STABILITY OF THE MISMATCH NEGATIVITY IN HEAD IMPACT EXPOSURE

THE STABILITY OF THE MISMATCH NEGATIVITY EVENT-RELATED POTENTIAL IN HEAD IMPACT EXPOSURE AND CONCUSSION

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Lay Abstract

Concussion is a form of traumatic brain injury that is associated with a variety of health effects. There is increasing evidence that individuals who are repeatedly exposed to head impacts, such as athletes in contact sports, may exhibit similar changes to brain function even without experiencing the symptoms of a concussion. EEG-based event-related potentials (ERPs) are a brain imaging technique that are useful in studying the effects of head impact exposure as they reflect brain function on the scale of milliseconds. One consideration of using ERPs is the amount of data required to obtain a reliable response. The present study investigated the minimum number of repetitions required for a reliable ERP. It found reliability to be consistent across histories of head impact exposure and with relatively few trials, providing preliminary evidence that ERPs may be a stable response that can serve as a reliable assessment tool for brain injured populations.

Abstract

Concussive injuries are well documented as having a variety of acute and chronic health effects, and there is increasing evidence for cognitive health effects following repetitive head impact exposure even without the clinical presentation of injury. Event-related potentials (ERPs) recorded from electroencephalography (EEG) are uniquely suited to examine these effects due to their temporal resolution and specificity. ERP research requires a balance between collecting enough data to obtain a reliable response and optimizing the length of the experimental task so as not to be onerous for the participant; however, there is limited research addressing the stability of ERPs with an increasing number of trials. The present study investigated the stability of the mismatch negativity (MMN), an ERP associated with pre-attentive processing, in the context of head impact exposure history. Forty-one athletes with varying histories of head impact exposure and concussion completed EEG recording during a three-deviant auditory oddball paradigm. Data were analyzed with an increasing number of MMN trials using multiple indices of robustness and stability including Pearson's correlation, Cronbach's alpha and R^2. Results indicated that head impact exposure did not influence the reliability of the MMN. A reliable response was obtained with a minimum of 40 trials for a duration deviant, 50 trials for a frequency deviant, and 60 trials for an intensity deviant. Moreover, over 70% of the variance in total MMN amplitude was uniquely explained by the average of as few as 30 MMN trials in all three deviant types. The study was limited by a small sample size and varying quantifications of head impact exposure. The findings provide preliminary evidence that the MMN can be reliably observed with fewer trials than is currently the

norm and can be applied to shorten paradigms and reduce the burden placed on participants.

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to the changing circumstances of the past year, and for being so reassuring when I was facing an abrupt change of thesis topic. You've really shown me how exciting this field of research can be.

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List of All Abbreviations and Symbols

Ag/AgCl: Silver/silver chloride

b: Unstandardized beta coefficient

BDI-II: Beck Depression Inventory – II

$CI_{.95}$: 95% confidence interval

CTE: Chronic traumatic encephalopathy

CVMT: Continuous visual memory task

d: Cohen's d

dB: Decibels

df: Degrees of freedom

EEG: Electroencephalography

EOG: Electrooculogram

ERN: Error-related negativity

ERP: Event-related potential

fMRI: Functional magnetic resonance imaging

Hz: Hertz

ICC: Intraclass correlation coefficient

ImPACT: Immediate Post-Concussion Assessment and Cognitive Test

MMN: Mismatch negativity

ms: Miliseconds

mTBI: Mild traumatic brain injury

n: sample size

PCSS: Post-concussion symptom scale

PSS: Perceived stress scale

r: Pearson’s correlation coefficient

SD: Standard deviation

SE: Standard error

SF-36: Short-form health survey 36

SPL: Sound pressure level

SR^2: semi-partial correlation

TBI: Traumatic brain injury

α: Cronbach’s alpha coefficient

μV: Microvolts

Declaration of Academic Achievement

I established the research question for the present study and completed the statistical analysis and writing and revision of the thesis. I also contributed to the interpretation of the results with the assistance of my supervisor. The supervisor and supervisory committee also provided feedback on the written thesis.

Introduction

Electroencephalography and Event-Related Potentials

Electroencephalography (EEG), as a measure of brain function, is well known for its excellent temporal resolution, and its ability to represent activity on the scale of milliseconds. Event-related brain potentials (ERPs) are a technique derived from EEG in which activity is associated in time with a specific event, such as an environmental stimulus or individual response, and subsequently provide insight into cognitive processes such as attention, memory, or response inhibition (Duncan et al., 2009; Polich, 2007). ERPs are examined as components that represent the summed activity of numerous cortical neurons firing in concert, and can be distinguished based on a combination of polarity, scalp distribution, onset latency, and the cognitive process from which they arise (Duncan et al., 2009; Münte et al., 2000). For example, the P3b component is an attention-related ERP, being a positive going component maximal over the temporoparietal regions and associated with the allocation of attentional resources (Polich, 2007).

The mismatch negativity (MMN), another ERP component and the primary focus of the present investigation, is a brain response associated with automatic attention and predictive coding, arising when a detectable change in stimulation occurs even in the absence of active attention placed on the stimuli (Duncan et al., 2009; Näätänen et al., 2004). The MMN was chosen as the focus of the present investigation for its frequency of application with various clinical populations, which is discussed further below. The MMN presents as negative activity recorded from the frontocentral region of the scalp

and typically peaks around 150 to 250 milliseconds after a stimulus has been presented (Näätänen et al., 1978; Näätänen & Kreegipuu, 2012). The MMN is often studied using an auditory so-called oddball paradigm. A series of frequently repeated tones are interspersed with infrequent tones that differ from the recurring tones on some characteristic. The frequent tones are referred to as standard tones and the infrequent ones as deviants. The MMN is elicited by the infrequent deviant tones when compared with the response to the standard tones. Common types of deviant stimuli used in auditory oddball paradigms include ones differing from the standard in intensity, frequency, duration, and location (Näätänen et al., 2004), with the resulting MMN distribution over the scalp electrode sites varying with the type of deviant (Giard et al., 1995). The MMN also varies based on the size of the difference between the standard and deviant tones, in that there is typically a larger electrophysiological response corresponding to a larger magnitude of difference (Pakarinen et al., 2007; Tiitinen et al., 1994).

The MMN has been widely used with different clinical populations, such as psychiatric populations or patients with various disorders of consciousness. For example, studies involving patients with major depression (e.g. Chen et al., 2015), schizophrenia (e.g. Todd et al., 2008), and coma (e.g. Fischer et al., 1999) have all utilized the MMN, typically by examining the size of the response in patients compared to that of healthy controls. More recently, the MMN has been applied to the study of concussion patients, and mixed results have been observed. Following a history of remote concussion, studied in a sample of retired professional football players, smaller MMN amplitudes were observed compared to participants with no history of prior concussion (Ruiter et al.,

2019). On the other hand, when looking at recent injury in a younger population, no MMN changes were observed in a sample of adolescents currently symptomatic of concussion (Ruiter et al., 2020). Thus, the MMN may be emerging as a useful tool in the assessment of automatic attention in populations with a history of numerous remote concussions. The MMN is but one ERP component that measures cognitive functioning, and others will be described with reference to their common characteristics when mentioned below.

Concussion and Head Impact Exposure

Concussion has gained attention as a public health concern both generally and in sports specifically. Concussion is a form of traumatic brain injury (TBI) caused by an impact to the head, neck, or other part of the body that transmits a direct or indirect force to the head (Guskiewicz & Mihalik, 2011; McCrory et al., 2017). Similar injuries may be described with varying terminology, such as mild TBI (mTBI) rather than concussion, and while the distinction between these concepts is subject to debate, the terms are often used interchangeably (McKinlay et al., 2011). In the present thesis, the term “concussion” will be used for the sake of consistency; however, it will be considered synonymous to mTBI so as not to exclude relevant previous work that represented the same concept with differing terminology. Concussive injuries are variable in their presentation both within and across individuals, and currently are without a specific diagnostic biomarker. Often considered a primarily functional injury, acute concussion typically does not display abnormalities when standard structural imaging methods are used (Belanger et al., 2007; McCrory et al., 2017). Therefore, such injuries are typically characterized by the onset of

a variety of clinical symptoms, signs, and altered neurological function, such as headache, nausea, confusion, or memory impairment (McCrory et al., 2017; Meehan & Bachur, 2009). In many cases, concussion symptoms resolve around 10 to 14 days postinjury; however, symptoms may persist beyond this timeframe (McCrea et al., 2009; McCrory et al., 2017; Williams et al., 2010). The variability in concussions across cases and lack of clear diagnostic markers make these injuries difficult to diagnose and assess, especially when occurring in the context of sport.

While concussions are known to arise from a force transmitted directly or indirectly to the head, it is well documented that not all impacts producing such a force subsequently result in the clinical presentation of a concussive injury (Guskiewicz & Mihalik, 2011). Head impact exposure without concussion has become an increasing focus of research for its potential long-term and cumulative health effects. Of particular concern are high contact or collision sports such as football, in which individuals may be exposed to a high volume of head impacts during athletic participation, accumulating over years of a career. Research suggests that during a single season, football players may sustain around 650 sub-concussive impacts at the high school level (Broglio et al., 2011) and around 950 to over 1000 impacts at the college level (Guskiewicz & Mihalik, 2011; Gysland et al., 2012).

One of the most prominent concerns of cumulative head impact exposure is the potential for long term effects that may later arise (Bailes et al., 2013). Among the most severe of these potential concerns is a condition called chronic traumatic encephalopathy (CTE). CTE refers to a specific form of neurodegeneration that has been observed in

individuals with a history of head trauma, including repetitive concussive or sub-concussive trauma, with symptoms often arising years or decades after the occurrence of impact exposure (Baugh et al., 2012; Omalu et al., 2011). Symptoms of CTE vary in severity and can include deteriorated attention and memory, executive dysfunction (e.g. poor planning or judgement), depression, suicidal behaviour, and dementia (McKee et al., 2009; Stern et al., 2011). CTE is diagnosed post-mortem based on a distinct accumulation of tau proteins in the brain. Historically, CTE has been diagnosed in individuals with an extensive history of concussion or other head injury, such as professional boxers or football players (Omalu et al., 2011); however, it has been suggested that head impact exposure without concussion also plays a significant role in the development and progression of the disease (Gavett et al., 2011; B. R. Huber et al., 2016). It is also widely regarded that, although necessary for the development of the disease, not all individuals with a history of head impact exposure will develop CTE, bringing into question its exact mechanism of development (Baugh et al., 2012; Stern et al., 2011).

Consequently, there is an emphasis on understanding the acute effects of head impact exposure, focusing on changes occurring over the course of an athletic season. The results of such research have been mixed, with changes often being dependent on the type of assessment used. For example, uninjured college football players did not display changes on concussion assessments such as the Standardized Assessment of Concussion (a screening tool for symptoms and cognitive changes in suspected concussion) and the Postconcussion Syndrome Checklist (an evaluation of potential symptoms) when assessed prior to and following a season of play (Gysland et al., 2012; Killam et al., 2005; Miller et

al., 2007). On the other hand, the results of studies using neuropsychological assessments to examine the effects of head impact exposure are less unequivocal. McAllister et al. (2012) compared neuropsychological function in college athletes in contact and noncontact sports at preseason and postseason, and reported no group differences on the Immediate Post-Concussion Assessment and Cognitive Testing (ImPACT), a widely used computerized neurocognitive test. Contact athletes did however display lower performance on a verbal learning test at the postseason compared to noncontact athletes (McAllister et al., 2012). In contrast, Talavage et al. (2014) examined high school football players with and without a concussion diagnosis over the course of a season. The authors found that a subset of players without a clinical concussion diagnosis exhibited decreased verbal and visual memory scores on the ImPACT, as well as reduced activation in the cerebellum and dorsolateral prefrontal cortex in a working memory task during functional magnetic resonance imaging (fMRI). The impairments observed on both ImPACT and fMRI measures were also stated to be at least as severe as those displayed by athletes with a diagnosed concussion, drawing similarity in the functional sequelae of head impact exposure and concussion (Talavage et al., 2014).

Head Impact Exposure and ERPs

As concussion is widely considered a primarily functional injury, it follows that functional assessment methods, such as those used by Talavage et al. (2014), might be most suitable for detecting subtle deficits following head impact exposure. As it stands, there is increasing support for the use of EEG in examining cognitive function following concussion, both in the acute and long-term stages following injury. Altered

neurophysiology has been observed for processes such as attention, inhibitory control, and working memory in concussed populations persisting after the resolution of clinical symptoms by months (Baillargeon et al., 2012), years (Broglio et al., 2009; Moore et al., 2014; Parks et al., 2015; Thériault et al., 2011), and even decades (De Beaumont et al., 2009; Ruiter et al., 2019).

There is also emerging evidence to support the use of EEG to assess cognitive function following head impact exposure without concussion. A comparison of athletes with a history of diagnosed concussion, sub-concussive head impact exposure, and no history of head impact exposure revealed a reduction in P3b amplitude, a response related to the allocation of attentional resources, in both the concussion and sub-concussion groups in relation to controls (Moore et al., 2017). Another study, while failing to show ERP changes across a single season, found P3b alterations in third- and fourth-year college football players compared to first-year players despite a lack of behavioural differences, suggesting an effect of multiple season exposure to head impacts on neurophysiology (Wilson et al., 2015). Additionally, Ewers (2020) reported altered neurophysiology during attention and memory tasks after head impact exposure, wherein contact athletes displayed a reduced P3b amplitude when compared to noncontact athletes. The author also reported a smaller MMN amplitude in contact athletes at both the preseason and postseason in comparison to noncontact athletes, and a shorter MMN latency for contact athletes at the postseason compared to the preseason. Not only may EEG be ideal for detecting acute and chronic cognitive changes of diagnosed concussion,

but it may also be a useful tool for examining changes associated with head impact exposure in the absence of clinical concussion.

