μV)	−0.02	0.089	0.03
Nontarget CV of amplitude (μV)	−0.036	−0.069	0.157
Nontarget latency (ms)	−0.076	−0.097	0.051
Nontarget CV of latency (ms)	0.097	−0.219	−0.176
Target amplitude (μV)	−0.099	0.138	0.009
Target CV of amplitude (μV)	0.108	−0.184	0.047
Target latency (ms)	−0.077	−0.026	0.278*
Target CV of latency (ms)	0.134	−0.132	0.034
Flanker behavior			
Congruent response accuracy (% correct)	−0.271	−0.144	−0.034
Congruent reaction time (ms)	0.042	0.065	0.253
Congruent CV of RT (ms)	0.025	0.089	0.295*
Incongruent response accuracy (% correct)	0.233	−0.219	−0.204
Incongruent reaction time (ms)	−0.238	0.121	0.377**
Incongruent CV of RT (ms)	0.054	0.104	0.289*
Overall response accuracy (% correct)	0.023	−0.213	−0.131
Overall reaction time (ms)	−0.12	0.089	0.347*
Overall CV of RT (ms)	0.039	0.116	0.325*
Flanker neuroelectric measures			
Congruent amplitude (μV)	0.053	0.133	−0.043
Congruent CV of amplitude (μV)	−0.007	−0.135	0.264
Congruent latency (ms)	0.235	−0.088	−0.098
Congruent CV of latency (ms)	0.032	−0.258	−0.005
Incongruent amplitude (μV)	0.076	0.196	−0.058
Incongruent CV of amplitude (μV)	−0.091	−0.12	0.09
Incongruent latency (ms)	−0.203	−0.147	−0.085
Incongruent CV of latency (ms)	−0.028	−0.108	−0.152
Overall amplitude (μV)	0.084	0.274	−0.032
Overall CV of amplitude (μV)	−0.068	−0.243	0.184
Overall latency (ms)	0.018	−0.075	−0.048
Overall CV of latency (ms)	0.023	−0.179	−0.034

* $p \leq 0.05$.
** $p \leq 0.01$.

3.2. Oddball task group differences in neuroelectric measures

Preliminary analyses of the number of trials used for ERP analysis revealed no significant differences between individuals with a history of concussion (target: 33.7 ± 6.6; non-target: 72.3 ± 28.4), and healthy controls (target: 35.5 ± 6.0; non-target: 73.5 ± 27.8; *t*'s (96) ≤ 1.4, *p*'s ≥ .16).

Analysis of P3 amplitude revealed a main effect of stimulus type, $F(1,96) = 269.1$, $p < .001$, $\eta_p^2 = .74$, with greater P3 amplitude for target (15.1 ± 7.1 μV) stimuli relative to non-target (5.2 ± 3.7 μV) stimuli. No main effects of Group, $F(1,96) = 1.2$, $p = .27$, $\eta_p^2 = .012$, or interactions of Group × Stimulus, $F(1,96) = .004$, $p = .95$, $\eta_p^2 < .001$, were observed for P3 amplitude (see Fig. 1). Examination of individual trial coefficient of variation of P3 amplitude, similarly, revealed no significant effects for Group, $F(1,96) = .38$, $p = .54$, $\eta_p^2 = .004$, Stimulus, $F(1,96) = .63$, $p = .43$, $\eta_p^2 = .007$, or interactions of Group × Stimulus, $F(1,96) = .22$, $p = .64$, $\eta_p^2 = .002$.

Analysis of P3 latency revealed no significant effects for Group, $F(1,96) = .09$, $p = .76$, $\eta_p^2 = .001$, Stimulus, $F(1,96) = .13$, $p = .72$, $\eta_p^2 = .001$, or interactions of Group × Stimulus, $F(1,96) = 1.5$, $p = .23$, $\eta_p^2 = .02$. A main effect of stimulus type was observed for individual trial coefficient of variation of P3 latency, $F(1,96) = 57.2$, $p < .001$, $\eta_p^2 = .37$, with greater variability for non-target (0.188 ± 0.015 ms) stimuli relative to target (0.162 ± 0.034 ms) stimuli. No main effects of Group, $F(1,96) = .5$, $p = .48$, $\eta_p^2 = .005$, or interactions of Group × Stimulus, $F(1,96) = 3.3$, $p = .07$, $\eta_p^2 = .03$, were observed for individual trial coefficient of variation of P3 latency.

