Do sport-related concussions result in long-term cognitive impairment? A review of event-related potential research

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Abstract

Sport-related concussions have become a major public health concern although the long-term effects on cognitive function remain largely unknown. Event-related potentials (ERPs) are ideal for studying the long-term impact of sport-related concussions, as they have excellent temporal precision and provide insight that cannot be obtained from behavioral or neuropsychological measures alone. We reviewed all available published studies that have used stimulus or response-locked ERPs to document cognitive control processes in individuals with a history of concussion. Collectively, cross-sectional evidence suggests consistent reductions in P3 amplitude in previously concussed individuals, as well as a possible impairment in cognitive processing speed (P3 latency) and error monitoring processes (ERN). The persistent neurophysiological changes found may be related to the number of previous concussions sustained and the time since injury. Future studies incorporating prospective research designs are warranted before definitive statements can be offered regarding the long-term impact of sport-related concussions on cognitive control.

1. Introduction

Approximately 1.6 to 3.8 million concussions occur annually in the U.S. as a result of competitive and recreational sports participation (Langlois et al. 2006). It is estimated that as many as 50% of these mild traumatic brain injuries (mTBIs) go undiagnosed or unreported (Faul et al. 2010; Harmon et al. 2013). Sport-related concussions have received increasing scientific and popular press attention over the past decade, driven in part by an increasing number of high profile cases involving former professional athletes who have suffered from debilitating and life threatening mental health conditions and the heightened incidence of chronic traumatic encephalopathy (CTE), a progressive neurodegenerative disease found in individuals with a history of repetitive brain trauma. As a result, a number of public health initiatives (e.g., Centers for Disease Control and Prevention’s HEADS UP; National Football League’s Play Smart, Play Safe) and research programs (e.g., Sports and Health Research Program) have been established to spur advancements in concussion prevention, injury detection, and post-injury treatment and management strategies. Despite the increased attention, much remains unknown about the immediate and long-term neuropsychological consequences of sport-related concussions.

Accurate diagnosis of concussion and evidence related to persistent symptoms remains elusive, in part due to individual differences and the nature of linear and/or rotational biomechanical forces resulting in injury. Acute symptoms include headache, dizziness, nausea, vomiting, abnormal balance and postural instability, cognitive deficits, sleep disruption, and sensitivity to light and noise. Such clinical symptoms are often used in addition to brief neuropsychological measures (e.g., Standardized Assessment of Concussion; SAC) to inform sideline concussion assessment and to assist on-the-field clinical decision making. Although these brief neuropsychological evaluations are practical and effective, they are not meant to replace more comprehensive neuropsychological testing aimed at documenting subtle deficits that may persist beyond the acute phase of injury (McCrorry et al. 2013). Standardized neuropsychological tests assessing memory, visuospatial processing, and executive function have advanced clinical practice and comprehensive concussion management. However, given the complexity of concussive injuries and the number of patients who develop persistent symptoms beyond the expected clinical recovery window (i.e., 10–14 days), there remains a critical need for unbiased, objective tools to aid in diagnosing injury, tracking progress toward recovery, and guiding return-to-play decision-making (Covassin et al. 2009).
One limitation surrounding traditional neuropsychological assessments is their lack of sensitivity to detect underlying cognitive processes that may be impaired by ‘silent’ (i.e., not readily observable) concussive injuries (Ellemberg et al. 2009). For instance, Broglio et al. (2014) contend that neuropsychological testing ‘...should never be used in isolation but rather in conjunction with symptom and motor-control assessments to support the clinical examination.’ (p. 252). In addition, Resch et al. (2013) reported variable test-retest reliability for the ImPACT and low sensitivity for classifying concussions among two separate groups from an Irish and U.S. university. Concussions may lead to disruptions in select aspects of cognitive function (e.g., attention, memory) and/or impairments in a single (e.g., sensory processing) or multiple (e.g., visual attention and working memory) cognitive processes, which are difficult to disentangle based on gross performance on standard neuropsychological tests. Furthermore, it is well known that most readily observable concussion-related symptoms resolve within 10–14 days in acutely injured athletes (Belanger and Vanderploeg 2005; McCrea et al. 2003) despite evidence suggesting persistent neuropsychological deficits that endure well beyond symptom reduction (Broglio et al. 2011; Daneshvar et al. 2011; Moore et al. 2015; Urukawa et al. 2004). The extent to which these persistent deficits impact long-term health and overall quality of life remains unknown. Fortunately, advancements in neuroscience techniques, including electroencephalography (EEG), functional magnetic resonance imaging (fMRI), resting-state functional connectivity (rsFC), diffusion tensor imaging (DTI), positron emission tomography (PET), and magnetic resonance spectroscopy (MRS) may provide valuable information on subtle, covert disruptions in cognitive function following sport-related concussion and assist in documenting persistent deficits. One such approach that has received increasing research attention is the event-related potential (ERP) technique. ERPs are useful in measuring mental operations that are time-locked to internal or external events and represent neural processes that are otherwise undetectable through overt measures of behavioral performance (e.g., response accuracy and reaction time). In addition, ERPs can be used to capture brain activity even when an overt behavioral response is not warranted or able to be made, which may be particularly important in the area of sport-related concussions. Accordingly, the purpose of this review is to provide an overview of the ERP technique and highlight strengths and limitations of using this method to gain insight into the relationship between sport-related concussions and potential for long-term impairment in cognitive control processes. Subsequently, we provide an overview of research that has used this methodology and outline important considerations for designing future ERP experiments.