Psychometric Properties

When attempting to assess concussion with ERPs, to draw conclusions with any degree of certainty it is important to ensure that the measures being used do in fact reflect the processes they are intended to measure. Two central properties that contribute to the efficacy of any form of measurement are validity and reliability. Validity refers to the degree to which a measurement tool fulfils its purported use, meaning that it evaluates the specific construct to which it claims relevance (Clayson & Miller, 2017; Kimberlin & Winterstein, 2008). Reliability refers to the stability of the outcome of measurement scores over time (test-retest reliability), across evaluators (interrater reliability), or across items (internal consistency) (Henson, 2001; Kimberlin & Winterstein, 2008). Reliability is also context dependent, being specific to testing conditions, population of interest, and in ERP measures relying on factors such as raw signal quality and component quantification method (Thigpen et al., 2017). Although separate concepts, validity and reliability are interrelated in that a measurement cannot be valid without also being reliable; therefore, establishing the reliability of a measurement is an important component of the ability to draw meaningful conclusions from the results of said measurement, especially when being used for the assessment of clinical populations.

Reliability of the Mismatch Negativity

Pertaining to the MMN, most reliability studies have investigated test-retest reliability, demonstrating the stability of this component and measurement replicability

across time. The terminology and thresholds used for reliability vary somewhat between studies, thus descriptions of prior studies presented here retain the authors' original terms and values were applicable. Reliability criteria employed in the present study are outlined in the Methods and discussed further in the Limitations section. A previous study by Hall et al. (2006) reported high test-retest reliability of the MMN component elicited from a duration deviant in an auditory oddball paradigm in which testing sessions occurred an average of 17.8 days apart. The intra-class correlation (ICC) for peak amplitude was 0.67 and for mean amplitude 0.66. The authors also noted similar results when the MMN was quantified with the peak amplitude and the mean amplitude in a time window of 50 to 200ms, suggesting that the amplitude quantification method may not exert a large impact on MMN reliability. However, the type of deviant stimulus may influence the test-retest reliability of the MMN, as a slightly higher correlation has been seen for responses to a tone duration deviant as opposed to tone frequency and intensity deviants (Tervaniemi et al., 1999).

Internal Consistency

Internal consistency provides an additional metric of robustness to test-retest reliability, indexing the degree to which test items combine to represent a singular concept and contribute to overall statistical power (Clayson & Miller, 2017; Henson, 2001). Internal consistency values are often reported with the results of psychological self-report measures or questionnaires and tests with multiple items; however, this practice is less common when reporting on ERP data. To that extent, several studies have examined the internal consistency of ERP components as it relates to the stability of the

signal when including an increasing number of trials in the average waveform. In all cases, the stability of the signal increased as more trials were included; however, the point at which internal consistency was reached varied with the component of interest. For example, the P3 component has been recorded as stabilizing with a minimum of 20 trials when assessed by analysis of variance (Cohen & Polich, 1997), with others observing adequate reliability with as few as 14 trials when indexed by Pearson's correlation and Cronbach's alpha ($r > 0.8$, $\alpha > 0.6$) (Rietdijk et al., 2014). Adequate internal consistency ($\alpha > 0.6$) has also been reported as occurring with 20 trials for the N2 component (Rietdijk et al., 2014), a negative-going response related to inhibition and conflict management with a typical latency between 180 and 325ms (Patel & Azzam, 2005). The error-related negativity (ERN) is an ERP component related to the identification of errors in behavioural response, that typically presents as a frontocentral negativity peaking around 100ms following an error (Gehring et al., 2016). The ERN has been reported to require eight trials for adequate reliability ($r > 0.8$, $\alpha > 0.6$) (Rietdijk et al., 2014), and 10 trials for high internal consistency ($\alpha > 0.7$) (Olvet & Hajcak, 2009). In the abovementioned studies, Pearson's correlations were calculated between subset averages of trials and the average of all trials for a given component (i.e., the "typical" response), to determine the association between these smaller subset responses and the typical response, providing an additional representation of ERP stability. Such estimates provide an index of the minimum number of trials necessary to obtain adequate reliability of a measure, and thus suggest a potential threshold which may be used to determine if enough trials for a given paradigm were recorded for a given participant. To date, no

studies have been done to examine the internal consistency of the MMN with an increasing number of trials; however, some reports suggest a minimum of 150 trials to be included for a strong signal (Duncan et al., 2009).

ERP Reliability in Clinical Populations

Because the reliability of a test is context dependent, to fully represent its utility it should be examined in consideration of the population of interest. In ERP studies, it is common to evaluate cognitive function in patient populations by drawing comparison to healthy populations. Rightly so, if an ERP is intended for use with a specific patient population, the reliability of said component should be examined for healthy participants and patient participants independently. A small number of studies have examined the reliability of ERP components in clinical populations with the intent of discerning their stability as they are used for assessment purposes. A study of test-retest reliability using a dual modality (auditory and visual) oddball task revealed comparable reliabilities for individuals recovering from chronic alcoholism and healthy controls on 27 of 28 ERP measures investigated, focusing on amplitudes of the N1, N2, and P3 components (Sinha et al., 1992), suggesting that in some cases reliability remains consistent between patient populations and controls.

While reliability is important to consider for the utility of a measurement, in the case of ERPs in clinical research a reduction in reliability can be indicative of pathology rather than a weakness of the test as such. Patient populations may display variability in responsiveness, resulting in an ERP not being consistently elicited by a stimulus. This can be due to a lack of consciousness, attention, or perception of the stimuli, reflected in an

attenuated waveform when responses are averaged and manifesting as a theoretically unreliable test. For example, in comatose patients an MMN response may occur in cycles with the response being both present and absent at different times within a single recording session. This may appear as an issue with test reliability although it is actually a result of pathology (Armanfard et al., 2019; Connolly et al., 2019). Therefore, variability in responsiveness of clinical populations further highlights the necessity of examining ERP reliability in the context of the population of interest, as this may allow for the identification of potential biomarkers.

To our knowledge, only one ERP reliability study has included patients with a history of TBI. It examined test-retest reliability in healthy controls and patients recently recovered from moderate to severe injuries (Lew et al., 2007). The authors examined four ERP components: the P3, MMN, N1, which is an early sensory response presenting as an anterior negativity around 50 to 150ms post-stimulus (Näätänen & Picton, 1987), and N4, which is a centroparietal negativity related to semantic processing (Kutas & Hillyard, 1983). Responses were recorded from an auditory oddball paradigm (single deviant: frequency) in which participants were required to make a button press following the presentation of the deviant stimulus. They found acceptable reliability (ICC $\geq$ 0.60) for all component amplitudes in the healthy control group, and acceptable reliability of latency for all components except the N4. In the TBI group, only the amplitude of the N1 had acceptable reliability across testing sessions, and the latencies of the N1 and MMN were relatively stable (ICC > 0.50) (Lew et al., 2007). Although it has been demonstrated that a history of moderate to severe TBI influences the reliability of ERP component measures,

it is presently not known how this may occur in concussion, a mild form of TBI. Furthermore, the internal consistency of ERP measures in this context, rather than their reliability across sessions, has not been studied.

When considering internal consistency rather than test-retest reliability, some differences have been observed between patient populations and healthy controls. Participants with a history of schizophrenia spectrum disorder or other psychotic disorder required fewer trials than controls to obtain fair reliability ($\alpha > 0.70$) in the ERN component from a flanker task; however, split-half reliability for the ERN was unacceptable for the patient group ($r < 0.70$) and good for the control group ($r > 0.80$) (Foti et al., 2013). Conversely, Baldwin et al. (2015) found that patients with major depression or anxiety disorders had lower internal consistency for the ERN than healthy controls when using both single and multiple electrode sites. Therefore, it has been seen that clinical diagnosis exerts an impact on ERP component internal consistency, although the specific effect may vary based on factors such as patient population and component of interest. Internal consistency, specifically targeting an increasing number of trials included in an ERP component average, could be a prudent characteristic of such measures as it would help to establish a minimum number of necessary trials for inclusion in analysis, and could potentially allow for paradigms to be shortened, decreasing the burden placed on patients.

The Present Study

In an effort to better understand the potential effects of cumulative head impact exposure, increasing attention is being placed on the unique suitability of ERPs for

outcome assessment. In particular, the MMN has recently shown promise in unveiling neurophysiological alterations that may be attributable to head impact exposure (Ewers, 2020; Ruiter et al., 2019). There is evidence that brain injury, such as moderate to severe TBI, can influence the reliability of ERP measures (Lew et al., 2007), which can serve as an indicator of potential pathology. With the lack of research on the internal consistency of the MMN in general, and following head impact exposure specifically, our objective was to examine the stability of the MMN in this context. The research questions we sought to address were: 1) Is the MMN stable as additional trials are included in the averaged response? 2) Is the MMN a stable response in individuals with a history of head impact exposure and concussion? Specifically, we aimed to examine the stability of the MMN to determine the minimum number of trials required to obtain a clear response that is both reliable and representative of the response resulting from a larger number of trials. Our secondary aim was to investigate how MMN reliability may be impacted by a history of head impact exposure, with the expectation that head impact exposure would be associated with a reduction in reliability. Finally, we also aimed to investigate the effects of acute head impact exposure by examining internal consistency of data obtained after a season of contact sport participation. The findings of the present study contribute to our understanding of the stability of the MMN ERP component, while also potentially strengthening the efficacy of its application as a clinical assessment tool in head impact exposure and concussion research.

Methods

Participants

The participants in the present study were recruited as part of a larger research protocol, the results of which are reported by Ewers (2020) . Two groups of participants were recruited from the McMaster University athletics community: contact sport athletes (n = 58), to serve as a participant sample with a history of head impact exposure, and noncontact sport athletes (n = 21), to serve as a control group. All contact sport athletes were members of the McMaster University football team and self-identified as male, and noncontact sport athletes were gender matched and recruited from various sports including running (n = 9), rock climbing (n = 6), rowing (n = 2), squash (n = 2), swimming (n = 1), and volleyball (n = 1). Contact athletes participated in the study at two timepoints, a baseline session prior to the start of their sports season and a follow-up session occurring approximately two months after the culmination of their season (mean = 58.2 days, SD = 4.12). Noncontact athletes were tested only once throughout their season to allow for the recruitment of a sufficient sample size.

Fourteen contact athletes did not return for postseason testing. Noncontact athletes were screened to ensure they had no previous history of diagnosed concussion, and one participant was excluded for failing to meet this criterion. Additionally, three contact and two noncontact athletes were excluded due to the use of medications that act on the central nervous system, such as those used to treat attention deficit hyperactivity disorder, and four contact athletes were excluded due to technical issues with the EEG recording. Participants with fewer than 100 trials available in any of the deviant types were excluded

from the present analysis. This included four noncontact sport participants and 10 contact sport participants, resulting in the final inclusion of 14 participants recruited from noncontact sports and 27 participants from contact sports at both preseason and postseason timepoints. The average number of trials available for each type of deviant and each group are presented in Table 1. No participants in either group reported any previous history of hearing or speech/language problems, and all were fluent English speakers with normal or corrected-to-normal vision. The present study was approved by the Hamilton Integrated Research Ethics Board.

Table 1

Average Number of Trials in Each Type of MMN Deviant by Group

Deviant Type	Mean Number of Trials (*SD*)		
	Current Noncontact Group	Preseason Group	Postseason Group
N	14	27	27
Frequency	133.21 (7.27)	131.96 (9.2)	131.48 (11.75)
Duration	133.14 (9.68)	132.52 (8.46)	130.81 (10.6)
Intensity	133.93 (8.05)	132.33 (9.75)	130.15 (9.99)

The mean ages of the contact and noncontact sport groups were 19.3 (*SD* = 1.4) and 20.5 (*SD* = 2.2) respectively. The average number of previously diagnosed concussions in the contact sport group was 0.85 (*SD* = 1.0, range = 0-4). Of the noncontact sport participants, 57.1% had previously participated in contact sports for less than one year, 14.3% one to two years, 7.1% four to six years, and 21.2% had eight or more years previous experience in contact sports. In comparison, 51.9% of the contact sport participants had spent more than 10 years participating in contact sports, 18.5% had

eight to 10 years of experience, and the remaining 29.6% had at least four years of experience participating in contact sports. To acknowledge various histories of previous participation in contact sports, participants recruited from noncontact sports will hereon be referred to as the "current noncontact" group, and those recruited from contact sports will be referred to as the "current contact" group or "preseason" and "postseason" groups depending on the timepoint in question.

Materials

Participants completed four surveys and completed three cognitive tasks during EEG recording. The four questionnaires administered were the Beck Depression Inventory-II (BDI-II; Beck et al., 1996), the Short Form Health Survey version 2 (SF-36; McHorney et al., 1993), the Post-Concussion Symptom Scale (PCSS; Chen et al., 2007), and the Perceived Stress Scale (PSS; Cohen et al., 1983). The BDI-II is a 21-item self-report questionnaire that assesses an individual's experiences with depressive symptoms over the previous two-week period (Beck et al., 1996). The SF-36 is a health survey that measures an individual's general and overall health over the previous four-week period, including physical health, emotional problems, and bodily pain and their impact on daily functioning and social interaction (McHorney et al., 1993). The PCSS assesses an individual's current experience with common concussion symptoms, such as headache and irritability, by rating their severity. It is common for some symptoms to be experienced even without the presence of concussion, thus scores on the PCSS may be greater than zero even at baseline (Chen et al., 2007). The PSS is also a self-report measure, inquiring as to participants' levels of stress (Cohen et al., 1983). Additional

survey questions pertaining to athletic participation and concussion history were also included. All questionnaires were administered online via LimeSurvey, excluding the BDI-II which was administered in a paper format. The online survey is available in the Appendix.