3.3. Oddball task correlations with concussion history

Spearman's rho correlations indicated that the number of concussions resulting in loss of consciousness (N = 27 never lost consciousness, N = 13 lost consciousness after one concussion, N = 6 lost consciousness following concussion two times, N = 2 lost consciousness following concussion three times) was associated with poorer response accuracy to the target stimulus ($r = -0.28$, $p = .05$), increased variability of reaction time as indexed by the coefficient of variation ($r = 0.31$, $p = .03$), and longer P3 latency to the Target stimulus ($r = 0.28$, $p = .05$; see Table 2).

3.4. Flanker task differences in behavioral performance

Analysis of response accuracy revealed a main effect of group, $F(1,96) = 3.9$, $p = .05$, $\eta_p^2 = .04$, with poorer response accuracy observed for individuals with a history of concussion (85.3 ± 8.3% correct) relative to controls (88.4 ± 7.1% correct; $d = .40$); in addition to a main effect of congruency, $F(1,96) = 158.6$, $p < .001$, $\eta_p^2 = .62$, with more accurate responses observed in response to the congruent (92.5 ± 6.8% correct) relative to the incongruent (81.3 ± 10.7% correct) stimuli. No Group × Congruency interaction was observed for response accuracy,

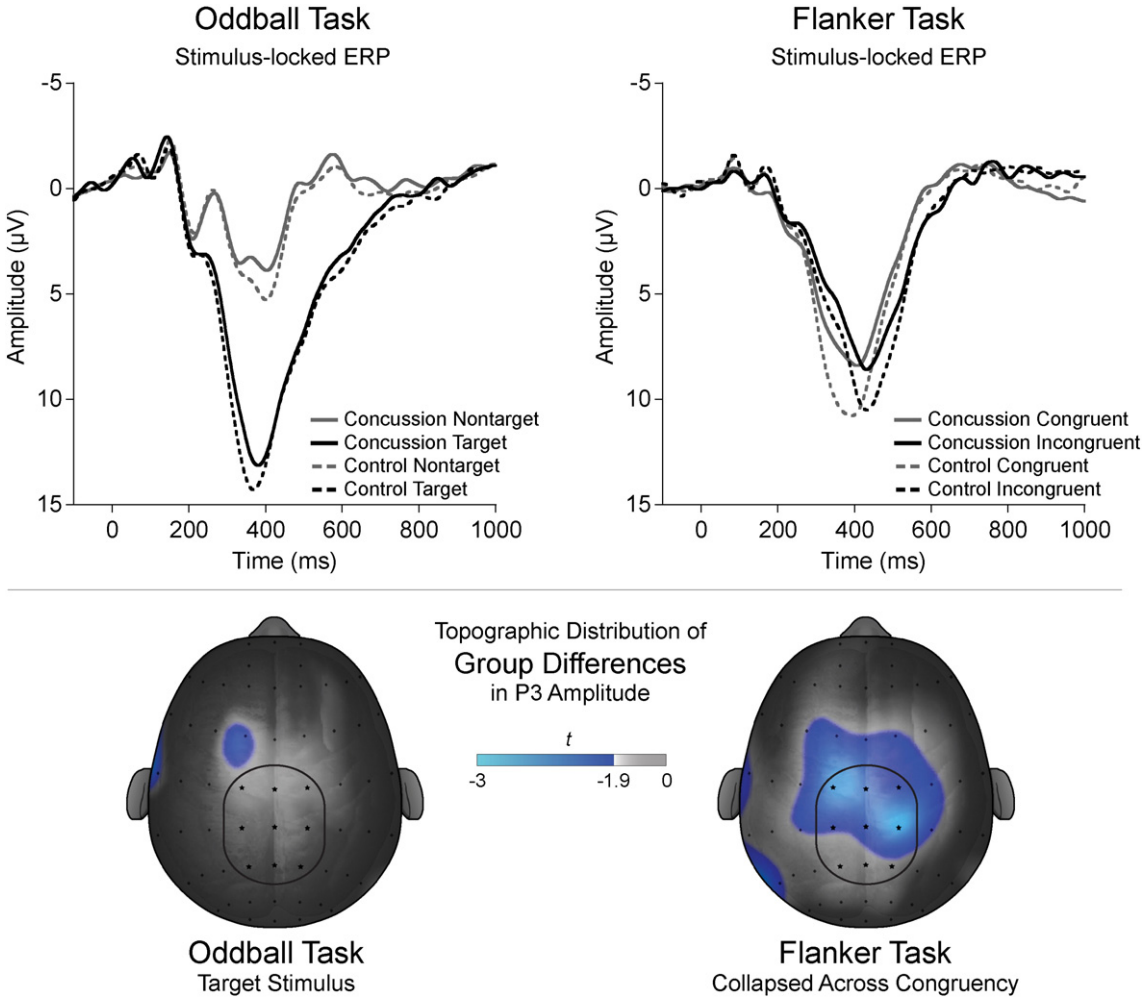

Fig. 1. Stimulus-locked ERP waveforms in response to the oddball task (left) and flanker task (right) as a function of group and stimulus type. The head plots provide the topographic distribution of the difference in P3 amplitude for the concussion group relative to the control group. The oddball data is presented only for the target stimulus which elicits the stereotypical P3 component (Polich, 2007), while the flanker data is collapsed across congruent and incongruent stimuli. The 9-electrode site region of interest used for analysis is indicated by the bounding box.