2. Event-related potentials

ERPs are voltage fluctuations in the ongoing EEG that are time-locked to a specific event, such as the presentation of a visual stimulus or execution of a manual response (Luck 2014). They are extracted from the continuous EEG signal and can provide insight into temporal mechanisms related to ongoing neural processes before, during, and after behavioral responses, thus providing insight that cannot be obtained solely from behavioral or neuropsychological measures (Luck and Kappenman 2012). The ongoing EEG activity is most commonly captured non-invasively via electrodes placed on the head to measure voltages at various locations across the scalp. The voltage fluctuations reflect the summation of postsynaptic potentials that occur simultaneously in cortical pyramidal neurons. Since ERPs are conducted nearly instantaneously through the brain and surrounding tissue, they provide excellent temporal resolution within the millisecond (ms) range. However, unlike other brain imaging techniques (e.g., fMRI and PET), ERPs provide relatively poor spatial resolution. That is, it is difficult to make assumptions about the actual source of an ERP signal, as the recorded activity at the scalp reflects the weighted sum of voltages from all active neural generators and not only those closest to the electrode sites (Freeman 1980; Jackson and Bolger 2014). Considering that postsynaptic potentials can occur simultaneously in multiple brain regions and spread rapidly and laterally across the scalp, voltages recorded at a given electrode site typically reflect activity from multiple brain areas (Luck 2014). Therefore, when designing ERP experiments, it is important to consider their main strength, which is the ability to capture moment by moment cognitive or mental processes as they unfold over time.

A growing body of literature incorporating various ERP components have investigated the long-term consequences of sport-related concussions across a variety of sensory and cognitive processes (Baillargeon et al. 2012; Broglio et al. 2011; Dupuis et al. 2000; Ellemberg et al. 2009; Gosselin et al. 2012). For the purpose of this review, the focus will be limited to ERP components related to cognitive control, which represents a collection of top-down mental processes necessary for governing more basic cognitive functions and emotions, as well as guiding goal-directed behaviors (Botvinick et al. 2001). Cognitive control impairments in information processing, planning, memory, and mental switching processes are commonly reported following concussions, which was outlined in the Summary and Agreement Statement of the first International Conference on Concussion in Sport (Aubry et al. 2002). Cognitive control processes are critical for cognitive, affective, and social development as well as success in school, at work, and in life (Diamond 2013). Thus, it is essential to understand how cognitive control processes may be impacted following sport-related concussions.

3. Selection of studies

The most commonly studied ERP components in the sport-related concussions and cognitive control literature include the stimulus-locked N2 and P3, and the response-locked error-related negativity (ERN) and error positivity (Pe) components (see Figs. 1 and 2 for examples of these ERP components). These components have garnered considerable interest due to their relevance to cognitive control, attention, and performance monitoring processes (Polich 2007; Resch et al. 2013; Rietdijk et al. 2014). Thus, we performed a literature search using the PubMed database for all available published studies through January 01, 2017 examining the relationship between a history of sport-related concussion and N2, P3, ERN, and Pe components. Relevant papers were identified by using various combinations of the following terms: concussion, sport, mild traumatic brain injury, cognitive control, attention, performance monitoring, event-related potential, electrophysiology, neurophysiology, neuroelectric, N2, P3, P300, ERN, and Pe. Additional papers relevant for inclusion were identified from the reference lists from all articles identified from the PubMed database.
search. Studies were included if the sample consisted of a majority of individuals (i.e., at least 50% of the study sample) with a history of sport-related concussion. Articles were excluded if they did not include sport-related concussion (e.g., those occurring from car accidents or falls) as an independent variable, and at least one cognitive control-related ERP component as a dependent variable.

4. Cognitive control-related ERP components

In the following sections, we highlight research that has incorporated N2, P3, ERN, and Pe components to characterize the potential long-term cognitive control deficits following sport-related concussion. A general description of the study characteristics and primary findings related to cognitive control are shown in Table 1.

4.1. N2: Inhibitory control and conflict monitoring

The N2 component is a negative deflection in the stimulus-locked ERP with a maximal frontocentral scalp distribution that peaks approximately 200–350 ms following stimulus onset (Folstein and Van Petten 2008; Larson et al. 2014). Differences in N2 amplitude are typically observed during varied trial types of inhibitory cognitive control tasks, such as the Eriksen flanker task, Stroop paradigm, or oddball task, where participants are instructed to respond to target stimuli while inhibiting task irrelevant stimuli. For instance, during a typical flanker task, individuals are encouraged to respond to the direction of a central arrow while ignoring the direction of incompatible flanking arrows. Incongruent trials (< < > < < or > > < > > > > ) require higher levels of conflict processing relative to congruent trials (< < < < < or > > > > > > > > ), as reflected by a more pronounced (more negative) N2 (Folstein and Van Petten 2008). Successful task performance is governed by the ability to modulate top-down cognitive control, particularly for incongruent flanker task trials (Alderman et al. 2015). Although it has been suggested that N2 elicited by different tasks might not represent the same cognitive processes (Larson et al. 2014), in general the N2 component is considered an index of conflict monitoring processes (Clayson and Larson 2011; Nieuwenhuis et al. 2003; Yeung et al. 2004).