EEG Stimuli and Recordings

EEG was recorded during three cognitive tasks pertaining to attention and memory: an active auditory oddball task (multi-deviant: frequency, duration, and intensity), the Continuous Visual Memory Test (CVMT), and a passive auditory oddball task (multi-deviant: frequency, duration, and intensity). The paradigms were presented with Presentation software on a computer monitor positioned approximately 90 cm from the participant. EEG data were recorded during all three cognitive paradigms. To examine the MMN response, only data collected from the passive auditory oddball task are analyzed in the present study.

The passive auditory oddball task was adapted from Todd et al. (2008), and was comprised of a series of four kinds of tones: a standard tone occurring for 82% of trials (1968 total repetitions), and three deviant tones each occurring for 6% of trials (144 repetitions each), for a total of 2400 trials. The standard tone was set at 1000 Hz, 80 dB Sound Pressure Level (SPL), and 50ms duration. The three deviant tones included a louder intensity deviant (1000 Hz, 90 dB SPL, 50ms), a higher pitch frequency deviant (1200 Hz, 80 dB SPL, 50ms), and a longer duration deviant (1000 Hz, 80 dB SPL, 100ms). The interstimulus interval ranged from 627ms to 673.4ms over the course of the paradigm, varying consistently within and across participants. The task did not require a

participant response, but rather participants were instructed to watch a silent nature film and ignore the tones while the paradigm was completed.

EEG was recorded from 64 Ag/AgCl electrodes placed according to the International 10-20 system using a BioSemi ActiveTwo system. Recordings were collected with a 0.01-100 Hz bandpass filter, 60 Hz notch filter, and 512 Hz sampling rate, with five external reference electrodes placed on the nose, left and right mastoids, and above and beside the outer canthus of the left eye. Electrodes above and beside the left eye were used for electrooculogram (EOG) recording. EEG recording was referenced online to the common mode sense (CMS) and driven-right leg (DRL), and reference voltage offsets were examined during setup to adhere to a threshold between -20 and +20 mV.

Procedure

Participants provided written informed consent upon arrival at the first testing session, and all other testing procedures were the same across the first and second sessions, and for contact and noncontact sport participants. Prior to EEG testing, participants were seated in a comfortable chair and completed a series of questionnaires. Participants were then fit with the EEG equipment and provided with a brief explanation and demonstration of EEG recording. They were asked to remain relaxed and as still as possible throughout the session. EEG recording began with the active oddball task, followed by the CVMT, and ended with the passive oddball task. Participants were thanked for their participation and provided with $30 remuneration at the end of each session. All participants completed the study within a timeframe of two hours.

EEG Data Analysis

Raw EEG data were processed offline with Brain Vision Analyzer software (v2.01). Data were filtered with a bandpass of 0.1-30 Hz (24 dB/oct). Manual raw data inspection was conducted to remove artifacts, such as those arising from muscle movement. Eye-movement artifacts were removed using Ocular Independent Component Analysis (ICA), and data were re-referenced to the average mastoids (Luck, 2014). Data for one participant in the contact group at baseline were referenced to the nose due to a technical issue with the mastoid recordings. Data were segmented into epochs beginning 200ms pre-stimulus onset and ending 1000ms post-stimulus. Data were averaged into bins with an increasing number of trials for each deviant type (i.e., 10 trials, 20 trials, 30 trials…100 trials, all available trials) and automated peak detection (Barr et al., 1978) was performed on each bin. Binning procedures used here were based on previous methods used to examine ERP stability (e.g., Foti et al., 2013; Olvet & Hajcak, 2009). Peak detection was also performed on the unaveraged data to obtain single trial values as is necessary for calculating Cronbach's alpha for internal consistency. The MMN peak amplitude was defined as the maximal negative-going electrophysiological response within the window of 150-250ms post-stimulus at electrode Fz.

Statistical Analysis

We examined the stability of the MMN with multiple metrics using similar methods as those employed by Foti et al. (2013) and Olvet and Hajcak (2009). MMN stability was examined separately for the current noncontact group, preseason contact group, and postseason contact group. To determine the number of trials at which the

amplitude of the MMN stabilizes, a series of paired t-tests was calculated between each successive trial bin (i.e., 10 trials vs 20 trials, 20 trials vs 30 trials…100 trials vs all trials). In this analysis, stability would be indicated by a nonsignificant difference between pairs, therefore a series of paired t-tests was chosen as a more conservative test than other alternatives that correct for familywise error and thus make a significant result less likely. For t-tests with a significant result, Cohen's d is reported as an index of effect size, where a value of 0.2 indicates a small effect, 0.5 a medium effect, and 0.8 a large effect (Cohen, 1988). To examine the association between each subset MMN and the typical total trial MMN, Pearson's correlation coefficient was calculated between the average of all MMN trials and each subset trial bin. Finally, Cronbach's alpha was calculated for a subset of 10 trials and for additional subsets increasing by 10 up to 100 total trials. Identical analyses were conducted for each deviant type of the oddball task: frequency, duration, and intensity deviants. In accordance with past research, a strong correlation was indicated by a Pearson coefficient of at least 0.8 (Akoglu, 2018; Olvet & Hajcak, 2009; Rietdijk et al., 2014) and Cronbach's alpha values were considered adequate at the minimum threshold of 0.7, good when reaching 0.8, and excellent at 0.9 (Cicchetti, 1994; Foti et al., 2013).

Results

Frequency Deviant

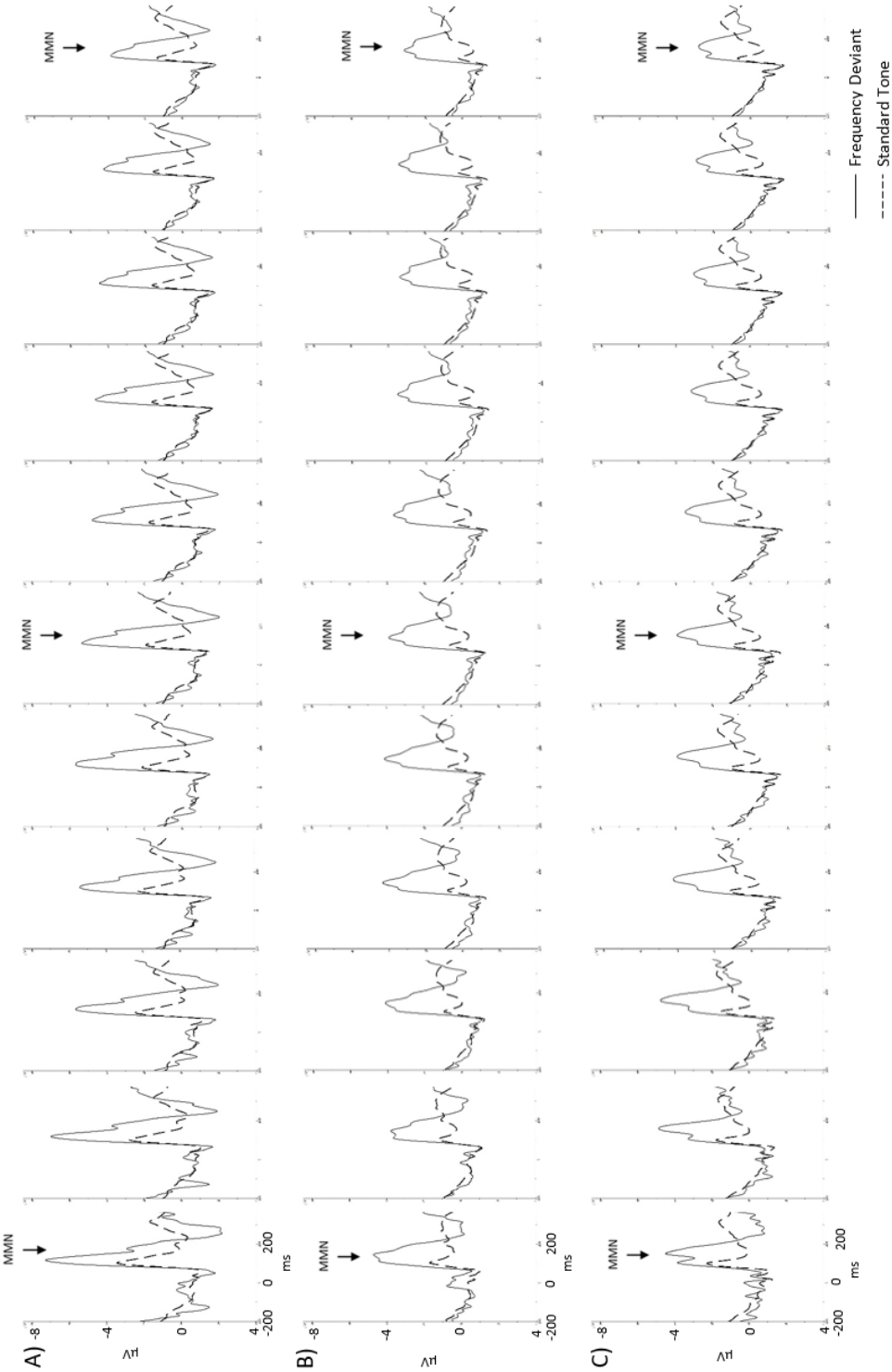
Grand averaged waveforms of increasing trial bins for the frequency deviant are presented in Figure 1. Paired t-tests were conducted to compare the MMN amplitude from successive bins with increasing numbers of trials in the three participant groups. For the

current noncontact group, a significant difference was observed for 70 trials versus 80 trials, $t(13) = -2.99$, $p = 0.01$, $d = 0.16$. For the preseason group, a significant difference was observed for 100 trials versus all trials, $t(26) = -2.41$, $p = 0.02$, $d = 0.12$. For the postseason group, significant differences were observed for 40 trials versus 50 trials ($t(26) = -2.96$, $p < 0.01$, $d = 0.14$), 60 trials versus 70 trials ($t(26) = -3.31$, $p < 0.01$, $d = 0.07$), 70 trials versus 80 trials ($t(26) = -4.15$, $p < 0.01$, $d = 0.13$), and 100 trials versus all trials ($t(26) = -2.12$, $p = 0.04$, $d = 0.08$). All other comparisons were nonsignificant (all ps > 0.05).

Pearson's correlation coefficients between different bin sizes and all trials for the MMN amplitude in the frequency deviant condition as a function of increasing trial bin size are presented in Figure 2. The correlation coefficient with 10 trials for the current noncontact group was not significant ($p = 0.1$), but all other correlation coefficients in all groups were significant. For the current noncontact group, a strong correlation ($r > .8$) to the amplitude of all trials was achieved with as few as 30 trials included in the average ($r = 0.81$, $CI_{.95} = 0.50, 0.94$), with a maximum correlation of 0.93 occurring with 100 trials.

Figure 1

Grand Average Waveforms of Increasing Trial Bins in the Frequency Deviant by Group

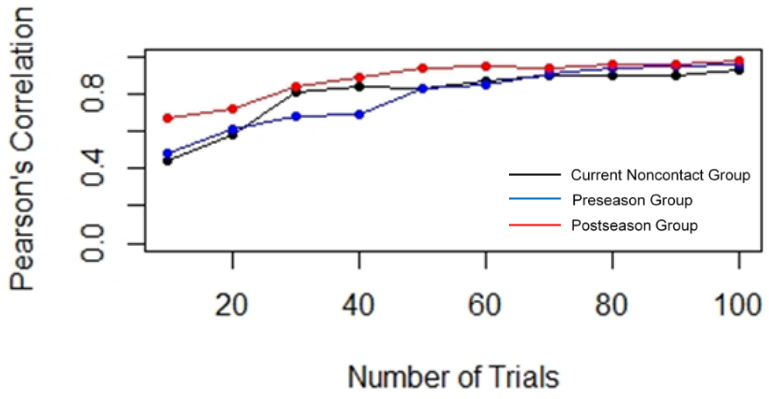


Note. A) Grand average MMN waveforms in the current noncontact group. B) Grand average MMN waveforms in the preseason group. C) Grand average MMN waveforms in the postseason group

For the preseason group, a strong correlation was obtained with as few as 50 trials (r = 0.83, $CI_{.95}$ = 0.67, 0.92), with a maximum correlation of 0.97 [$CI_{.95}$ = 0.93, 0.99] occurring with 100 trials. A strong correlation was obtained for the postseason group with 30 trials included in the average (r = 0.84, $CI_{.95}$ = 0.68, 0.93) and the maximum correlation occurring with 100 trials was 0.98 [$CI_{.95}$ = 0.95, 0.99].

Figure 2

Pearson's Correlation Coefficient between Increasing Trial Bin Sizes and Total Trials for Amplitude in the Frequency Deviant Condition

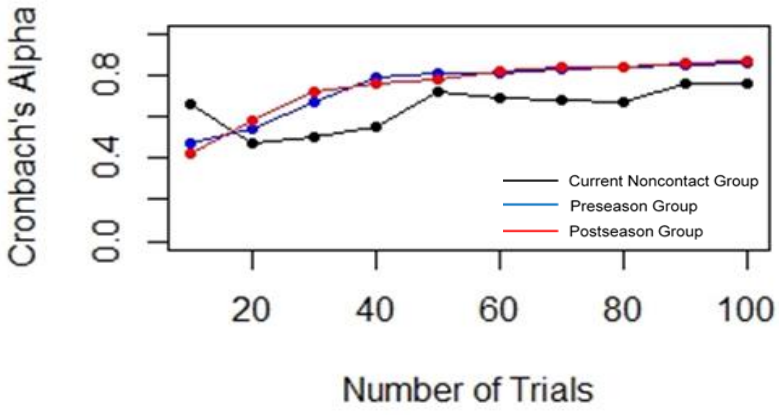


Cronbach's alpha as a function of increasing trial bin sizes in the frequency deviant condition are presented in Figure 3. Fair internal consistency (α > .7) was achieved in the current noncontact group when 50 trials were included (α = 0.72, $CI_{.95}$ = 0.52, 0.92), but dropped slightly below this threshold with an alpha coefficient of 0.68 before rising again with 90 trials (α = 0.76, $CI_{.95}$ = 0.59, 0.93). For the preseason group, fair internal consistency was achieved with as few as 40 trials (α = 0.79, $CI_{.95}$ = 0.68, 0.90) and good internal consistency (α > .8) was achieved with 50 trials (α = 0.81, $CI_{.95}$ = 0.71, 0.91). Fair internal consistency was achieved for the postseason group with 30 trials

(α = 0.72, $CI_{.95}$ = 0.57, 0.87) and good internal consistency was achieved with 60 trials (α = 0.82, $CI_{.95}$ = 0.73, 0.92).