$F(1,96) = .13$, $p = .72$, $\eta_p^2 = .001$. Examination of early vs late trials revealed a main effect of Time, $F(1,96) = 11.6$, $p = .001$, $\eta_p^2 = .11$, with greater response accuracy for early trials (88.0 ± 8.0) relative to later trials (85.5 ± 9.4). No other interactions with Time were observed for response accuracy, F's$(1,96) \leq 1.5$, p's $\geq .22$, $\eta_p^2 \leq .02$.

Analysis of mean RT revealed a main effect of congruency, $F(1,96) = 291.2$, $p < .001$, $\eta_p^2 = .75$, with shorter RT in response to congruent (397.6 ± 48.3 ms) relative to incongruent (458.0 ± 58.3 ms) stimuli. No main effects of Group, $F(1,96) = .76$, $p = .38$, $\eta_p^2 = .008$, or interactions of Group × Congruency, $F(1,96) = .09$, $p = .76$, $\eta_p^2 = .001$, were observed for mean RT. Follow up analysis observed a main effect of Time, $F(1,96) = 13.0$, $p < .001$, $\eta_p^2 = .12$, with shorter RT for early trials (422.7 ± 46.8) relative to later trials (434.0 ± 59.4). No other interactions with Time were observed for mean RT, F's$(1,96) \leq 2.5$, p's $\geq .12$, $\eta_p^2 \leq .03$. Analysis of intra-individual coefficient of variation of RT revealed a main effect of Group, $F(1,96) = 5.6$, $p = .02$, $\eta_p^2 = .06$, with greater variability observed for individuals with a history of concussion (0.196 ± 0.04 ms), relative to controls (0.177 ± 0.038 ms; $d = .48$); as well as a main effect of congruency, $F(1,96) = 12.0$, $p = .001$, $\eta_p^2 = .11$, with larger coefficient of variation of reaction time in response to congruent (0.192 ± 0.048 ms) relative to incongruent (0.18 ± 0.038 ms) stimuli. No interaction of Group × Congruency was observed for intra-individual coefficient of variation of RT, $F(1,96) = .5$, $p = .48$, $\eta_p^2 = .005$. Follow up analysis revealed a main effect of Time, $F(1,96) = 24.7$, $p < .001$, $\eta_p^2 = .2$, with decreased variability for early trials (0.176 ± 0.039 ms) relative to later trials (0.192 ± 0.044 ms). No other interactions with Time were observed, F's$(1,96) \leq 1.9$, p's $\geq .18$, $\eta_p^2 \leq .02$.