Seven cross-sectional studies have investigated N2 as an index of conflict-related processing among individuals with a history of sport-related concussion (Broglio et al. 2009; Gaetz et al. 2000; Gosselin et al. 2012; Ledwidge and Molfese 2016; Moore et al. 2016; Moore et al. 2014). Across these studies, three found larger N2 amplitude among individuals with a history of concussion relative to non-concussed comparison subjects (Ledwidge and Molfese 2016; Moore et al. 2014 [switch task]; Moore et al. 2015), while only one study (Broglio et al. 2009) reported smaller N2 among previously concussed athletes, notably without a significant between group difference on the ImPACT. In this study, Broglio et al. examined N2 amplitude and latency measures in young adult male and female athletes with (n = 46) and without (n = 44) a self-reported history of a physician-diagnosed concussion (average time since concussion = 3.4 years). N2 was elicited by a three stimulus oddball task and amplitude was measured as the maximum peak amplitude occurring 150–300 ms post-stimulus while latency was measured as the time point corresponding to the maximum peak amplitude. Relative to controls, those with a concussion history had smaller N2 amplitudes at Fz and Cz electrode sites, while no between group differences in N2 latency were found. In contrast, Ledwidge and Molfese (2016) examined N2 amplitudes elicited during a two-tone auditory oddball task among a sample of previously concussed male NCAA Division I athletes relative to non-concussed athletes. The amount of time since the most recent concussion ranged from 4 months to 11 years, with an average of 4 years. Although no differences were found for N2 latency, a larger N2 amplitude was found in athletes with a concussion history leading the authors to speculate that this larger N2 represents greater cognitive conflict and inefficient recruitment of neural resources to successfully meet task demands. Using visual oddball, switch, and flanker tasks, Moore et al. (2014) also observed larger N2 amplitude and increased N2 latency in 19 previously concussed young adults relative to 21 control participants during the switch task, while no differences in N2 amplitude or latency were observed during the oddball and flanker tasks. Interestingly, although there were no significant between group differences in behavioral performance (reaction time, accuracy) for the oddball task, participants in the concussed group were significantly less accurate on the flanker task relative to the non-concussed control group.

In addition to the adult literature, recent research has also examined concussion outcomes in pediatric samples, which is significant given the lack of evidence on the neurophysiological effects of sport-related concussion in youth and emerging research suggesting that concussions during childhood may be most devastating to healthy development (Zemek et al. 2013). Using a modified flanker task, Moore et al. (2015) examined N2 amplitude and latency in 32 children aged 8–10 years (n = 16 with a concussion history) and observed increased N2 amplitude during the incongruent trials and longer N2 latency during both task conditions among children with a concussion history. Based on their findings, the authors concluded that neurocognitive processing deficits extend past the acute recovery period, and that children injured earlier in life may experience poorer outcomes. Moore et al. (2016) followed this study by measuring N2 amplitude and latency in a sample of thirty 8–10 year old children (n = 15 with a concussion history) using two separate conflict-related tasks, including the switch and go/no-go tasks. On average, children with a concussion history did not differ from healthy controls in N2 amplitude; however, there was a delay in N2 latency for those with concussion history, indicating disrupted stimulus-response conflict detection, which are indicative of subtle deficits in conflict-related processing. Previously concussed children also demonstrated subtle impairments in behavioral performance on both the switch task and go/no-go tasks. Furthermore, the age in which children were injured was related to the magnitude of several concussion-related deficits, highlighting age as a potential moderator of the long-term effects of pediatric concussion. To date, it remains unclear whether concussion results in a differential pattern of N2 responses between children and adults. In order for more definitive conclusions to be made, future research efforts should explore this relationship by examining the N2 component and prolonged symptoms following concussion using similar experimental designs.

Despite the previous findings, four studies to date have failed to find any between group differences by concussion status on N2 amplitude (Gaetz et al. 2000; Gosselin et al. 2012; Moore et al. 2016; Moore et al. 2014 [oddball and flanker]). Similar to the lack of between-group findings in the oddball and flanker tasks, other studies have not supported differences in N2 amplitude and latency measures (Gaetz et al. 2000; Gosselin et al. 2012), besides revealing injury variables that may be associated with altered conflict-related processing. For example, Gaetz et al. (2000) investigated the influence of multiple concussions on functional systems related to cognitive ERPs during a visual oddball task in a group of 60 athletes with a variable history of concussion. The
Summary of research investigating the relationship between sport-related concussion and ERP measures of cognitive control.

**Publication Sample Paradigm ERP Components ERP Measurements and Time Main ERP Findings**

**Baillargeon et al. (2012)** 96 male athletes (32 children, 34 adolescents, 30 adults), 48 concussed, 48 non-concussed. Visual Oddball P3a, P3b No differences in P3a amplitude or latency. Lower P3b amplitude for concussed athletes across all age groups. Reduced P3 amplitude relative to controls. No group differences in N2 latency. No group differences in the post-concussion symptom scale. Reduced P3b amplitude was positively associated with accuracy on the Rey-Osterrieth Complex Figure Test.

**De Beaumont et al. (2007)** 45 university football players (15 with a history of one concussion, 15 with two or more concussions, and 15 non-concussed controls). Visual Search Oddball P3 No amplitude or latency differences in the concussed group relative to controls. In former concussed athletes, there were negative relationships between P3a amplitude and incorrect trial accuracy and P3b amplitude and fractional accuracy interference effect. Longer P3a latency and reduced amplitudes in the concussed group relative to controls. In former concussed athletes and flasher incongruent trial accuracy and fractional accuracy interference effect. Reduced P3 amplitude for rare stimuli and P3 amplitude rare-frequent difference wave for concussed football players, even concussive relative to controls. No differences in P3b amplitude or latency and no differences in the post-concussion symptom scale. There was a negative association between concussion symptom severity and the P3 rare-frequent difference wave. No P3 latency differences between groups.