Figure 3

Cronbach's Alpha as a Function of Increasing Trials for the Frequency Deviant Condition

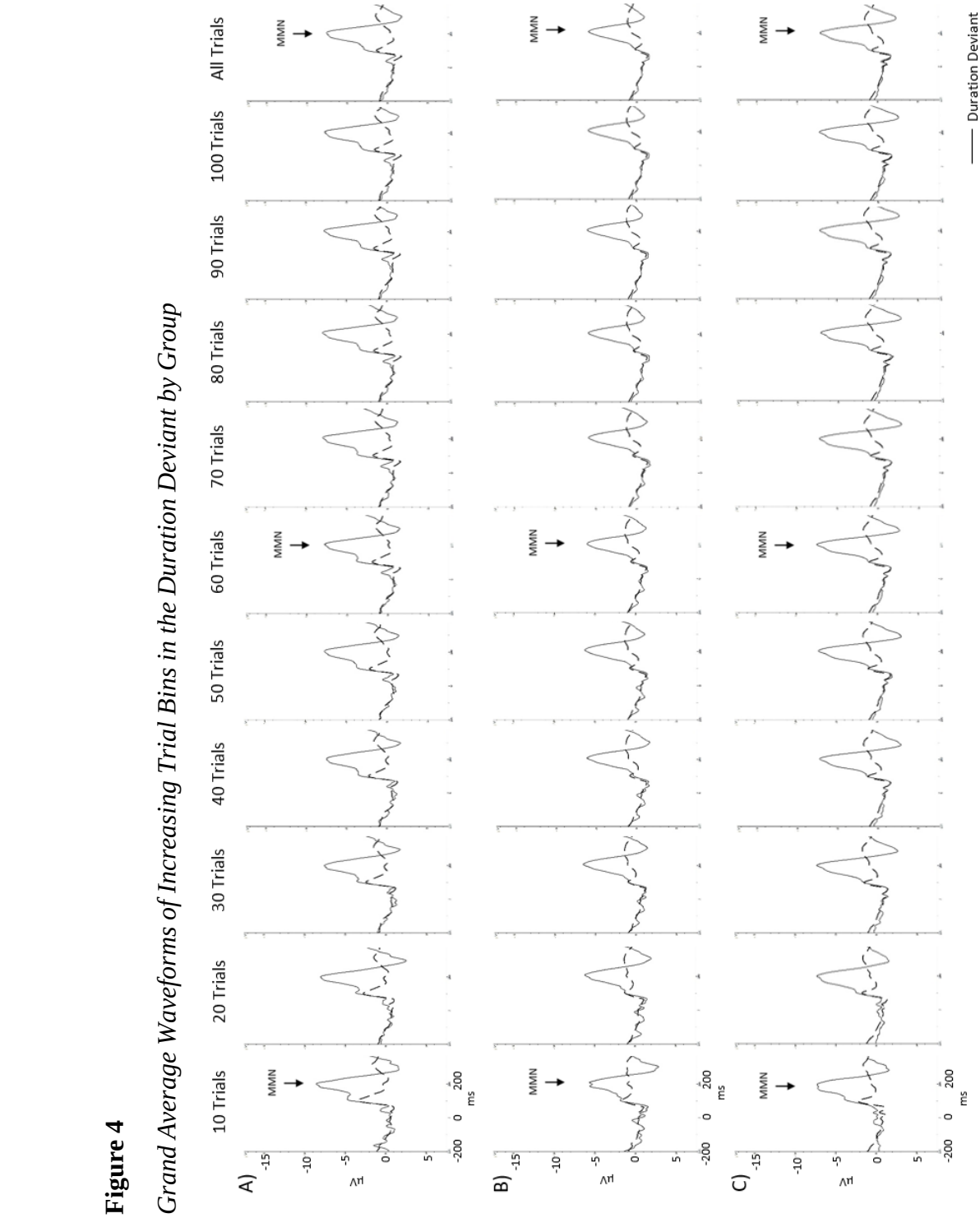


Duration Deviant

Grand averaged waveforms of increasing trial bin sizes for the duration deviant condition are presented in Figure 4. No significant differences in amplitude were found between any successive bins for the current noncontact group (all *p*s > 0.05). For the preseason group, a significant difference was found in the amplitude of 50 trials versus 60 trials, $t(26) = -2.12$, $p = 0.04$, $d = 0.11$; all other trial pairs were nonsignificant. No significant differences were found between any trial pairs for the postseason group (all *p*s > 0.05).

Figure 4

Grand Average Waveforms of Increasing Trial Bins in the Duration Deviant by Group

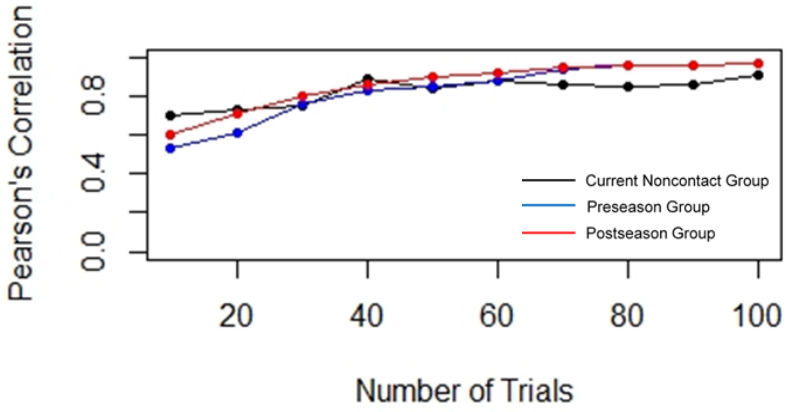


Note. A) Grand average MMN waveforms in the current noncontact group. B) Grand average MMN waveforms in the preseason group. C) Grand average MMN waveforms in the postseason group

Pearson's correlation coefficients with MMN amplitude from all trials as a function of increasing trial bin sizes for the duration deviant condition are presented in Figure 5. All correlation coefficients were significant ($p < 0.05$). A strong correlation ($r > .8$) to the amplitude of all trials was obtained for all three groups when as few as 40 trials were included in the average (current noncontact group: $r = 0.90$, $CI_{.95} = 0.70, 0.97$; preseason group: $r = 0.84$, $CI_{.95} = 0.67, 0.92$; postseason group: $r = 0.87$, $CI_{.95} = 0.73, 0.94$). The maximum correlation coefficients obtained for the current noncontact, preseason, and postseason groups were 0.92 [$CI_{.95} = 0.75, 0.97$], 0.98 [$CI_{.95} = 0.95, 0.99$], and 0.97 [$CI_{.95} = 0.93, 0.99$] respectively.

Figure 5

Pearson's Correlation Coefficient between Increasing Trial Bin Sizes and Total Trial Amplitude in the Duration Deviant Condition

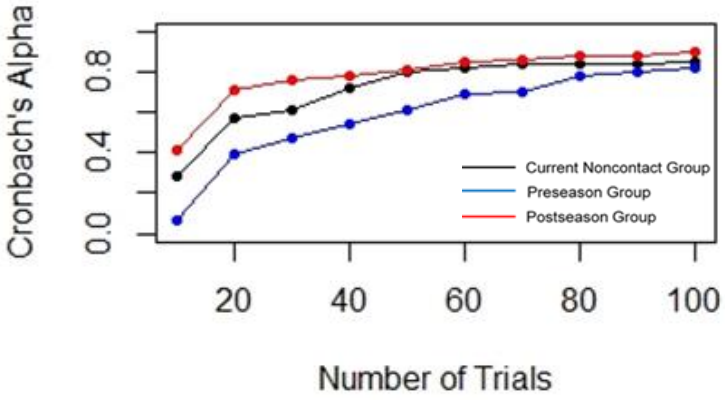


Cronbach's alpha coefficients for the duration deviant are presented in Figure 6. The current noncontact group reached fair internal consistency ($\alpha > .7$) for the amplitude of the MMN with as few as 40 trials included in the analysis ($\alpha = 0.72$, $CI_{.95} = 0.53, 0.91$), and good internal consistency with as few as 50 trials ($\alpha = 0.80$, $CI_{.95} = 0.67, 0.94$). The preseason group reached fair internal consistency with 70 trials ($\alpha = 0.70$, $CI_{.95} = 0.54,$

0.86) and good internal consistency with 90 trials (α = 0.80, $CI_{.95}$ = 0.70, 0.91), while the postseason group reached fair and good internal consistency at 20 trials (α = 0.71, $CI_{.95}$ = 0.56, 0.87) and 50 trials (α = 0.81, $CI_{.95}$ = 0.71, 0.91) respectively.

Figure 6

Cronbach's Alpha as a Function of Increasing Trials for the Duration Deviant Condition

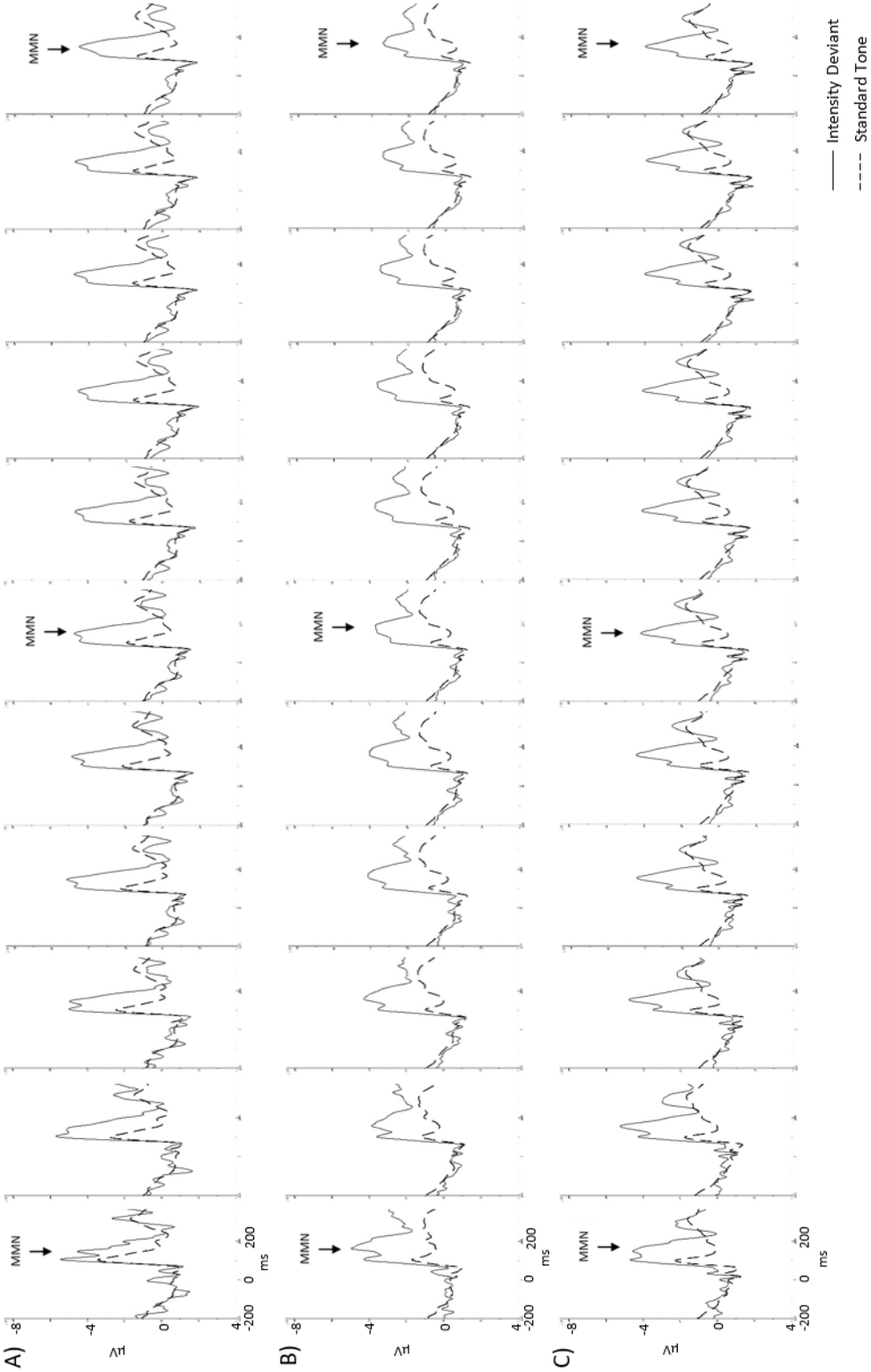


Intensity Deviant

Grand averaged waveforms of increasing trial bin sizes for the intensity deviant condition are presented in Figure 7. Using paired t-tests, significant differences in amplitude between successive trial bin sizes were observed in the current noncontact group for 20 trials versus 30 trials ($t(13) = -2.50$, $p = 0.03$, $d = 0.39$) and 70 trials versus 80 trials ($t(13) = -2.53$, $p=0.03$, $d = 0.11$). For the preseason group, a significant difference was observed for 50 trials versus 60 trials ($t(26) = -2.07$, $p = 0.048$, $d = 0.14$), and for the postseason group significant differences were found between 20 trials versus 30 trials ($t(26) = -2.37$, $p = 0.03$, $d = 0.20$) and 50 trials versus 60 trials ($t(26) = -2.51$, $p = 0.02$, $d = 0.11$). All other comparisons were nonsignificant (all ps > 0.05).