3.5. Flanker task differences in neuroelectric measures

Preliminary analyses of the number of trials used for ERP analysis revealed no significant differences between individuals with a history of concussion (congruent: 58.6 ± 25.8; incongruent: 55.3 ± 23.8) and healthy controls (congruent: 67.8 ± 28.1; incongruent: 61.9 ± 29.2; t's $(96) \leq 1.7$, p's $\geq .09$).

Analysis of P3 amplitude revealed a main effect of Group, $F(1,96) = 4.4$, $p = .04$, $\eta_p^2 = .04$, with smaller P3 amplitude exhibited by individuals with a history of concussion (9.3 ± 5.0 μV) relative to controls (11.3 ± 4.9 μV; $d = .43$, see Fig. 1). No main effects of Congruency, $F(1,96) = .19$, $p = .67$, $\eta_p^2 = .002$, or interactions of Group × Congruency, $F(1,96) = .75$, $p = .39$, $\eta_p^2 = .008$, were observed for P3 amplitude. Examination of individual trial coefficient of variation of P3 amplitude, similarly, revealed no main effects of Group, $F(1,96) = .36$, $p = .55$, $\eta_p^2 = .004$, Congruency, $F(1,96) = 3.4$, $p = .07$, $\eta_p^2 = .03$, or interactions of Group × Congruency, $F(1,96) = .82$, $p = .37$, $\eta_p^2 = .009$.

Analysis of P3 latency observed a main effect of Congruency, $F(1,96) = 88.2$, $p < .001$, $\eta_p^2 = .48$, with longer P3 latency in response to incongruent (431.7 ± 37.3 ms) relative to congruent (395.6 ± 33.4 ms) stimuli. However, no main effect of Group, $F(1,96) = 1.4$, $p = .24$, $\eta_p^2 = .02$, or interaction of Group × Congruency, $F(1,96) = .04$, $p = .85$, $\eta_p^2 < .001$, was observed for P3 latency. A main effect of Congruency was observed for individual trial coefficient of variation of P3 latency, $F(1,96) = 8.0$, $p = .006$, $\eta_p^2 = .08$, with greater variability in response to congruent (0.164 ± 0.029 ms) relative to incongruent (0.156 ± 0.025 ms) stimuli. No main effects of Group, $F(1,96) = 1.1$, $p = .3$, $\eta_p^2 = .01$, or interactions of Group × Congruency, $F(1,96) = .42$, $p = .52$, $\eta_p^2 = .004$, were observed for individual trial coefficient of variation of P3 latency.

3.6. Flanker task correlations with concussion history

Spearman's rho correlations indicated that the number of concussions resulting in loss of consciousness was associated with increased reaction time for incongruent trials ($r = 0.38$, $p = .01$) and greater variability of reaction time for coefficient of variation across all trials of the flanker task ($r = 0.33$, $p = .02$; see Table 2).

4. Discussion

The present study provides initial evidence indicating that a previous concussive injury is associated with long-term increases in intra-individual variability. During the simple stimulus discrimination task (i.e., oddball task), negligible differences were observed between individuals with and without a history of concussion, regardless of the method for quantifying behavioral or neuroelectric measures. In response to the flanker task, however, lower overall mean response accuracy and greater intra-individual variability (as indexed by larger CV of RT) were observed for individuals with a history of concussive injury, relative to controls. At the neural level, although a history of concussive injury was associated with a reduction in the allocation of attentional resources (as indexed by smaller P3 amplitude) during the flanker task, no differences between groups were observed during the oddball task in terms of P3 amplitude or latency. Furthermore, no differences between groups were observed for ERP measures of intra-individual variability for either task. Collectively, the behavioral and neuroelectric differences between individuals with a history of concussion and controls were observed only in response to the flanker task.