**De Beaumont et al. (2009)** 90 young adults (46 with mTBI history, 44 without mTBI). Visual Oddball N2 No amplitude or latency differences in the concussed group relative to controls. In former concussed athletes and flasher incongruent trial accuracy and fractional accuracy interference effect. Reduced P3 amplitude relative to control athletes. In formerly concussed athletes, there was a negative relationship between number of concussions sustained and ERN-CRN difference wave. No differences in P3b amplitude relative to controls. There was a positive relationship between P3 latency and increasing severity of post-concussion symptom reports.

**Dupuis et al. (2000)** 30 athletes (10 controls, 10 symptomatic, 10 asymptomatic). Auditory Oddball P3 No amplitude differences in the concussed group relative to controls. In former concussed athletes and flasher incongruent trial accuracy and fractional accuracy interference effect. Reduced P3 amplitude relative to control athletes. In formerly concussed athletes and flasher incongruent trial accuracy and fractional accuracy interference effect. Reduced P3 amplitude in symptomatic concussed individuals relative to formerly concussed athletes, three concussions or more relative to controls. No differences in P3 latency differences between groups. No differences in N2 amplitude or latency. No differences in Pe amplitude by group. Reduced ERN amplitude in athletes with 3+ concussions relative to formerly concussed athletes, three concussions or more relative to controls. No differences in Pe latency differences between groups. No differences in Pe amplitude by group. Reduced ERN amplitude in athletes with 2+ concussions relative to formerly concussed athletes, three concussions or more relative to controls. No differences in Pe latency differences between groups. No differences in Pe amplitude by group. Reduced ERN amplitude in athletes with 3+ concussions relative to formerly concussed athletes, three concussions or more relative to controls. No differences in Pe latency differences between groups. No differences in Pe amplitude by group. Reduced ERN amplitude in athletes with 2+ concussions relative to formerly concussed athletes, three concussions or more relative to controls. No differences in Pe latency differences between groups. No differences in Pe amplitude by group. Reduced ERN amplitude in athletes with 3+ concussions relative to formerly concussed athletes, three concussions or more relative to controls. No differences in Pe latency differences between groups. No differences in Pe amplitude by group. Reduced ERN amplitude in athletes with 2+ concussions relative to formerly concussed athletes, three concussions or more relative to controls. No differences in Pe latency differences between groups. No differences in Pe amplitude by group. Reduced ERN amplitude in athletes with 3+ concussions relative to formerly concussed athletes, three concussions or more relative to controls. No differences in Pe latency differences between groups. No differences in Pe amplitude by group.
<table>
<thead>
<tr>
<th>Publication</th>
<th>Sample</th>
<th>Main ERP Findings</th>
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<tbody>
<tr>
<td>Gosselin et al. (2006)*</td>
<td>84 participants (44 mTBI, 40 controls)</td>
<td>Reduced P3 amplitude in individuals with mTBI. Greater severity of depression symptoms was correlated with smaller P3 amplitude. Time since injury and post-traumatic amnesia were positively associated with P3 amplitude. Reduced P3 latency in asymptomatic and symptomatic concussed athletes relative to controls. No differences in P3 amplitude or latency.</td>
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<tr>
<td>Gosselin et al. (2012)*</td>
<td>82 participants (44 mTBI, 40 controls)</td>
<td>Reduced P3 amplitude in individuals with mTBI. Greater severity of depression symptoms was correlated with smaller P3 amplitude. Time since injury and post-traumatic amnesia were positively associated with P3 amplitude. Reduced P3 latency in asymptomatic and symptomatic concussed athletes relative to controls. No differences in P3 amplitude or latency.</td>
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<tr>
<td>Larson et al. (2012)</td>
<td>82 participants (36 individuals with mTBI and 46 healthy controls)</td>
<td>Reduced P3 amplitude in individuals with mTBI. Greater severity of depression symptoms was correlated with smaller P3 amplitude. Time since injury and post-traumatic amnesia were positively associated with P3 amplitude. Reduced P3 latency in asymptomatic and symptomatic concussed athletes relative to controls. No differences in P3 amplitude or latency.</td>
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<tr>
<td>Lavoie et al. (2004)</td>
<td>30 athletes (10 concussed with symptoms, 10 nonconcussed controls).</td>
<td>Reduced P3 amplitude during rare trials for symptomatic and asymptomatic concussed athletes. A positive association emerged between P3 amplitude and time since last concussion. No differences in P3 latency.</td>
</tr>
<tr>
<td>Moore et al. (2014)</td>
<td>40 young adults (19 concussed, 21 nonconcussed controls).</td>
<td>Reduced P3 amplitude across both trial types. No differences in P3 latency. Reduced P3 amplitude during incompatible trials. These trials were observed. A positive association emerged between P3 amplitude and time since last concussion. No differences in P3 latency.</td>
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<tr>
<td>Moore et al. (2015)</td>
<td>32 children ages 8–10 yrs. (16 concussed, 16 nonconcussed controls).</td>
<td>Reduced P3 amplitude across both trial types. No differences in P3 latency. Reduced P3 amplitude during incompatible trials. These trials were observed. A positive association emerged between P3 amplitude and time since last concussion. No differences in P3 latency.</td>
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<td>Publication</td>
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<td>Moore et al. (2016)</td>
<td>30 children ages 8-10 yrs. (15 concussed, 15 control).</td>
<td>n-Back, Go/No-Go, and Switch Task</td>
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<tr>
<td>Moore et al. (2017)</td>
<td>49 male university soccer athletes (14 concussed, 16 sub-concusive, 19 non-contact controls).</td>
<td>Oddball</td>
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<td>Ozen et al. (2013)</td>
<td>34 participants (17 concussed and 17 nonconcussed controls).</td>
<td>N-back</td>
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<tr>
<td>Parks et al. (2015)</td>
<td>50 controls and 48 college students (22 with one concussion, 26 with two or more concussions)</td>
<td>Flanker and Visual Oddball</td>
</tr>
<tr>
<td>Pontifex et al. (2009)</td>
<td>66 college-aged athletes (30 concussed and 36 nonconcussed controls).</td>
<td>Flanker</td>
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<tr>
<td>Theriault et al. (2009)</td>
<td>32 university varsity athletes (10 recently concussed (5–12 months post-injury), 12 late concussed (22–60 months post-injury, and 10 nonconcussed controls).</td>
<td>Auditory Oddball</td>
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* amplitude measured as the difference between the mean pre-response baseline and the designated amplitude measurement.
$ ± 1.5$ ms mean interval surround the largest peak.
% ± 25 ms mean interval surround the largest peak.
* study also investigated ERP components not related to cognitive control.
sample was divided into four evenly divided groups (0, 1, 2, 3+ concussions), each consisting of 15 athletes. Regardless of concussion history, there were no group differences for N2 amplitude and latency. More recently, Gosselin et al. (2012) evaluated the relationship between ERP indices of cognitive control elicited during a working memory task on postconcussion symptoms, type of injury (sport concussion or other), and time since last injury in 44 patients with mTBI compared to 40 age- and sex-matched control volunteers. No significant between group differences or group by region interactions were found for N2 amplitude and latency, although they did find impaired accuracy for the more difficult working memory task condition among the mTBI patients.