Figure 7

Grand Average Waveforms of Increasing Trial Bins in the Intensity Deviant by Group

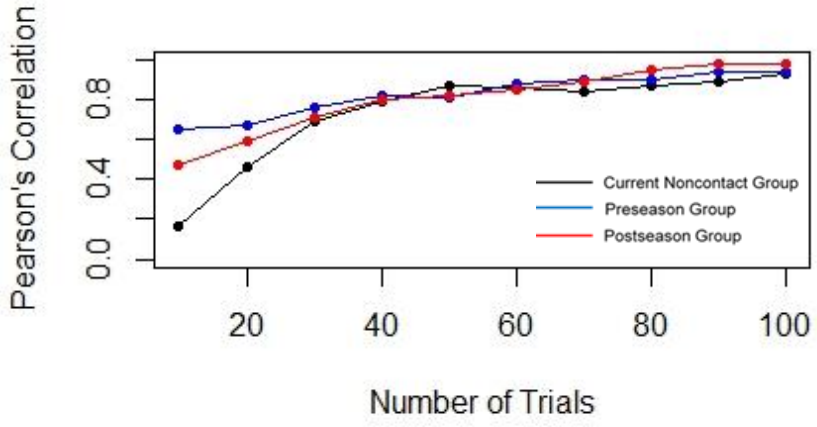


Note. A) Grand average MMN waveforms in the current noncontact group. B) Grand average MMN waveforms in the preseason group. C) Grand average MMN waveforms in the postseason group

Pearson's correlation coefficients of MMN amplitude in all trials as a function of increasing trial number for the intensity deviant condition are presented in Figure 8. Correlation coefficients for 10 and 20 trial averages in the current noncontact group were not significant (10 trials $p = 0.56$; 20 trials $p = 0.09$); all other coefficients were significant. For the current noncontact group, a strong correlation to the average of all trials was obtained with as few as 50 trials ($r = 0.87$, $CI_{.95} = 0.63, 0.96$), with a maximum correlation of 0.94 [$CI_{.95} = 0.80, 0.98$] occurring with 100 trials. A strong correlation was achieved with the inclusion of 40 trials for both the preseason and the postseason groups (preseason: $r = 0.82$, $CI_{.95} = 0.64, 0.92$; postseason: $r = 0.80$, $CI_{.95} = 0.61, 0.91$), and maximum correlations of 0.94 [$CI_{.95} = 0.88, 0.97$] and 0.98 [$CI_{.95} = 0.96, 0.99$] respectively were obtained with 100 trials.

Figure 8

Pearson's Correlation Coefficient for Increasing Trial Bin Sizes and Total Trial Amplitude in the Intensity Deviant Condition

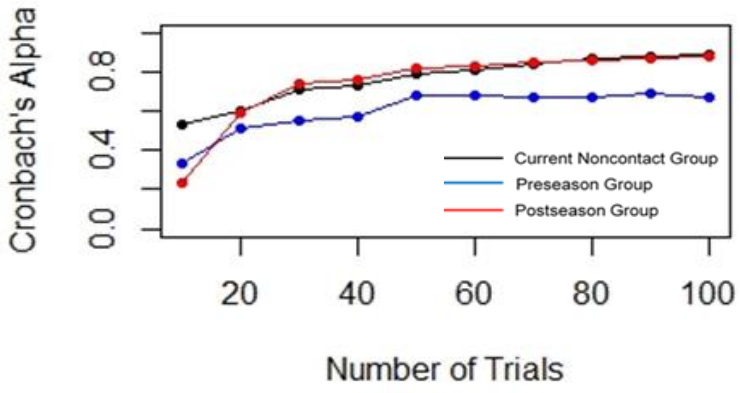


Cronbach's alpha coefficients for the amplitude of the MMN as a function of increasing trials for the intensity deviant are presented in Figure 9. For the current

noncontact group, fair internal consistency (α > .7) was reached with the inclusion of 30 trials (α = 0.72, $CI_{.95}$ = 0.52, 0.91) and good internal consistency (α > .8) was reached with as few as 60 trials (α = 0.82, $CI_{.95}$ = 0.69, 0.95). The preseason group did not reach the threshold for fair internal consistency but was approaching this threshold with an alpha value of 0.69 ($CI_{.95}$ = 0.52, 0.85) occurring with 50 trials included in the analysis. Fair internal consistency was reached for the postseason group with 30 trials (α = 0.74, $CI_{.95}$ = 0.61, 0.88) and good internal consistency was reached with 50 trials (α = 0.82, $CI_{.95}$ = 0.73, 0.92).

Figure 9

Cronbach's Alpha as a Function of Increasing Trials for the Intensity Deviant Condition



Regression Analyses

As some participants in the current noncontact group reported having previously participated in contact sports, and thus are more likely to have a history of head impact exposure, additional analyses were conducted to examine the influence of previous contact sport participation on the MMN regardless of current sport. To do so, the current noncontact group and the preseason group were combined, which also helps to improve

the sample size limitations that were present in the previous analyses. Participants' previous involvement in contact sports is described in Table 2. A series of linear regression analyses was calculated, the purpose of which was two-fold: 1) to examine the influence of previous contact sport participation on the MMN and 2) to examine the relationship between subset MMN and total trial MMN, focusing on the magnitude of the association. For each regression, the outcome variable was the amplitude of the total trial MMN, and the predictor variables were years of participation in contact sports and the amplitude of a subset MMN trial bin. Because the focus of this analysis was the magnitude of the association between the subset MMN and the total trial MMN, and to minimize issues stemming from the inclusion of highly related predictor variables within a single regression, each subset MMN was entered into a separate regression analysis, akin to the procedure used for the Pearson's correlation analyses reported above. Separate analyses were also conducted for responses to each type of deviant tone.

Table 2

Sample Size for Previous Participation in Contact Sports by Group and Total

	Current Noncontact Group	Preseason Group	Total *N*
None	4	/	4
>1 year	4	/	4
1-2 years	2	/	2
2-4 years	/	/	/
4-6 years	1	3	4
6-8 years	/	5	5
8-10 years	2	5	7
10+ years	1	14	15

Overall model statistics and regression coefficients for all models in the frequency deviant condition are presented in Table 3. All overall models were significant, and in each bin size case, the average trial subset amplitude was significantly associated with the total trial amplitude. Previous participation in contact sports did not significantly predict total trial amplitude in any model (all *p*s > 0.05). As seen in Table 3, adjusted R^2 ranges from 0.18 to 0.92, with the model explaining at least 50% of the variance in MMN amplitude when including at least 40 trials in the average, and over 70% of the variance when at least 50 trials were included. Independent of previous participation in contact sports, subset amplitude accounted for 46.9% to 95.9% of the variance in total MMN amplitude depending on the number of trials included in the subset, with over 70% of the variance explained when at least 30 trials were included.

Overall model statistics and regression coefficients for all models in the duration deviant condition are presented in Table 4. In each in size case, the overall model was significant, as was the contribution of each subset of trials. Participation in contact sports was not significantly associated with MMN amplitude in any of the models (all *p*s > 0.05). Adjusted R^2 ranged from 0.34 to 0.94. At least 50% of the variance in MMN amplitude was explained by the model when including at least 30 trials in the average, with over 70% of the variance accounted for by the models including at least 40 trials. Independent of participation in contact sports, subset amplitude accounted for 52.1% to 91.7% of the variance in total MMN amplitude depending on the number of trials included, with over 70% of the variance explained when at least 30 trials were included.

Overall model statistics and regression coefficients for all models in the intensity deviant condition are presented in Table 5. All overall models were significant, and each bin size subset amplitude was significantly associated with the overall trial amplitude. Participation in contact sports was not significantly associated with MMN amplitude in any model (all *p*s > 0.05). Adjusted R^2 ranged from 0.22 to 0.88. At least 50% of the variance in MMN amplitude was explained by the model when including at least 30 trials in the average, with over 70% of the variance accounted for by the models including at least 60 trials in the average. Subset bin amplitudes accounted for 48.8% to 93.0% of the variance in total MMN amplitude independent of participation in contact sports, with over 70% of the variance explained when at least 30 trials were included in the average.

Table 3

Model Statistics and Regression Coefficients for Total MMN Amplitude by Increasing Trial Subset in the Frequency Deviant

Trial Subset	Overall Model Statistics				Subset Amplitude Statistics			
	F	df	*p*	Adjusted R^2	b (SE)	$CI_{.95}$	*p*	SR^2
10 trials	5.5	2, 38	0.008	0.184	0.22 (0.07)	0.09, 0.36	0.002	0.469
20 trials	11.1	2, 38	<0.001	0.337	0.42 (0.09)	0.24, 0.60	<0.001	0.604
30 trials	20.3	2, 38	<0.001	0.491	0.60 (0.10)	0.41, 0.80	<0.001	0.715
40 trials	21.4	2, 38	<0.001	0.505	0.57 (0.09)	0.39, 0.75	<0.001	0.724
50 trials	48.8	2, 38	<0.001	0.705	0.66 (0.07)	0.53, 0.80	<0.001	0.845
60 trials	54.9	2, 38	<0.001	0.730	0.77 (0.07)	0.62, 0.91	<0.001	0.859
70 trials	88.9	2, 38	<0.001	0.815	0.83 (0.06)	0.71, 0.96	<0.001	0.905
80 trials	126.6	2, 38	<0.001	0.863	0.88 (0.06)	0.77, 0.99	<0.001	0.930
90 trials	161.7	2, 38	<0.001	0.889	0.91 (0.05)	0.81, 1.02	<0.001	0.943
100 trials	230.8	2, 38	<0.001	0.920	0.93 (0.04)	0.85, 1.02	<0.001	0.959

Note. df = degrees of freedom; b = unstandardized beta coefficient; SE = standard error; $CI_{.95}$ = 95% confidence interval; SR^2 = semi-partial correlation

Table 4

Model Statistics and Regression Coefficients for Total MMN Amplitude by Increasing Trial Subset in the Duration Deviant

Trial Subset	Overall Model Statistics				Subset Amplitude Statistics			
	F	df	*p*	Adjusted R^2	b (SE)	$CI_{.95}$	*p*	SR^2
10 trials	11.2	2, 38	<0.001	0.339	0.36 (0.09)	0.18, 0.53	<0.001	0.521
20 trials	15.0	2, 38	<0.001	0.412	0.53 (0.11)	0.31, 0.75	<0.001	0.584
30 trials	27.8	2, 38	<0.001	0.573	0.69 (0.10)	0.48, 0.89	<0.001	0.703
40 trials	52.3	2, 38	<0.001	0.719	0.77 (0.08)	0.61, 0.93	<0.001	0.796
50 trials	49.5	2, 38	<0.001	0.708	0.78 (0.08)	0.61, 0.95	<0.001	0.789
60 trials	71.8	2, 38	<0.001	0.780	0.80 (0.07)	0.65, 0.94	<0.001	0.831
70 trials	134.0	2, 38	<0.001	0.869	0.90 (0.06)	0.78, 1.01	<0.001	0.881
80 trials	180.0	2, 38	<0.001	0.900	0.87 (0.05)	0.77, 0.97	<0.001	0.897
90 trials	210.9	2, 38	<0.001	0.913	0.95 (0.05)	0.85, 1.04	<0.001	0.904
100 trials	303.8	2, 38	<0.001	0.938	0.98 (0.04)	0.90, 1.07	<0.001	0.917

Note. df = degrees of freedom; b = unstandardized beta coefficient; SE = standard error; $CI_{.95}$ = 95% confidence interval; SR^2 = semi-partial correlation

Table 5

Model Statistics and Regression Coefficients for Total MMN Amplitude by Increasing Trial Subset in the Intensity Deviant

Trial Subset	Overall Model Statistics				Subset Amplitude Statistics			
	F	df	*p*	Adjusted R^2	b (SE)	$CI_{.95}$	*p*	SR^2
10 trials	6.6	2, 38	0.003	0.220	0.27 (0.08)	0.11, 0.42	0.001	0.488
20 trials	11.8	2, 38	<0.001	0.352	0.40 (0.08)	0.23, 0.57	<0.001	0.603
30 trials	23.8	2, 38	<0.001	0.533	0.55 (0.08)	0.39, 0.72	<0.001	0.732
40 trials	35.8	2, 38	<0.001	0.635	0.67 (0.08)	0.50, 0.83	<0.001	0.796
50 trials	41.3	2, 38	<0.001	0.668	0.72 (0.08)	0.56, 0.88	<0.001	0.815
60 trials	61.1	2, 38	<0.001	0.750	0.78 (0.07)	0.63, 0.92	<0.001	0.862
70 trials	65.8	2, 38	<0.001	0.764	0.84 (0.07)	0.69, 0.99	<0.001	0.869
80 trials	76.8	2, 38	<0.001	0.791	0.89 (0.07)	0.74, 1.04	<0.001	0.884
90 trials	111.6	2, 38	<0.001	0.847	0.92 (0.06)	0.79, 1.05	<0.001	0.913
100 trials	147.6	2, 38	<0.001	0.880	0.95 (0.06)	0.84, 1.06	<0.001	0.930

Note. df = degrees of freedom; b = unstandardized beta coefficient; SE = standard error; $CI_{.95}$ = 95% confidence interval; SR^2 = semi-partial correlation

Discussion

The present study evaluated the robustness and the reliability of the MMN component of the ERP both in general and following repetitive head impact exposure and concussion by investigating the minimum number of trials necessary to clearly elicit this response. The stability of the MMN was not found to be related to varying histories of head impact exposure, remaining similar despite both prolonged and sporadic participation in contact sports. The amplitude of the MMN was most likely to be robust with fewer trials when elicited by a duration deviant as compared to frequency and intensity deviants. Based on the observed degree of similarity to the MMN response obtained from the inclusion of all trials in the paradigm, the MMN may be reliably elicited by a minimum of 40 to 60 trials depending on the type of deviant used, while maintaining a high degree of similarity to that obtained with a larger number of trials.