The current study replicates and extends previous behavioral research in failing to observe concussion-related deficits during relatively simple cognitive tasks, both at the mean-level (Broglio et al., 2006, 2009; Collie et al., 2006; Guskiewicz et al., 2002; Iverson et al., 2006) and in terms of intra-individual variability (Broglio et al., 2006, 2009; Collie et al., 2006; Guskiewicz et al., 2002; Halterman et al., 2006; Iverson et al., 2006; Makdissi et al., 2001; Sosnoff et al., 2007). Thus, as suggested by Pontifex et al. (2009), tasks requiring lower-order cognitive operations appear to lack the requisite sensitivity required to detect the subtle, yet persistent deficits stemming from concussion in a young adult population. Although, it should be noted, that the number of times an athlete lost consciousness was related to both behavioral and neuroelectric function during the oddball task, suggesting that even lower-level cognitive processes may be effected with multiple, higher grade concussive injuries.

In the present study the concussion group exhibited an overall decrease in response accuracy relative to the control group during the flanker task, further validating the requisite sensitivity of flanker tasks for detecting persistent concussion-related deficits with a relatively large sample size (Collins et al., 1999; Ellemberg et al., 2007; Moore et al., 2014; Pontifex et al., 2009). The lack of any differential findings between congruent and incongruent trials of the flanker task, however would appear to suggest that such concussion related decrements in performance may not necessarily manifest as a function of demands placed on cognitive control operations; but rather appear to manifest when attentional systems are stressed above some threshold. That is, the oddball task used in the present investigation places relatively minimal demands on the attentional system, whereas the flanker task requires selectively attending only to a target stimulus and attentionally gating out the lateral flanking stimuli. Some insight into the mechanisms underlying this specificity is provided by recent findings by Moore et al. (2014) whom observed that concussed athletes exhibit a persistent decrease in P1 amplitude suggesting reduced sensory capture, and that this decrease in sensory capture was directly related to flanker performance. Thus, the combination of sensory and attentional demands of the flanker task may explain the general pattern of flanker deficits observed here and in other studies (Pontifex et al., 2009; Moore et al., 2014).

Such claims would also support recent findings by Karr et al. (2014), who observed a selective relationship between a previous concussive injury and impairments on multiple measures of cognitive control tasks. In a similarly sized sample of 52 concussed college-athletes and 86 athletes without a concussive-injury, Karr et al. (2014) observed

concussion-related impairments in cognition only for aspects of set-shifting (assessed using a global–local task) with no relationship observed for inhibition (assessed using a Go/Nogo task) or working memory (assessed using a n-back task). These discrepant results may simply reflect the heterogeneity of concussive outcomes (Aubry et al., 2002; Livingston et al., 2010); however, as the authors note and further reinforcing the assertion made herein, the lack of a relationship for behavioral inhibition and working memory may also be a function of the ease at which participants were able to complete those tasks relative to the shifting task (Karr et al., 2014). Thus, while the Go/Nogo task is well established as demanding of inhibitory control, the sensory and attentional demands of such a task on an individual stimulus level are more similar to oddball task than the flanker task used within the present investigation. Although speculative, from this perspective then it would seem that the sensory and attentional characteristics of a task may more strongly relate to deficits related to concussive injury than the cognitive demands alone. Indeed a number of recent investigations observing concussion related impairments in cognition have utilized tasks with high sensory and attentional demands (i.e., the attentional-networks task/flanker task, and task switching paradigms; Howell et al., 2013; Mayr et al., 2014; Moore et al., 2015). These findings highlight the inherent difficulty of investigating the long-term cognitive consequences of a concussive injury as individuals appear to be cognitively healthy; with deficits emerging only with increasing environmental demands, such that these subtle, yet persistent deficits stemming from concussive injuries may go undetected in the absence of an appropriate assessment.