In sum, the current evidence related to the relationship between a history of sport-related concussion and conflict-related processing (N2) is inconsistent. A majority of the findings suggest that sport-related concussion does not impact upon N2 amplitude or latency measures collected months to years following injury; however, some studies suggest an increase in conflict monitoring processes during conflict detection tasks in both children and young adults (Ledwidge and Molfese 2016; Moore et al. 2016; Moore et al. 2014), with one study (Broglie et al. 2009) reporting reduced N2 amplitude. The lack of consistent findings in this area is likely due to a number of reasons, including the considerable variation in cognitive tasks employed (i.e., oddball, working memory task, flanker, switch, n-back, and go/no-go tasks), study sample heterogeneity (e.g., gender, presence of mental health disorders, injury-related moderators such as loss of consciousness), and study designs. These methodological considerations will be further addressed below.

4.2. P3: Information processing and attention

The P3, or P300, first discovered in 1965, is one of the most commonly studied ERP components within the broader psychology literature. P3 represents a positive deflection observed at midline parietal scalp recording sites that arises approximately 300–800 ms after stimulus presentation. The P3 is typically elicited during stimulus probability tasks, such as the “oddball” paradigm, where participants attend to target stimuli that are presented infrequently among more frequently occurring standard stimuli. For instance, in a three stimulus oddball task, participants are presented with a frequently occurring standard stimulus (e.g., the letter “X”) and a distractor stimulus that occur with lower probability. Although a precise understanding of the P3 remains elusive (Polich 2012), the amplitude is sensitive to the amount of attentional resources engaged during task performance, while the latency is believed to index stimulus evaluation speed (Kutas et al. 1977; Magliero et al. 1984).

Like the broader ERP literature, the P3 component has garnered the most attention within the area of sport-related concussions. Seventeen of the 21 included studies examined P3 amplitude and/or latency measures in individuals with a history of concussion relative to a matched comparison group. The most consistent finding among these 17 studies is an attenuated or reduced P3 amplitude across a number of cognitive control tasks among previously concussed individuals (Baillargeon et al. 2012; Broglie et al. 2009; De Beaumont et al. 2007; De Beaumont et al. 2009; Dupuis et al. 2000; Gosselin et al. 2012; Gosselin et al. 2006; Lavoie et al. 2004; Moore et al. 2016; Moore et al. 2014; Moore et al. 2017; Moore et al. 2015; Ozen et al. 2013; Parks et al. 2015; Theriault et al. 2009). Four studies also demonstrated longer P3 latency in previously concussed individuals (De Beaumont et al. 2009; Gaetz et al. 2000; Gosselin et al. 2006; Ledwidge and Molfese 2016), although the majority of studies have found no between group differences in P3 latency. In one of the earliest studies in this area, Dupuis et al. (2000) assessed P3 amplitude and latency in 30 athletes (n = 10 asymptomatic concussed; n = 10 asymptomatic concussed; n = 10 controls) to determine if variation in concussion history was related to deficits in cognition. During a visual oddball task, athletes who recently experienced a concussion (1.7 ± 2 months post-injury) and experienced post-concussion symptoms at the time of testing exhibited reduced P3 amplitudes relative to a group of asymptomatic concussed individuals (9.8 ± 7.8 months post-injury) and healthy controls. Interestingly, the P3 amplitude difference wave (i.e., rare-minus-frequent waveforms) diminished as a function of symptom severity, indicating a potential neurocognitive marker of the relationship between concussion severity and cognitive processes represented by P3. Despite amplitude differences, the authors reported no significant P3 latency differences between the three groups. Using a similar study design, Gosselin et al. (2006) examined P3 amplitude and latency among 30 former athletes (n = 10 symptomatic concussed; n = 10 asymptomatic concussed; n = 10 controls) using an auditory oddball task. The findings revealed attenuated amplitudes and delayed P3 latencies in both symptomatic and asymptomatic concussed athletes compared to controls, while no differences were observed between symptomatic and asymptomatic athletes. Further examination of post-injury related variables indicated that symptoms of headaches and difficulties in concentration were related to reductions in P3 amplitude. Such studies are reflective of the majority of ERP research indicating smaller P3 amplitude when measured months to years following a sport-related concussion. However, it should be noted that six studies have found no between-group differences while one study (Ledwidge and Molfese 2016) reported increase in P3 amplitude and delayed latency among athletes with a concussion history. Although the increased P3 latency is similar to several previous investigations, this is the only study to date that has found increased, rather than decreased, P3 amplitude among a previously concussed sample. The sample in this study included 44 current NCAA Division I football players (22 with a history of concussion) and P3 was elicited by a two-tone auditory oddball task. It is unclear why the P3 findings in this study were divergent from the majority of the findings to date, although it is notable that the time window for P3 adaptive mean amplitude was from 260 to 388 ms post-stimulus, a relatively early time window in comparison to other published studies.