Comparing the stability of the three deviant types, the amplitude elicited by the duration deviant exhibited little to no difference in a series of paired t-tests between trial bin sizes when subsequent trials were added, whereas a greater number of differences between adjacent trial bin sizes were displayed by the responses to the other deviant types. This provides evidence that the duration deviant may be the most robust for eliciting a reliable MMN when compared to frequency and intensity deviants. Previous studies of MMN test-retest reliability (Tervaniemi et al., 1999) displayed a similar pattern, reporting higher reliability between testing sessions for a duration deviant when compared to frequency and intensity deviants. Furthermore, specifically in the current contact groups (both at preseason and postseason), stability was found with fewer trials

for the intensity deviant compared to the frequency deviant, for which differences in amplitude were found between bins with higher trial numbers. The postseason group in the frequency deviant condition displayed the most instability of any group/deviant combination, with significant amplitude differences seen in four trial bin pairs, suggesting the possibility of a reduction in stability of MMN amplitude for this deviant type after head impact exposure during a contact sports season. This also demonstrates the importance of using different types of deviants in the same protocol.

In contrast, in comparisons of participant groups, the minimum number of trials required to obtain a representative MMN amplitude was comparable across the three groups. It differed by 20 trials at the most, suggesting that a history of head impact exposure or concussion does not have a large influence on the reliability of the MMN. The postseason group did not require the highest number of trials to achieve reliability in any deviant type, but rather required an equal number or fewer trials, suggesting that acute exposure to repetitive head impacts may exert minimal influence on MMN reliability. Based on these similarities, although slight differences in amplitude may be found with the inclusion of additional trials, as demonstrated by the paired t-tests between adjacent trial bin sizes, this does not seem to impact the reliability of the response in terms of the strength of the association between a subset of responses and all available data. Therefore, smaller trial numbers may be used to reliably elicit the MMN. However, the average number of trials and range of accepted trials for each group should always be reported to account for any potential amplitude differences, such as a larger amplitude arising due to the inclusion of significantly fewer trials in one group.

Furthermore, when considering the Cronbach's alpha internal consistency results, the reliability coefficients of the preseason group were lower than that of the postseason group in some cases, especially for the smaller trial numbers. The same pattern also emerged when examining the correlation between all trials and different bin size subsets of trials. This discrepancy could potentially be attributed to a difference in the strength of the memory trace developed for stimuli on the first versus second exposure to the paradigm. Näätänen et al. (1993) investigated the relationship between the strength of a memory trace and the associated MMN response using a single-deviant auditory oddball paradigm consisting of complex sound stimuli in which the standard and deviant stimuli were minimally discriminable. The authors found that the presence of an MMN response developed gradually over the course of the task as participants became more capable of discriminating the deviant tone from the standard, which the authors attributed to a strengthening of the sensory memory trace. A similar process could account for the differences in reliability between the preseason and postseason observed here because participants at the postseason timepoint were more familiar with the experiment and therefore may have had a stronger memory trace for the stimuli, resulting in higher reliability.

A further comparison between the results obtained with Pearson's correlation coefficient and Cronbach's alpha coefficient revealed discrepancies in the number of trials required for reliability. Although in some cases these discrepancies were minor (e.g., in the intensity deviant condition for the postseason group), there were multiple cases, particularly including the current noncontact group and the preseason group, in

which more trials were required for reliability when based on Cronbach's alpha compared to robustness as reflected by Pearson's correlation between trial bins of different sizes and total trials. For example, in the intensity deviant condition for the preseason group, a strong correlation to the amplitude of all MMN trials ($r \geq 0.8$) was obtained with 40 trials, however adequate internal consistency ($\alpha \geq 0.7$) was not achieved with even 100 trials. These discrepancies may be attributable to differences in calculating each coefficient, and subsequent differences in how the ERP data is extracted from the EEG signal. Pearson's correlation was calculated between the average of each trial bin subset and the average of all trials, where the amplitude is obtained from the averaged ERP data. On the other hand, Cronbach's alpha examines the similarity of items, requiring each individual value, and thus required the amplitude value be obtained at the single trial level. Differences in results between these two analyses may be attributable to differences in formed waveforms compared to unextracted, unaveraged data. As the MMN is a relatively small response, there is more variability at the single trial level than occurs with the averaged responses, resulting in a larger amount of data being necessary to achieve reliability. Although Cronbach's alpha has been used in the past to examine the internal consistency of ERPs (e.g., Foti et al., 2013; Olvet & Hajcak, 2009; Rietdijk et al., 2014), this has primarily been done with larger components such as the P3 and the ERN, which are typically obtained from far fewer repetitions. Indeed, recommendations for the use of the ERN are as low as eight trials (Olvet & Hajcak, 2009), which is a fraction of that typically recommended for the MMN, and suggests that these larger components may be better represented at the single trial level than is the MMN. Consequently, optimal

methods for ERPs could be determined in part by the size of the component. Although the Cronbach's alpha and Pearson's correlation methods address different questions regarding stability and internal consistency, previous studies have interpreted these results in concert when discussing the minimum trials required for a robust ERP response (e.g., Olvet & Hajcak, 2009; Rietdijk et al., 2014). Therefore, taking the size of the component into consideration, in the present context the Pearson's correlation results should potentially be considered over Cronbach's alpha as they share more similarity to typical research practices in its quantification of the MMN.

The results of the regression analyses reinforce the conclusions drawn from the group findings, providing additional evidence that a history of cumulative head impact exposure may not influence the MMN, and that this response is highly stable even with a small number of repetitions. Rather than operationalizing cumulative head impact exposure based on current sport participation as was done in the group analyses, for the regression analyses we investigated this variable based on lifetime participation in contact sports. This provides an additional approach to address potential confounds in our quantification of chronic head impact exposure by accounting for previous experience in high contact activity. The operationalization of head impact exposure is discussed further in the Limitations section. When including previous participation in contact sports in regressions predicting the results from all trials, over 70% of the variance in MMN amplitude was explained by a subset of at least 40, 50, and 60 trials for the duration, frequency, and intensity deviants, respectively. Furthermore, when controlling for participation in contact sports, this was achieved with as few as 30 trials for all three

deviant types. The explanatory power of subset MMN trial bins on total trial MMN was slightly higher when contact sport participation was controlled, which could indicate a potential influence of contact sport participation on MMN stability. However, contact sport participation alone did not significantly influence the amplitude of the MMN. Additionally, the minimum number of trials required to account for the majority of the variance in total trial MMN amplitude was comparable when contact sport participation was included (i.e., 40 to 60 trials) or controlled (i.e., 30 trials), suggesting that any potential influence of contact sport participation on MMN stability is likely minimal. Not only do these results support the assertion that the MMN may be obtained with relatively few trials, but they are also comparable to the Pearson's correlation results obtained from the group analyses. In this way, accordant results were obtained when applying two methods of operationalizing head impact exposure, serving as concurrent evidence, and strengthening the conclusion that the MMN may be a robust assessment method regardless of head impact exposure history.

Although the results of the present study run contrary to the hypothesis that head impact exposure would impact the reliability of the MMN, there are a small number of previous studies reporting similar findings of comparable ERP reliability between clinical populations and healthy controls. For example, Sinha et al. (1992) investigated the test-retest reliability of the N1, N2, and P3 components elicited by a dual-modality (auditory and visual) oddball paradigm in individuals recovering from chronic alcoholism and healthy controls. All patients in the study met the National Council on Alcoholism criteria for alcoholism, had an average of over 10 years of alcoholism, and had been detoxified

for three to six weeks prior to participating in the study. When comparing within-subjects ERP measures over a 14 month period, no differences in test-retest reliability were found between patients and controls for 27 of 28 measures, with differences only arising for the visual N2 recorded at electrode Oz. Male and female participants were also equally reliable on ERP measures (Sinha et al., 1992). Despite having comparable reliability, group ERP differences were observed for male participants such that patients exhibited lower visual N1 and P3 amplitudes than controls, but no differences were observed for female participants (Parsons et al., 1990; Sinha et al., 1992). In this way, there can in some cases be a separation between ERP reliability and pathology, such that altered neurophysiological function is observed without the loss of measurement reliability.

In some cases, a seeming lack of reliability for a given ERP measurement in a clinical population may occur because a given response presents inconsistently over time. This looks like an unreliable manifestation of the ERP because of the typical averaging procedure that includes all trials of a stimulus type whether the person paid attention and perceived the stimulus or not. Variable participant brain responsiveness has been observed in comatose patients both across testing sessions, wherein an MMN response was absent in initial recording sessions but later appeared in others (Kane et al., 1996), and within a single session, as responsiveness has been observed to occur in cycles of presence and absence (Armanfard et al., 2019; Connolly et al., 2019). Although in such a case it would appear as though the reliability of the measurement is inadequate, this can serve as an indication of altered cognitive processing for the population in question. In the context of a single testing session, variability in responsiveness could manifest as an

attenuated waveform when responses are averaged and would subsequently impact the reliability of the measurement. In comparison, when the responses obtained from a clinical population are reliable, as was the case in Sinha et al. (1992) discussed above, this may suggest that observed ERP attenuations occur consistently, rather than resulting from variability in participant responsiveness. Such patterns may be more easily identified by examining responses across time in an experiment rather than for an increasing number of trials. This should be addressed by future research to further elucidate patterns of ERP reliability in clinical populations.

Although head impact exposure is becoming an increasing area of research focus, particularly pertaining to sports injuries, the mechanism of associated deficits and relation to clinical conditions such as concussion and CTE is not well understood. Deficits associated with head impact exposure without concussion appear to be situationally specific, depending on the method of assessment and the characteristics of the impact (Gysland et al., 2012; McAllister et al., 2012; Miller et al., 2007; Talavage et al., 2014). For example, in their cross-season study of high school football players, Talavage et al. (2014) reported that only a subset of athletes displayed impaired cognitive function in the absence of clinical injury, but this impairment was comparable to that of those athletes who did sustain a clinical injury. Impaired cognitive function was also associated with having sustained a greater number and magnitude of collision events at the top frontal location of the head as measured by an accelerometer. Incorporating additional specificity into the assessment and analysis of head impact exposure can thus be crucial in elucidating outcomes. To apply these findings to the present study, it is possible that

examining neurophysiological function, specifically ERP stability, based on the specific magnitude and location of sustained head impacts may provide additional insight into the manifestation of subsequent cognitive dysfunction.

As applied to the study of concussion and head impact exposure, the MMN is also an emerging technique that has yielded inconsistent results. Specifically, a reduction in amplitude of the MMN has been observed in a sample of retired professional football players (Ruiter et al., 2019); however, no differences were found in a sample of recently concussed adolescents compared to controls (Ruiter et al., 2020). The discrepancy in these findings may be attributable to differences in the recency of injury or in cumulative exposure to concussion and head impacts, as older individuals who have participated in sports at higher levels of competition are likely to have sustained a greater number and magnitude of such injuries (Boshra et al., 2020; Boshra, Ruiter, et al., 2019; Broglio, 2017). Furthermore, Boshra et al. (2020) suggested that such a pattern of responses may be indicative of a progression of concussion wherein cognitive dysfunction in early ERP measures emerges with aging as a chronic stage of injury, while not being present in the short-term post-injury, signifying a dynamic nature of concussive symptoms. Although the results of the current study suggest that years of participation in contact sports do not influence the MMN, this was found with a relatively young, small sample. Therefore, future research should focus on older adults to address longer participation histories and a longer delays from injury to further elucidate the progression of concussion and determine if the present results remain consistent.

Furthermore, there is currently limited research that compares concussion and repetitive head impact exposure independently. This in part may be attributable to the interdependent nature of these two concepts and the complexities of separating them. In the present study, we examined head impact exposure in a sample including participants who also had a history of diagnosed concussion, thus the present results cannot be isolated purely to one concept. Previous investigations of the test-retest reliability of the MMN found that this component was not stable over time in a sample with a history of moderate to severe TBI (Lew et al., 2007), and as concussion is a form of TBI (McCrory et al., 2017), albeit more mild, future research would benefit from examining the reliability of the MMN in concussion specifically.

In addition to examining the reliability of the MMN in concussion specifically, future research would benefit from addressing the psychometric properties of other ERPs that may be affected by this type of injury. For example, the P3b, a centroparietal positivity associated with attentional resource allocation, has served as a robust assessment tool for cognitive function following concussion in a variety of contexts, including recent (Baillargeon et al., 2012) and remote (De Beaumont et al., 2009) concussion and repetitive head impact exposure (Moore et al., 2017; Wilson et al., 2015). The N2b, a frontocentral negativity associated with inhibitory executive function, is also a component of interest that would be beneficial to examine in terms of stability as its outcome in concussion is less consistent (Boshra et al., 2020; Boshra, Dhindsa, et al., 2019; Krokhine et al., 2020; Ruiter et al., 2020). Previous studies have reported the N2b to be smaller in some cases (Broglio et al., 2009; Hudac et al., 2018; Ruiter et al., 2019)

and larger in others (Ledwidge & Molfese, 2016; Moore et al., 2015); therefore, understanding the consistency of this response both within and across testing sessions could contribute to unraveling these inconsistencies.

