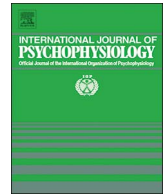




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# A history of sport-related concussion is associated with sustained deficits in conflict and error monitoring<sup>☆</sup>

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## ABSTRACT

Previous research has demonstrated long-term deficits in neurocognitive function in individuals with a history of sport-related concussion. The purpose of this study was to examine the relationship between a history of concussion and behavioral and event-related potential (ERP) indices of pre- and post-response conflict and error monitoring. A secondary aim was to determine whether years of high risk sport participation were related to impairments in these cognitive control processes. Forty-seven former athletes (age = 20.8 ± 2.2 years) with ( $n = 25$ ; 5 females) and without ( $n = 22$ ; 9 females) a history of concussion completed a modified flanker task while behavioral performance, N2, error-related negativity (ERN), and error positivity (Pe) components were assessed. An increase in post-response error-related (ERN) brain activity and a nonsignificant trend of increased pre-response conflict (N2) was observed in individuals with a prior sport-related concussion relative to non-concussed controls; however, no behavioral performance differences were found between groups. No significant associations were found between ERP and behavioral measures and the number of years of high-risk sport participation; however, time since last head injury was associated with shorter N2 latency. Together, these findings suggest a persistent impairment in cognitive control and error-related processing in individuals with a history of concussion. These findings are interpreted within the framework of the compensatory error-monitoring hypothesis.

## 1. Introduction

Sport-related concussions have received increasing media attention, in part due to their high prevalence rates and potential for long-term consequences. Although an estimated 1.6 to 3.8 million sport-related concussions occur annually in the United States (Langlois et al., 2006), many of these mild traumatic brain injuries (mTBIs) go unreported (Meehan et al., 2013). Despite this underreporting, concussion incidence rates have increased over the past two decades in part due to the increased awareness and improved diagnostic criteria surrounding these injuries (Clark and Guskiewicz, 2016). A recent meta-analysis of 57 studies demonstrated that a history of TBI, including concussions, is associated with increased risk for Alzheimer's disease, Parkinson's disease, mild cognitive impairment, depression, mixed affective disorders, and bipolar disorder (Perry et al., 2016). Therefore, advancing understanding of the dynamic process of brain recovery and the potential for intervention following injury remains paramount.

Concussions are often associated with a diverse range of neuro-pathological symptoms that affect normal, healthy functioning. Many of these symptoms (e.g., headache, balance problems, feeling “in a fog”) appear immediately, while others may not be observable for days or even months following injury (McCrory et al., 2017). However, most of these symptoms gradually resolve and observable neurological status typically returns to baseline levels within 7–10 days following injury (Harmon et al., 2013; Pontifex et al., 2009). Although there is rapid restoration of symptomatology following an acute injury, there are growing concerns about the potential long-term effects of sport-related concussions on brain and cognitive function. Indeed, evidence suggests that cognitive impairment may persist much longer than subjective symptoms following a concussion (e.g., Harmon et al., 2013; McCrea et al., 2003). Unfortunately, the majority of studies examining the relationship between a history of concussion and cognitive function have relied solely on behavioral performance measures of reaction time and response accuracy and standard neuropsychological tests, such as the

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Immediate Post-Concussion Assessment and Cognitive Testing (ImPACT). This is problematic since these behavioral measures may not have the requisite sensitivity and specificity to reveal subtle, persistent impairments in cognition after symptoms have resolved (Broglio et al., 2006; Guskiewicz et al., 2002; Iverson, 2005). Thus, enhancing the reliability and precision of neurocognitive testing following concussion remains a priority.

To advance clinical practice, experts have recommended combining sensitive neuroscientific techniques with neuropsychological and symptom-based assessments (Slobounov et al., 2012). Numerous neuroscientific techniques, including electroencephalography (EEG), functional magnetic resonance imaging (fMRI), diffusion tensor imaging (DTI), positron emission tomography (PET), and magnetic resonance spectroscopy (MRS) offer promise for advancing the clinical management of concussions. Event-related potentials (ERPs) represent one particularly useful approach to document subtle neurocognitive deficits following concussion (see Broglio et al., 2011 for a review). ERPs reflect voltage fluctuations in the ongoing EEG that are time-locked to an event, such as the presentation of a visual stimulus or execution of a manual response (Kappenman and Luck, 2012). Importantly, the millisecond-level resolution of the ERP technique allows for the detection of subtle changes in the stream of information processing to be isolated and quantified (Kappenman et al., 2016; Moore et al., 2017). ERPs have allowed for the identification of select alterations in sensory, motor, and cognitive functions following concussive injuries (Broglio et al., 2011).