In several studies, P3 amplitude and latency measures were derived from more than one cognitive domain, using multiple cognitive tasks, or were separated into P3a and P3b subcomponents. Parks et al. (2015) examined P3 in 98 college students (n = 50 controls, n = 22 with one concussion, n = 26 with two or more concussions) using flanker and visual oddball tasks. Individuals with a history of concussion displayed reduced P3 amplitude during the flanker task while no differences were found during the oddball task. These neurophysiological deficits among the concussed group were accompanied by impaired accuracy and reaction time variability to the flanker task. Similarly, Gaetz et al. (2000) found no differences in P3 amplitude using a visual oddball task used to elicit both N2 and P3 in 60 individuals (15 controls, 45 with a variable concussion history). More recently, Moore et al. (2017) conducted a study to examine the independent contribution of concussive and sub-concussive impacts on P3a and P3b components elicited by a three-stimulus oddball task. This is important because the relative contribution of subconcussive hits or years of playing contact sports may help to explain variability of P3 findings within the literature. Athletes in the sub-concussion and concussion groups exhibited reduced P3a and P3b amplitudes relative to non-contact athletes, although only athletes in the concussion group exhibited slower response time during the oddball task. Their findings suggest that in addition to diagnosed concussions, sub-concussive impacts may also be associated with alterations in the neurophysiological and behavioral indices of cognitive control.

A majority of the studies have observed no differences in P3 latency, with very few reporting longer P3 latency in concussed individuals, suggesting a potential slowing of cognitive processing speed. Importantly, impairments in stimulus categorization speed following a concussion may not be immediately present following injury. As De Beaumont et al. (2009) showed, older adults with a concussive event in early adulthood display longer P3b latencies to an auditory oddball task.
compared to non-concussed adults. Similarly, severity of concussion injury and number of concussions may also lengthen P3 latency (Gaetz et al. 2000). Although the clinical significance of longer P3 latency is not well understood, delayed P3 latencies have been associated with severity of cognitive impairment in neuropsychiatric patients (Polich et al. 1986). Future concussion-related research should consider examining trajectories of P3 latency over the lifespan of athletes to see whether and how this neurophysiological measure covaries with cognitive impairment across time.

4.3. ERN and Pe: Response monitoring

The ERN is a negative deflection in the ongoing ERP that occurs approximately 50–100 ms following an incorrect response (Gehring et al. 2012; Holroyd and Coles 2002). That is, the ERN may serve as an “alarm” signal from the anterior cingulate cortex (ACC) and supplementary motor regions of the medial prefrontal cortex (mPFC) to the lateral PFC that an error has occurred, resulting in the recruitment of greater cognitive resources to optimize future performance (Moran et al. 2015; Shenhav et al. 2013). The Pe, or error positivity, is a positive deflection elicited approximately 200–500 ms following error commission, with a midline and parietal scalp distribution. Although the Pe is observed following the ERN, its functional significance is still widely debated, with many believing that it either represents conscious error awareness (Endrass et al. 2007; Nieuwenhuis et al. 2001) or is simply a P3-like response to errors (Arbel and Donchin 2011; Ridderinkhof et al. 2009). Analogous to N2 and P3, ERN and Pe are assessed during tasks that require variable levels of inhibitory control, attention, and working memory. Common paradigms used to assess these measures include the Eriksen flanker, Stroop, and go/no-go tasks, all of which have established validity in eliciting error-related brain activity (Riesel et al. 2013).

Relative to the stimulus-locked components (N2 and P3), ERN and Pe have received less attention, with four studies examining the potential influence of sport-related concussions on response monitoring processes. Three studies have revealed attenuated ERN amplitudes (De Beaumont et al. 2013; Moore et al. 2015; Pontifex et al. 2009), while one study found differences in Pe amplitude for individuals with a concussion history relative to healthy controls (Moore et al. 2015). Therefore, preliminary cross-sectional evidence indicates that deficits in performance and error monitoring processes may persist for months to years following concussive injuries. As an example, Moore et al. (2015) found that children with a history of concussion exhibited smaller ERN and Pe amplitudes elicited by a flanker task, with significantly larger group differences during the more difficult incongruent task condition. Interestingly, a significant association between Pe amplitude and post-error accuracy was found, suggesting that children with a concussion history may have persistent impairments in conflict monitoring and error detection processes (ERN and Pe), leading to a subsequent failure to correct behavioral responses following errors (post-error task performance).