In the interpretation of the present findings, the specific features of the paradigm used to elicit the MMN should also be considered. We used a multi-deviant auditory oddball paradigm consisting of frequency, intensity, and duration deviants, which is one possible alternative used to study this response. The differences in reliability between deviant types reported here are minimal, and while this encompasses three types of deviants that are frequently used in the literature, it is not exhaustive of all possibilities. Other deviants including density, perceived sound-source location, gap, brightness, and noise level have also been used to elicit the MMN, and the amplitude of the response is reported to vary based on the type of deviant used (Näätänen et al., 2004; Pakarinen et al., 2010). It is also well established that the magnitude of difference between the standard and deviant tones impacts the amplitude and latency of the observed response (Pakarinen et al., 2007; Tiitinen et al., 1994). The specific type of deviant presented can also influence the results observed for different clinical populations. For example, in patients with schizophrenia MMN amplitude is consistently reduced in the duration deviant, but not in the frequency deviant (Michie et al., 2000), whereas in individuals with dyslexia an opposite pattern is observed (Baldeweg et al., 1999). Therefore, the observed MMN response can vary based on the context and the features of the stimuli presented, which should be accounted for when considering the reliability of the response. The results presented here suggest that the stability of the MMN is persistent across deviant types;

however, considering deviant-specific differences observed in clinical populations, widening our understanding of MMN reliability based on deviant type and population of interest would be beneficial.

The oddball paradigm, namely a stimulus presentation sequence consisting of the repetition of a frequent standard stimulus and infrequent deviant stimulus, has historically been the paradigm of choice for eliciting the MMN (Pakarinen et al., 2010); however, more recently multi-feature paradigms have been developed with the goal of optimizing MMN recording. These optimized multi-feature paradigms allow for the simultaneous presentation of numerous deviant stimuli, with up to eight deviant types being used without drastically increasing the length of the experiment (Näätänen et al., 2004; Pakarinen et al., 2010). This has been accomplished in two ways: 1) by reducing the occurrence of the standard stimulus to alternate between standard and deviant on each stimulus presentation (Näätänen et al., 2004) and 2) by eliminating the standard tone altogether and presenting a range of tones, each varying on one characteristic (Pakarinen et al., 2010). These multi-feature paradigms are reported to consistently elicit an MMN response, but these responses can vary in amplitude and latency to those elicited from a standard oddball paradigm, thus the stability of the MMN in these contexts may vary as well.

In addition to deviant type and paradigm structure, the MMN can also be elicited in different modalities. Though primarily recorded in the auditory modality, there is increasing support for a visual MMN elicited from stimuli presented in an oddball sequence varying in pattern or colour (Czigler et al., 2002; Winkler et al., 2005). The

visual MMN is described as a posterior negativity occurring around 100 to 250ms post-stimulus and is believed to represent similar attention and memory processes of the auditory MMN, as it occurs following unattended infrequent stimuli (Czigler et al., 2002; Kimura et al., 2009; Winkler et al., 2005). As the MMN has not been studied as extensively in the visual domain as in the auditory, future research would benefit from examining the stability of the visual MMN. Moreover, the specificities of the paradigm in which this response is elicited should be considered when interpreting and applying the present results.

Applications

The results of our study provide evidence supporting a strong relationship between the MMN as obtained from a large number of trials to that obtained from a relatively small subset, which can be applied to the use of the MMN as a cognitive assessment tool in future research. Overly long paradigms are undesirable in human research as participants may experience boredom, loss of focus, fatigue, or discomfort, all of which can reduce the quality of the data collected and make participants less willing or able to participate. The MMN has an advantage over other ERPs as it does not require active attention to be elicited, so loss of attention is not a critical factor for data collection in this case, but shorter paradigms are still preferable to promote the comfort of the participant. As previous recommendations for eliciting the MMN suggested the use of at least 150 trial repetitions (Duncan et al., 2009), the present results suggest that this number could be reduced while still allowing for a reliable MMN to be recorded, which would reduce the burden placed on participants.

Although some previous studies used randomized trial selection across the entire presentation period for subset ERP averages (e.g., Baldwin et al., 2015; Foti et al., 2013; Rietdijk et al., 2014), we analyzed subset averages based on consecutively occurring trials, to examine responses obtained with both relatively few trials and relatively few exposures to the target stimuli. It is possible that responses may vary over the course of an experiment, specifically as participants become more familiar with the deviant stimuli; thus, by examining a subset of early responses our results are more applicable to employing a shortened paradigm in which fewer exposures to the stimuli would occur. Furthermore, the present results revealed strong reliability of the MMN with a small number of trials using a single electrode, as is common for this type of analysis (e.g., Foti et al., 2013; Olvet & Hajcak, 2009; Rietdijk et al., 2014). Huffmeijer et al. (2014) reported that ERP reliability improves with the inclusion of additional electrode sites, specifically comparing a single electrode to a region of interest including seven electrodes, suggesting that the results presented here may also be improved when the MMN is analyzed as a region of interest.

Limitations

One limitation of the present study stems from the application of somewhat arbitrary threshold criteria for Cronbach's alpha and Pearson's correlation coefficients for determining when adequate reliability has been achieved. Although these methods are common in previous literature for determining a minimum number of trials necessary for a given ERP, there is a lack of consistency in the criteria used to make these decisions. Regarding Cronbach's alpha, the minimum threshold at which reliability is considered

acceptable ranges from 0.5 to 0.7 depending on the study (Baldwin et al., 2015; Foti et al., 2013; Moran et al., 2013; Olvet & Hajcak, 2009; Rietdijk et al., 2014). The language with which these values are described also varies, with alpha of 0.7 being described as "fair" (Foti et al., 2013) or "high" (Moran et al., 2013). Thresholds for Pearson's correlation coefficients have a similar range from 0.5 to 0.8 and are described as "acceptable" or "strong" depending on the context (Moran et al., 2013; Olvet & Hajcak, 2009; Rietdijk et al., 2014). Inconsistency in reliability criteria limits the generalizability of results across studies as the minimum number of trials stated by one study will vary compared to those employing a different criteria level. Therefore, it is important that studies reporting these coefficients explicitly state the criteria used, and future research would benefit from adhering to a more consistent standard.

Inconsistency in the interpretation of Cronbach's alpha and Pearson's correlation coefficients is not specific to the field of ERP reliability, but is a common criticism of reporting internal consistency results (Akoglu, 2018; Mukaka, 2012). Moreover, the language used to describe these results (i.e., "fair" versus "strong") has implications for how they are perceived. In some cases, this may result in overstating the strength of the relationship, so it has been recommended that authors exert caution when making such statements (Akoglu, 2018). The criteria applied in the present study were chosen based on recommendations from statistical literature for the use of such coefficients in research (Akoglu, 2018; Cicchetti, 1994) and on the criteria used in previous ERP reliability literature, so that the current interpretations would remain similar to those in the field without overstating the strength of the results. Furthermore, including R^2 in the present

analysis provides a more concrete representation of the explanatory power of the independent variable beyond a descriptive association, which helps to strengthen the conclusions drawn from the other analyses.

Another limitation of the present study arises from the quantification of head impact exposure. Contact sport athletes were tested at preseason and postseason timepoints to examine the influence of repetitive exposure to head impacts in the short term (i.e., over the course of a few months) based on the assumption that impacts would be obtained over the course of the season. Operationalizing head impact exposure in such a way limits the present results as impact exposure was not measured directly, so details such as the specific number of impacts sustained, their location, and their cumulative magnitude are unknown. Additionally, a subset of participants in the current noncontact group reported having previously participated in contact sports, which indicates a potential previous history of head impact exposure and limits the distinction between the two groups. We addressed this limitation by combining the current noncontact and preseason contact groups and conducting an analysis based on previous years participation in contact sports, which is discussed further below. Future research should include a direct measurement of head impacts, such as an accelerometer attached to athletes' helmets, which would provide a more accurate representation of this concept while also allowing for a more in-depth analysis including the frequency, magnitude, and location of sustained impacts.

We also quantified head impact exposure based on previous years participation in contact sports, which introduces additional considerations for the generalizability of our

findings. Like the comparison of preseason and postseason, years participating in contact sports is limited as it does not directly measure sustained head impacts; however, it does provide the advantage of examining participants on a continuum, based on the assumption that more years participating in contact sports would be associated with a higher number of sustained impacts. That being said, there are additional variables that influence the likelihood of sustaining an impact, such as type of sport and level of competition (Broglio et al., 2011; Guskiewicz & Mihalik, 2011; Gysland et al., 2012; Huber et al., 2021), which were not measured in the present study and thus reduce the robustness of present conclusions. For those participants not currently competing in contact sports, it is also not known when exactly this participation occurred, introducing an additional variable of time since exposure. However, because the present sample consisted of young adults, there is a smaller window in which participation could have occurred than in an older population, especially for those with a longer history (i.e., eight or more years), minimizing the potential impact of this confounder.

Finally, the group analysis is also limited due to the absence of a second testing session for the current noncontact group. While current contact athletes were tested prior to the start of their season and following its culmination, noncontact athletes were only tested once to allow for the recruitment of a sufficient sample size, which limits the conclusions that can be drawn when comparing the preseason and postseason timepoints. Recruitment and testing of current noncontact athletes was severely limited by laboratory closures due to the COVID-19 pandemic. While particularly true for the current

noncontact group, the present study as a whole was also limited by the use of a small sample size, and thus the results provide a preliminary representation of MMN stability.

Conclusion

There is increasing evidence of impaired cognitive health following repetitive head impact exposure and concussion, which are believed to be associated with possible longer term health effects such as CTE (Gavett et al., 2011; Huber et al., 2016; McAllister et al., 2012; Talavage et al., 2014). In the present study, we investigated the stability of the MMN, an electrophysiological response associated with pre-attentive processing and predictive coding, in the context of repetitive head impact exposure and concussion, with the goal of identifying the minimum amount of data required to observe this response. Although the current results are limited by a small sample size and the quantification of head impact exposure, MMN reliability was observed to be consistent regardless of acute or chronic head impact exposure, potentially suggesting that automatic attention may be a robust process as recorded in a single experiment and that any attenuations in this process may occur consistently across responses. While the amplitude of the MMN elicited by a duration deviant was most consistent with the inclusion of increasing trials, reliability was comparable across responses to duration, frequency, and intensity deviants, indicating that the MMN is robust with a variety of experimental features. Previous research has suggested that the MMN should be recorded from at least 150 trial repetitions for each deviant (Duncan et al., 2009). Our results provide preliminary evidence that this response can be observed with far fewer exposures, as low as 40 to 60 depending on the context, however these estimates are distinct from the total number of trials that would need to be

recorded, as they depend on the amount of data that is of insufficient quality to be included in analysis. These results can be applied to shorten paradigms used to elicit the MMN and consequently reduce the burden placed on participants, particularly patients. When making such applications, future research should consider the features of the paradigm used, such as stimulus modality and mode of presentation, as these features could impact the generalizability of results.

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Appendix – Online Survey

LMB Varsity Survey (2019-2020)

There are 58 questions in this survey.

Researcher Input

Participant code: *

Please write your answer here:

What is the purpose of today's testing? *

Choose one of the following answers
Please choose **only one** of the following:

- ◯ Baseline
- ◯ Concussion 1
- ◯ Concussion 2
- ◯ Concussion 3
- ◯ Concussion 4
- ◯ Concussion 5
- ◯ Concussion 6+
- ◯ Post-season

Do you play a contact or non-contact sport? *

Choose one of the following answers
Please choose **only one** of the following:

- ◯ Contact
- ◯ Non-contact

Test date: *

Answer must be greater or equal to 09.08.2019
Please enter a date:

Screening Form

Sex: *

Choose one of the following answers
Please choose **only one** of the following:

- ◯ Male
- ◯ Female
- ◯ Other

Highest level of education: *

Choose one of the following answers
Please choose **only one** of the following:

- ◯ No Formal Education
- ◯ High School
- ◯ College
- ◯ University
- ◯ Some College/University
- ◯ Vocational Training
- ◯ Masters
- ◯ Doctorate / PHD
- ◯ Other

Handedness: *

Choose one of the following answers
Please choose **only one** of the following:

- ◯ Right
- ◯ Left
- ◯ Ambidextrous

Date of birth: *

Please complete all parts of the date.
Answer must be less or equal to 31.12.2002
Please enter a date:

Highest level of education: *

Choose one of the following answers
Please choose **only one** of the following:

- ◯ No Formal Education
- ◯ High School
- ◯ College
- ◯ University
- ◯ Some College/University
- ◯ Vocational Training
- ◯ Masters
- ◯ Doctorate / PHD
- ◯ Other

Handedness: *

Choose one of the following answers
Please choose **only one** of the following:

- ◯ Right
- ◯ Left
- ◯ Ambidextrous

Date of birth: *

Please complete all parts of the date.
Answer must be less or equal to 31.12.2002
Please enter a date:

Language(s) in order of fluency:

Is English your native language? *

Choose one of the following answers
Please choose **only one** of the following:

- ◯ Yes
- ◯ No

How old were you when you first learned English? *

Only answer this question if the following conditions are met:
Answer was 'No' at question '10 [L1]' (Is English your native language?)

Only numbers may be entered in this field.
Please write your answer here:

Please enter a numerical value (e.g. if you were 5 years old, write "5").

Were you born in Canada? *

Choose one of the following answers
Please choose **only one** of the following:

- ◯ Yes
- ◯ No

How old were you when you moved to Canada? *

Only answer this question if the following conditions are met:
Answer was 'No' at question '12 [Canada]' (Were you born in Canada?)

Only numbers may be entered in this field.
Please write your answer here:

Please enter a numerical value (e.g. if you were 5 years old, write "5").

Is your vision normal or corrected-to-normal? *

Choose one of the following answers
Please choose **only one** of the following:

- ◯ Yes
- ◯ No

Please describe any vision issues. *

Only answer this question if the following conditions are met:
Answer was 'No' at question '14 [Vision]' (Is your vision normal or corrected-to-normal?)