Numerous studies examining different ERP components have been conducted to enhance our understanding of the immediate and potential delayed consequences of sport-related concussions (Broglio et al., 2011; Ellemberg et al., 2009; Moore et al., 2015; Pontifex et al., 2009). The majority of studies in this area have focused on the P3 (P300 or P3b) component, suggesting that it may serve as an ERP index of chronic cognitive impairments associated with a history of concussion (Broglio et al., 2011). Recently, the stimulus-locked N2 and response-locked error-related negativity (ERN) components have also received considerable research attention due to their relevance to cognitive control. Cognitive control is a broad term used to describe the set of mental functions or operations involved in guiding thoughts and actions in the service of goal-directed behaviors, and importantly, may be particularly affected by concussion history (Pontifex et al., 2009). The N2 and ERN components are most often elicited during cognitive control tasks involving inhibition (e.g., the flanker task), where individuals must override and control a strong internal disposition or external lure (i.e., stimuli) to successfully complete a particular goal (Folstein and Van Petten, 2008). The N2 is a negative deflection in the stimulus-locked waveform with a frontocentral scalp distribution that peaks approximately 250–350 ms after stimulus presentation (Botvinick et al., 2004; Clawson et al., 2013; Folstein and Van Petten, 2008) while the ERN is a negative deflection in the response-locked waveform that occurs within 100 ms after the commission of an error (Gehring et al., 2012; Holroyd et al., 1998). Previous evidence suggests that the N2 represents *pre-response* conflict generated by activation of competing response options, such as the target stimulus and flanking stimuli during a typical flanker task (Olvet and Hajcak, 2008). Thus, the N2 component relates to the process of conflict monitoring immediately prior to task completion and is typically more negative for trials of higher conflict (i.e., incongruent trials relative to congruent trials; Folstein and Van Petten, 2008). The ERN, on the other hand, represents an index of *post-response* conflict generated by a competing mental representation of an error response and a subsequent corrective response prompted by the target stimulus (Larson et al., 2014). Previous research suggests that the ERN represents neural activity signaling the need to adjust behavior and upregulate cognitive control processes for subsequent performance (Falkenstein et al., 1991; Gehring et al., 1993; Holroyd and Coles, 2002). More specifically, the ERN is thought to function as an ‘alarm’ that signals 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, in order to optimize subsequent performance (Moran et al., 2015; Shenhav et al., 2013). In addition, almost immediately following the ERN, a positive deflection is observed following error trials and is referred to as the error positivity (Pe). The Pe is maximal approximately 200–400 ms after error commission (Falkenstein et al., 2000; Nieuwenhuis et al., 2001) and has been suggested to reflect error awareness (Leuthold and Sommer, 1999; Nieuwenhuis et al., 2001), an affective or emotional response (Falkenstein et al., 2000), or a P3-like orienting response to errors (Hajcak et al., 2003). Relative to the N2 or ERN, the Pe component has received much less attention in ERP studies among individuals with a history of concussion.

In a recent study examining the potential long-term consequences of pediatric concussion, children who previously suffered a concussion exhibited increased amplitude and longer latency of the N2 during a modified flanker task (Moore et al., 2015). These findings were interpreted as impairments in monitoring and resolving stimulus conflict, indicating subtle but persistent deficits in attention and cognitive control processes. More recently, Ledwidge and Molfese (2016) found no between-group differences among 44 varsity football athletes with and without a history of concussion on neuropsychological tests or behavioral performance measures during an auditory oddball task. However, athletes with a concussion history exhibited significantly larger N2 amplitudes, suggesting increased recruitment of inhibitory control processes in order to successfully meet task demands. In contrast, Broglio et al. (2009) reported smaller N2 amplitudes elicited by a three-stimulus oddball task among a group of young athletes with a self-reported history of concussion relative to those athletes who reported no previous concussion history. Moreover, a number of previous studies have not found differences in N2 amplitude or latency to be associated with a history of concussion (e.g., Gaetz et al., 2000; Gosselin et al., 2012; Moore et al., 2016). Importantly, although the N2 is elicited during various tasks such as the go/no-go, stop signal, and oddball paradigm, the N2 elicited by these tasks may reflect different cognitive processes such as response inhibition, target probability, perceptual novelty, and mismatch (Folstein and Van Petten, 2008). This evidence led Larson et al. (2014) to conclude that “not all N2s are created equally” and to recommend caution when attempting to compare N2 findings across different cognitive tasks or paradigms. Collectively, the initial findings are mixed relative to the impact of a previous concussion history on long-term impairment of pre-response cognitive control processes, as indexed by N2.

Findings related to the post-response ability to detect errors and adaptively regulate behavior in a changing environment (reflected by the ERN) are also currently mixed. For instance, young adults with a history of concussion (average of 2.9 years since last injury) had a significantly smaller flanker ERN amplitude compared to non-concussed, otherwise healthy controls, even in the presence of normal functioning on the ImPACT test (Pontifex et al., 2009). Interestingly, a negative association was found between the number of previous concussions and ERN, such that an increased number of reported concussions was associated with lower ERN amplitudes. In a recent study of pediatric concussion, Moore et al. (2015) demonstrated decreased flanker ERN amplitudes in children with a history of concussion, with significantly larger ERN group differences for the more difficult incongruent flanker task condition, suggesting long-term impairments for tasks that require greater amounts of cognitive control. In contrast, Larson et al. (2012) used a modified color-naming version of the Stroop task and found no significant differences in ERN amplitudes between 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%) and 46 neurologically-healthy controls. Differences between these studies could be due to a number of moderating variables that have yet to be examined in the concussion and neurocognitive function relationship. For instance, individual

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