It is important to note, however, that such a premise was not explicitly tested within the present investigation, thus further research is needed to better address the apparent importance of sensory and attentional demands for detecting concussion related deficits. Indeed, a limitation of the present investigation was that such differences between groups may have occurred as a function of the fixed order of the presentation of the oddball and the flanker tasks. Although analysis separating early relative to later trials within each tasks would seem to indicate that such differences are not occurring as a result of fatigue; other differences inherent in the tasks such as the response frequency characteristics, the total number of stimuli presented, and the probability of the target-response indicating stimulus occurring may be important for establishing the context for concussion related deficits to become apparent. As work in this area continues, it will be important to more carefully control such task characteristics to determine how they may factor-in for detecting the prolonged effects of concussive injury for cognition.

Also of importance is consideration of how performance on such tasks is assessed. Beyond poorer overall response accuracy during the flanker task, individuals with a history of concussive injury also responded less consistently as indexed by larger CV of RT. Thus, the flanker task may be of dynamic utility for evaluating cognition in individuals with a history of concussion, as multiple performance indices appear sensitive to concussive injury. Although the precise underlying mechanisms accounting for the observed concussion-related differences in response variability are uncertain, theoretical proposals have suggested that these inconsistencies in performance may result from failures in the ability to sustain attentional focus (Bunce et al., 1993) and impairments in the frontal gray and white matter of the brain. A growing body of research has also highlighted an association between increases in variability resulting from age-related changes in cerebral blood flow, cortical thinning, vascular injury, and neurological conditions with structural and functional alterations in frontal gray and white matter (Britton et al., 1991; Bunce et al., 2007; Sowell et al., 2003; Stuss et al., 2003; Walhovd and Fjell, 2007; but see Garrett et al., 2013 for review). Relative to concussion related injuries; in contrast to claims that concussion related impairments resolve within 10 to 14 days (McCrea et al., 2009; McCrory et al., 2013), a growing body of literature has observed decreased gray matter volumes in formerly concussed individuals in areas supporting high level cognitive operations, including the dorsolateral prefrontal cortex, anterior cingulate cortex (Chen et al., 2004, 2008) and hippocampus (Tremblay et al., 2013). Further, evidence from human autopsy and animal investigations implicate axonal pathology – hypothesized to be the result of stretching and shearing of axonal fibers when the concussive impact is transmitted throughout the brain – as potentially underlying clinical symptomologies of a traumatic brain injury such as a concussion (Bigler, 2013). Indeed, differences in white matter volume, diffusivity and connectivity have been observed in association with a history of concussive injury (Chu et al., 2010; Messe et al., 2011; Tremblay et al., 2011; Wilde et al., 2008) and have been strongly associated with response variability during performance on cognitively taxing tasks in other neurological populations (Tamnes et al., 2012). Further, coupled with such damage to axonal tracts within white matter, a concussive injury also appears to result in an excessive release of GABA within the brain, which has been linked to deficits in functional neural plasticity (de Beaumont et al., 2009). Thus, following initial perturbations associated with the concussive impact, neuro-inflammatory processes – related to dysregulation between metabolic demands for restoring neural tissue and deficits in cerebral glucose availability – and impaired functional plasticity may contribute to these deficits in cognition associated with a history of concussion (Bigler, 2013). However, additional research is necessary to gain insight into the relation between differences in response variability associated with a previous concussive injury and the structural and functional integrity of such neural networks.