Pontifex et al. (2009) similarly found that young adults with a history of concussion (mean = 2.9 years since last injury) had significantly smaller flanker ERN amplitudes, yet similar Pe amplitudes. In this study, a significant negative association between number of previous concussions and ERN amplitude was found, suggesting lower ERN amplitude with an increasing number of self-reported concussions. Interestingly, response accuracy was also significantly lower in the concussed than in the control group. De Beaumont et al. (2013) also observed lower ERN amplitude in university football players reporting a history of 2 or more concussions relative to their non-concussed teammates, but no differences in Pe amplitude were found. These ERP findings were observed in the absence of behavioral performance differences between the groups. Although there have been few studies to date that have examined ERN/Pe in relation to a concussion history, these emerging findings provide support for diminished response monitoring processes following a sport-related concussion.

In contrast to these findings, Larson et al. (2012) examined ERN and Pe responses to a modified color-naming version of the Stroop task in 36 individuals with a history of mTBI from sports-related incidents (n = 25; 69%), falls (n = 7; 19%), motor vehicle accidents (n = 2; 6%), and other accidents (n = 2; 6%), compared to 46 neurologically-healthy controls. No between-group differences were observed for behavioral performance measures, ERN amplitude, or Pe amplitude between individuals with and without a previous mTBI. Contrary to previous findings, the mTBI group exhibited longer ERN centroid latency, suggesting an apparent delay in upregulating cognitive control processes following an error. Correlational analyses were also performed to examine the relationship between potential injury-related variables and response monitoring processes, and both Pe and Pe difference waveform amplitudes (error trials minus correct trials) were associated with a longer length of post-traumatic amnesia and longer time since last injury. Clearly, additional studies are needed to document any persistent effect of sport-related concussions on performance related monitoring processes. Examining neurophysiological responses and behavioral performance simultaneously may also provide deeper insight into the functional significance of the ERN and allow for a better understanding of performance monitoring in previously concussed individuals.

4.4. Summary of ERP findings

Collectively, the research evidence to date demonstrates selective impairments in ERP measures of cognitive control among individuals with a concussion history. The most consistent finding is diminished P3 amplitude, with some emerging evidence indicating a possibility for reduced ERN amplitude. Regardless of latency measures, the majority of studies have found no consistent between-group differences in N2, P3, ERN, or Pe components, although some evidence exists for prolonged P3 latency (see Table 2 for a summary of findings of between-group differences in amplitude and latency measures). There is growing interest in determining whether sport-related concussions result in long-term, persistent effects on cognitive function. The findings from this review suggest consistent reductions in P3 amplitude in individuals with a history of concussion, and a possible influence on cognitive processing speed (P3 latency) and error monitoring processes (ERN). Also, the persistent neurophysiological changes may be related injury-specific moderators such as number of concussions sustained and time elapsed since injury. Notably, these ERP alterations have often been observed without any differences in task performance measures, which illustrates the potential utility and sensitivity of the ERP technique in measuring long-term effects of concussions on cognitive control processes. Importantly, these tentative conclusions should be tempered by the fact that this area of research is still completely reliant on cross-sectional studies. That is, all of the published studies to date have examined neurophysiological measures of cognitive control in individuals with a history of one or more concussions relative to a comparison group without a history of concussions; thus, no causal evidence exists. Definitive conclusions attributing cognitive control deficits to sport-related concussion await future methodologically sophisticated studies using individual baseline measures of cognitive control and examining individual-level change in ERP component measures over time following a sport-related concussion.

5. Methodological considerations and future directions

Although evidence exists to suggest a detrimental influence of sport-
related concussions on select aspects of cognitive control, a number of experimental design, analytic, and practical issues should be addressed in future studies to provide greater clarity of this complex relationship. First, studies using ERPs should take advantage of the temporal precision of the technique to answer important timing related questions related to mental processes that unfold over time. Other neuroimaging techniques, such as fMRI and PET, are arguably better suited to address neuroanatomical questions or source localizing activity implicated in select cognitive processes (Kappenman and Luck 2016). ERPs may be useful to identify specific cognitive processes, neural circuits, or transmitter-receptor systems that may be influenced by concussion. In addition, ERPs may be particularly effective at determining when specific cognitive processes have recovered back to a preclinical baseline level, thus assisting with clinical return-to-play guidelines.

Although consistent P3 amplitude effects have been observed following sport-related concussion, there are largely inconsistent findings related to the other ERP component measures of cognitive control. Several methodological reasons may explain the discrepant findings. First, the cognitive tasks used have varied widely across studies, which makes direct comparisons between studies challenging. Published studies assessing the P3 component have included seven different tasks (visual oddball, auditory oddball, working memory task, flanker, switch, go/no-go, and n-back), although the majority of investigations employed visual and auditory versions of the oddball task. Across studies, seven tasks were used to elicit N2, while four different tasks (N2pc paradigm, SPCN paradigm, stroop, flanker) were employed for ERN and Pe. In terms of response monitoring processes, Riesel et al. (2013) reported a large amount of task-specific variation in error-related brain activity (i.e., ERN and Pe) across three separate cognitive tasks (flanker, stroop, go/no-go), likely due to differences inherent to each task (e.g., difficulty, error type, stimulus-response mapping). Relative to study samples, most studies have used a relatively small sample size and most lack a priori power analyses for sample size determination; thus, many of the studies may be underpowered or effects influenced by random error (Button et al. 2013). Recent calls have been made for human electrophysiology studies to include sample size calculations in order to reduce bias and reporting of false or inflated effects associated with small samples and improve the overall scientific rigor of our findings (Larson and Carbine 2017; Larson and Moser 2017).

