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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 (McCrory 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).

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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 neurophysiological 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 neuroscientific 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 (Folstein and Van Petten 2008; Larson et al. 2014; Nieuwenhuis et al. 2011; Polich 2007; Ridderinkhof et al. 2004; 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

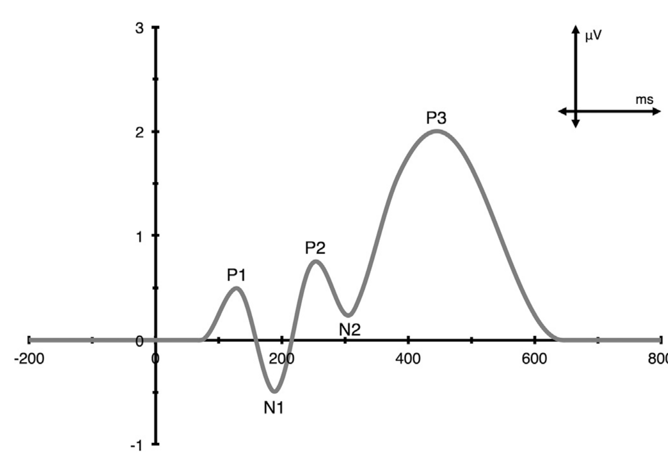

Fig. 1. Stimulus-locked grand-averaged waveform depicting several ERP components (including N2 and P3).