Also novel to the present investigation was the assessment of neuroelectric variability in response to both a simple stimulus discrimination task and a more demanding flanker task. Findings from this investigation revealed that a previous concussive injury was also associated with a reduction in the allocation of attentional resources (as indexed by smaller overall P3 amplitude) only in response to the flanker task. Thus, contrary to previous research indicating a reduction in the allocation of attentional resources in the service of context updating (i.e., decreased mean P3 amplitude) and delays in processing speed (i.e., longer mean P3 latency) during simple stimulus-discrimination tasks, we found no difference between individuals with and without a history of concussion (Broglio et al., 2009; de Beaumont et al., 2009; Gaetz et al., 2000; Theriault et al., 2009). As prior investigations assessing neuroelectric indices of attention exhibit large variations in participant characteristics in terms of age range, sex, time since previous injury, age at injury, numbers of concussions incurred, and injury severity; it is not necessarily surprising that some differences within the literature exist. In particular, it is important to note the heterogeneity in the length of time since the occurrence of a concussive injury with some participants being only a year out whereas others incurred the concussive injury a decade prior. Thus a key limitation in examining how such factors may moderate these findings within the present investigation is the small sample size, with sufficient power to detect only those relationships which exhibited moderate or stronger correlations. Accordingly, as the moderating effects of these factors may be smaller than the present investigation was powered to detect, this remains an area in need of further research. However, as over 40% of our concussion group had a history of concussive injury that resulted in loss of consciousness, we were able to examine the moderating effect of loss of consciousness. Although loss of consciousness following a concussive injury has been minimized as a relevant indicator of injury severity in recent position statements regarding concussion/mTBI; the finding of an association between the number of concussions resulting in loss of consciousness and greater variability in performance across cognitive tasks suggests that such statements relative to injury severity may have been premature, and highlight the importance of going beyond behavioral measures of central tendency.

The participant characteristics also highlight a limitation within this investigation, which focused only on post-concussion assessments without regard to baseline differences prior to injury. This limitation

may also be waged at the vast majority of the literature aimed at the long-term influences of a concussive injury. Specifically, given the cross-sectional nature of this investigation, it is possible that individual differences or some other factor may account for the observed differences between individuals with and without a previous concussive injury. While this possibility is minimized by the collection of other demographic variables (e.g., IQ, years of education); such retrospective reporting can limit the generalizability and consistency of the currently observed findings relative to other investigations. Given the substantial cost of longitudinal, controlled, prospective designs, as well as limitations that occur with test administration at multiple time points (e.g., learning effect, desensitization); cross-sectional findings are of substantial utility not only for elucidating persistent neurocognitive deficits, but also for guiding the design and implementation of future longitudinal paradigms. Accordingly, findings from this and other cross-sectional investigations have furthered the field of concussion research, and collectively indicate that careful consideration of the specificity and difficulty of cognitive assessments is required to fully elucidate the long-term neurocognitive sequelae stemming from concussive injuries (Bigler, 2013; Broglio et al., 2009; Moore et al., 2014).

The current study provides evidence that the examination of intra-individual variability may provide complementary information to measures of central tendency, yielding a more refined understanding of neurocognition as it relates to concussive outcomes. In addition, the current results further reinforce the idea that relatively simple stimulus-discrimination tasks are ill-suited to detect subtle deficits stemming from concussion in the long-term stage of injury, such that only with multiple higher grade concussive injuries do impairments in the speed of stimulus-processing and classification manifest. These findings also suggest that the sensory and attentional demands of the task may be of particular importance to facilitate detection of concussion related impairments. In concert, the implementation of more sensitive and challenging paradigms as well as a more deft approach to data analysis (intra-individual variability) may provide unique identifiers of cognitive dysfunction to detect subtle deficits indicative of long-term cognitive impairment. These findings further reaffirm claims associated with impairments in the allocation of attentional resources associated with a history of concussion, providing evidence that such findings are not merely reflective of greater underlying neural variability. Thus, it appears that the observed increases in behavioral variability manifest at some point between attentional engagement and response production. Clearly, additional longitudinal research is necessary to advance the current findings and further delineate the nature and selectivity of the relationship between concussion history and neurocognition across a variety of environmental demands. Ultimately, the current patterns of results suggest that the persistent influence of concussion on brain and cognitive health may relate not only to overall performance, but also to the consistency of cognitive performance as well.

Conflicts of interest

None of the authors have potential conflicts of interest to be disclosed.

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