5.1. Quantification of ERP amplitude and latency

A number of studies included in this review used peak amplitude and latency measures. Assessing amplitude and latency measures using the peak approach was necessary when powerful computers were not readily available and EEG signals were plotted on paper to identify large components that could be visually observable (Donchin and Heffley 1978). Individual subject measures of peak amplitude and latency can be distorted by high-frequency noise and can introduce error into the data, particularly with clinical patients (Clayson et al. 2013; Luck 2014). This may be a critical issue to consider in this area of research, since a lower signal-to-noise ratio (SNR) could be expected for concussed individuals relative to never concussed healthy controls. To help overcome some of these issues, some ERP and concussion studies have used an adaptive mean or peak interval approach which centers an averaging window around a single subject peak. This approach entails establishing the peak amplitude within a specified time window for each subject, and then create a time window surrounding each identified peak. An alternative option to the peak amplitude approaches is measuring the mean voltage of an ERP over a broad a priori time window, which is particularly advantageous since latency variability and noise would have less influence on the extracted data. Moreover, this method allows for comparison of subjects across the same time window as opposed to peak approaches that compare subjects or groups at different timepoints following stimulus presentation or response. Depending on the severity and time since injury, concussed individuals may also be presenting with movement and postural deficits, which could influence the EEG signal. Additionally, any physical head movement due to impaired balance resulting from vestibulocochlear and cerebellar damage (Guskiewicz 2011; Valovich McLeod and Hale 2015) can also reduce the SNR of the collected ERPs. Although perhaps less recognizable, other issues that can be problematic include attentional lapses during task engagement among concussed individuals, which may result in delays in re-engaging attention and result in a greater number of omission errors during cognitive testing (see e.g., Pontifex et al. 2012).

Similar to amplitude measures, many studies have used a peak latency approach. Of the 20 studies eligible for this review, 13 used peak amplitude measures, five used mean amplitude, and two failed to report measurement specifications. Furthermore, 18 out of the 20 studies assessed ERP component latency. Of the 18 studies, 15 used a peak measurement approach, one used centroid measures, and two did not report measurement specifications. Future studies should aim for consistency in ERP measurement approaches (e.g., using similar time measurement windows) and use less biased measures of amplitude and latency to reduce variability in the findings due to different time windows and artifactual noise.

5.2. Prospective cohort studies

To date, all of the research in this area is cross-sectional in nature. Consequently, differences in ERP measures of cognitive control could potentially be explained by a variety of factors besides concussion history. As Broglio (2017) recently mentioned, a number of studies “...suggest a correlation between concussion and long-term neurodegeneration, but there has yet to be a prospective longitudinal investigation demonstrating causation” (p. 113). Future prospective studies should be performed using a pre-posttest design to assess within-subject change in cognitive function compared to the pre-injury assessment. Given the high temporal stability and internal consistency of ERP components (Kappenman and Keil 2017; Larson et al. 2010), they may be a well suited methodology to use in carefully designed prospective studies. Prospective studies would be useful for ruling out a number of lifestyle risk factors and behaviors, such as years of high-risk sport participation, which likely influence or obscure any effects. A prospective research design would also allow for a more stringent test of the temporal sequence of concussions on cognitive function, including on recovery, which a cross-sectional design would not allow.

Table 2
Summary of between-group findings across published studies of sport-related concussions and cognitive control.

<table>
<thead>
<tr>
<th>ERP Component</th>
<th>Measure</th>
<th>Between-Group Differences</th>
<th>Decreased</th>
<th>Null</th>
<th>Increased</th>
</tr>
</thead>
<tbody>
<tr>
<td>Stimulus-Locked ERPs</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>N2</td>
<td>Amplitude</td>
<td>1</td>
<td>7</td>
<td>3</td>
<td></td>
</tr>
<tr>
<td>P3</td>
<td>Amplitude</td>
<td>20</td>
<td>10</td>
<td>1</td>
<td></td>
</tr>
<tr>
<td></td>
<td>Latency</td>
<td>0</td>
<td>14</td>
<td>6</td>
<td></td>
</tr>
<tr>
<td>Response-Locked ERPs</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>ERN</td>
<td>Amplitude</td>
<td>3</td>
<td>1</td>
<td>0</td>
<td></td>
</tr>
<tr>
<td>Pe</td>
<td>Amplitude</td>
<td>1</td>
<td>3</td>
<td>0</td>
<td></td>
</tr>
<tr>
<td></td>
<td>Latency</td>
<td>–</td>
<td>–</td>
<td>–</td>
<td></td>
</tr>
</tbody>
</table>

Note: Data indicate the number of significant between-group differences between individuals with a history of concussion and healthy non-concussed controls on cognitive control-related ERPs. Amplitudes and latencies are referenced to the control group. Studies that assessed several ERP components using different tasks are reported multiple times.
6. General conclusions

The long-term consequences of sport-related concussion are not well understood and the field is in its infancy. The literature to date suggests a consistent relationship between sport-related concussions and prolonged alterations in cognitive processes reflected by P3 amplitude, with less consistent but suggestive effects on cognitive processing speed (P3 latency) and performance monitoring (ERP). Based on the available and emerging evidence, ERPs seem especially well-suited for identifying aspects of cognitive control that remain disrupted for an extended period of time following injury, which are often not detectable using standard neuropsychological tests. ERPs may be particularly useful for determining which aspects of cognition continue to present dysfunction following injury and may be an important component of best-practice guidelines for the treatment of concussion. Although all of the published studies to date investigating the potential long-term consequences of sport-related concussions on cognitive control have been cross-sectional in nature, future prospective within-subject designs may benefit from the temporal stability, consistency, and excellent temporal resolution of ERPs. Future research incorporating ERPs within the standard concussion management protocol may help to elucidate the neuropathology behind these injuries and establish their utility in advancing clinical practice.

Disclosure statement.

The authors declare that they have no conflict of interest.

References


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