Please write your answer here:

Is your hearing normal or corrected-to-normal? *

Choose one of the following answers
Please choose **only one** of the following:

- ◯ Yes
- ◯ No

Please describe any hearing issues. *

Only answer this question if the following conditions are met:
Answer was 'No' at question '16 [Hearing]' (Is your hearing normal or corrected-to-normal?)

Please write your answer here:

Have you ever had any neurological, psychological, or psychiatric problems?

*

Choose one of the following answers
Please choose **only one** of the following:

- ◯ Yes
- ◯ No

Please describe any neurological, psychological, or psychiatric problems. *

Only answer this question if the following conditions are met:
Answer was 'Yes' at question '18 [NPPProblems]' (Have you ever had any neurological, psychological, or psychiatric problems?)

Please write your answer here:

Describe age, length, and recovery

Have you ever had any perceptual (such as colour blindness), learning, or language problems?

*

Choose one of the following answers
Please choose **only one** of the following:

- ◯ Yes
- ◯ No

Please describe any perceptual (such as colour blindness), learning, or language problems.

*

Only answer this question if the following conditions are met:
Answer was 'Yes' at question '20 [PLLProblems]' (Have you ever had any perceptual (such as colour blindness), learning, or language problems?)

Please write your answer here:

Describe age, length, and recovery

Are you presently taking any medication?

*

Choose one of the following answers
Please choose **only one** of the following:

- ◯ Yes
- ◯ No

Which medications are you presently taking? *

Only answer this question if the following conditions are met:
Answer was 'Yes' at question '22 [Medications]' (Are you presently taking any medication?)

Please write your answer here:

Have you taken any medications in the last 24 hours?

*

Choose one of the following answers
Please choose **only one** of the following:

- ◯ Yes
- ◯ No

Which medications have you taken in the last 24 hours? *

Only answer this question if the following conditions are met:
Answer was 'Yes' at question '24 [MedicationCont]' (Have you taken any medications in the last 24 hours?)

Please write your answer here:

How often do you consume the following? *

Please choose the appropriate response for each item:

	A few times a week	About once a week	At least once a month	A few times a year	Never
Alcohol	◯	◯	◯	◯	◯
Cigarettes/vapes	◯	◯	◯	◯	◯
Cannabis	◯	◯	◯	◯	◯
Other recreational drugs	◯	◯	◯	◯	◯

Have you ever lost consciousness, had any fainting spells, paralysis, or dizziness?

*

Choose one of the following answers
Please choose **only one** of the following:

- ◯ Yes
- ◯ No

Please describe the time(s) you lost consciousness, had any fainting spells, paralysis, or dizziness? *

Only answer this question if the following conditions are met:
Answer was 'Yes' at question '27 [ConsciousnessHistory]' (Have you ever lost consciousness, had any fainting spells, paralysis, or dizziness?)

Please write your answer here:

Describe age, length, and recovery

How alert do you feel right now? (1 = not very, 5 = very alert) *

Please choose the appropriate response for each item:

	1	2	3	4	5
Level of alertness	◯	◯	◯	◯	◯

How many hours did you sleep last night? *

Only numbers may be entered in this field.
Please write your answer here:

Please enter a numerical value.

Did you sleep more, less, or about an equal number of hours as compared to your average amount? *

Choose one of the following answers
Please choose **only one** of the following:

◯ More
◯ Less
◯ Average

How well have you been sleeping for the past week? (1 = not very, 5 = very well) *

Please choose the appropriate response for each item:

	1	2	3	4	5
Sleep quality	◯	◯	◯	◯	◯

Your Health and Well-Being (SF-36)

This survey asks for your views about your health. This information will help keep track of how you feel about how well you are able to do your usual activities.

In general, would you say your health is: *

Please choose the appropriate response for each item:

	Excellent	Very good	Good	Fair	Poor
	◯	◯	◯	◯	◯

Compared to one year ago, how would you rate your health in general now? *

Please choose the appropriate response for each item:

	Much better now than one year ago	Somewhat better now than one year ago	About the same now as one year ago	Somewhat worse now than one year ago	Much worse now than one year ago
	◯	◯	◯	◯	◯

The following questions are about activities you might do during a typical day. Does your health now limit you in these activities? If so, how much? *

Please choose the appropriate response for each item:

	Yes, limited a lot	Yes, limited a little	No, not limited at all
Vigorous activities, such as running, lifting heavy objects, participating in strenuous sports	◯	◯	◯
Moderate activities, such as moving a table, pushing a vacuum cleaner, bowling, or playing golf	◯	◯	◯
Lifting or carrying groceries	◯	◯	◯
Climbing several flights of stairs	◯	◯	◯
Climbing one flight of stairs	◯	◯	◯
Bending, kneeling, or stooping	◯	◯	◯
Walking more than a mile	◯	◯	◯
Walking several blocks	◯	◯	◯
Walking one block	◯	◯	◯
Bathing or dressing yourself	◯	◯	◯

During the past 4 weeks, have you had any of the following problems with your work or other regular daily activities as a result of your physical health? *

Please choose the appropriate response for each item:

	Yes	No
Cut down on the amount of time you spent on work or other activities	◯	◯
Accomplished less than you would like	◯	◯
Were limited in the kind of work or other activities	◯	◯
Had difficulty performing the work or other activities (for example, it took extra effort)	◯	◯

During the past 4 weeks, have you had any of the following problems with your work or other regular daily activities as a result of any emotional problems (such as feeling depressed or anxious)? *

Please choose the appropriate response for each item:

	Yes	No
Cut down on the amount of time you spent on work or other activities	◯	◯
Accomplished less than you would like	◯	◯
Did work or other activities less carefully than usual	◯	◯

During the past 4 weeks, to what extent has your physical health or emotional problems interfered with your normal social activities with family, friends, neighbors, or groups? *

Please choose the appropriate response for each item:

	Not at all	Slightly	Moderately	Quite a bit	Extremely
Answer:	◯	◯	◯	◯	◯

How much bodily pain have you had during the past 4 weeks? *

Please choose the appropriate response for each item:

	None	Very mild	Mild	Moderate	Severe	Very severe
Answer:	◯	◯	◯	◯	◯	◯

During the past 4 weeks, how much did pain interfere with your normal work (including both work outside the home and housework)? *

Please choose the appropriate response for each item:

	Not at all	A little bit	Moderately	Quite a bit	Extremely
Answer:	◯	◯	◯	◯	◯

These questions are about how you feel and how things have been with you during the past 4 weeks. For each question, please give the one answer that comes closest to the way you have been feeling. How much of the time during the past 4 weeks... *

Please choose the appropriate response for each item:

	All of the time	Most of the time	Some of the time	A little of the time	None of the time
Did you feel full of pep?	◯	◯	◯	◯	◯
Have you been a very nervous person?	◯	◯	◯	◯	◯
Have you felt so down in the dumps that nothing could cheer you up?	◯	◯	◯	◯	◯
Have you felt calm and peaceful?	◯	◯	◯	◯	◯
Did you have a lot of energy?	◯	◯	◯	◯	◯
Have you felt downhearted and blue?	◯	◯	◯	◯	◯
Did you feel worn out?	◯	◯	◯	◯	◯
Have you been a happy person?	◯	◯	◯	◯	◯
Did you feel tired?	◯	◯	◯	◯	◯

During the past 4 weeks, how much of the time has your physical health or emotional problems interfered with your social activities (like visiting with friends, relatives, etc.)? *

Please choose the appropriate response for each item:

	All of the time	Most of the time	Some of the time	A little of the time	None of the time
Answer:	◯	◯	◯	◯	◯

How TRUE or FALSE is each of the following statements for you? *

Please choose the appropriate response for each item:

	Definitely true	Mostly true	Don't know	Mostly false	Definitely false
I seem to get sick a little easier than other people	◯	◯	◯	◯	◯
I am as healthy as anybody I know	◯	◯	◯	◯	◯
I expect my health to get worse	◯	◯	◯	◯	◯
My health is excellent	◯	◯	◯	◯	◯

Perceived Stress Scale (PSS)

The questions in this scale ask you about your feelings and thoughts during the last month. In each case please indicate your response representing how often you felt or thought a certain way.

In the last month... *

Please choose the appropriate response for each item:

	Never	Almost never	Sometimes	Fairly often	Very often
How often have you been upset because of something that happened unexpectedly?	○	○	○	○	○
How often have you felt that you were unable to control the important things in your life?	○	○	○	○	○
How often have you felt nervous and "stressed"?	○	○	○	○	○
How often have you felt confident about your ability to handle your personal problems?	○	○	○	○	○
How often have you felt that things were going your way?	○	○	○	○	○
How often have you found that you could not cope with all the things that you had to do?	○	○	○	○	○
How often have you been able to control irritations in your life?	○	○	○	○	○
How often have you felt that you were on top of things?	○	○	○	○	○

	Never	Almost never	Sometimes	Fairly often	Very often
How often have you been angered because of things that were outside your control?	◯	◯	◯	◯	◯
How often have you felt difficulties were piling up so high that you could not overcome them?	◯	◯	◯	◯	◯

Concussion Screening

What is the **total** number of concussions you have sustained to date? If you have sustained more than 6, please indicate how many in the "other" section. *

ⓘ Choose one of the following answers
Please choose **only one** of the following:

◯ 0
◯ 1
◯ 2
◯ 3
◯ 4
◯ 5
◯ 6
◯ Other

Of the concussions you have sustained, how many were **sports-related**? *

Only answer this question if the following conditions are met:
Answer was NOT '0' at question '45 [NOCs]' (What is the total number of concussions you have sustained to date? If you have sustained more than 6, please indicate how many in the "other" section.)

Choose one of the following answers
Please choose **only one** of the following:

- ◯ 0
- ◯ 1
- ◯ 2
- ◯ 3
- ◯ 4
- ◯ 5
- ◯ 6
- ◯ Other

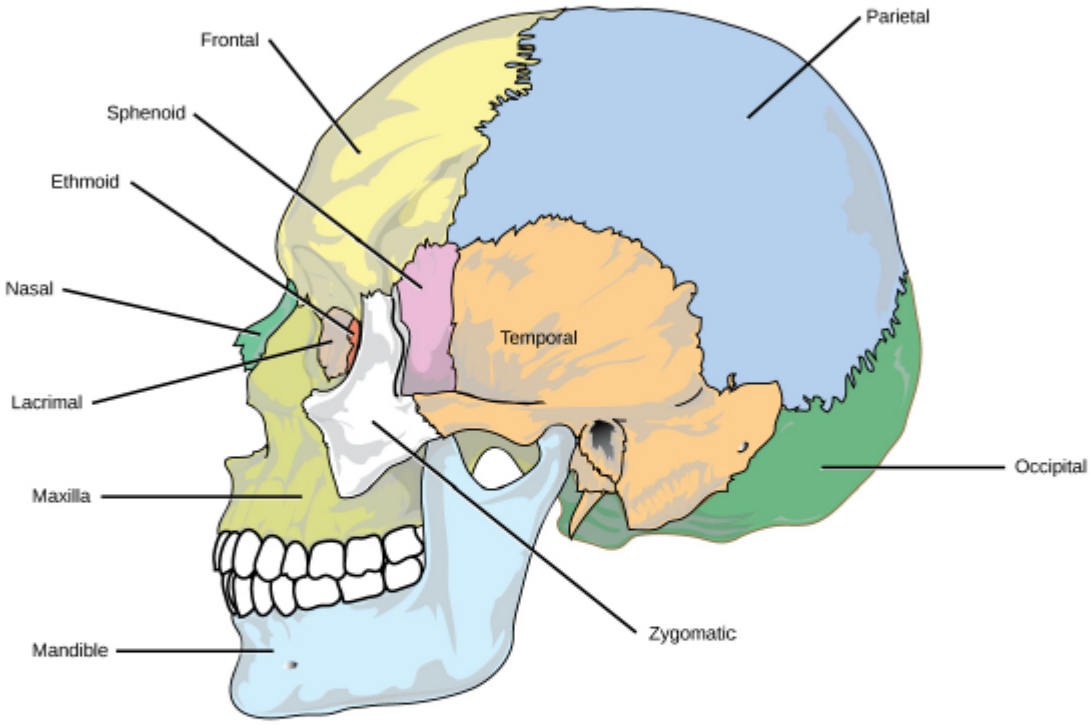
When did you sustain your most recent concussion? *

Only answer this question if the following conditions are met:
Answer was NOT '0' at question '45 [NOCs]' (What is the total number of concussions you have sustained to date? If you have sustained more than 6, please indicate how many in the "other" section.) *and* Answer was 'Concussion 1' *or* 'Concussion 2' *or* 'Concussion 3' *or* 'Concussion 4' *or* 'Concussion 5' *or* 'Concussion 6+' at question '2 [Testing]' (What is the purpose of today's testing?)

Answer must be greater or equal to 09.08.2019
Please enter a date:

If you cannot remember the exact date please provide an estimate.

If you were hit on the head, or your head hit an object (e.g. dashboard of a car), please specify where the PRIMARY contact occurred during your most recent concussion. Note: indirect force is an option.



*

Only answer this question if the following conditions are met:
Answer was NOT '0' at question '45 [NOCs]' (What is the total number of concussions you have sustained to date? If you have sustained more than 6, please indicate how many in the "other" section.) *and* Answer was 'Concussion 1' *or* 'Concussion 2' *or* 'Concussion 3' *or* 'Concussion 4' *or* 'Concussion 5' *or* 'Concussion 6+' at question '2 [Testing]' (What is the purpose of today's testing?)

Choose one of the following answers
Please choose **only one** of the following:

- ◯ Frontal (forehead)
- ◯ Occipital (back

- ◯ Left Temporal (close to ear)
- ◯ Right Temporal (close to ear)
- ◯ Left Parietal (top)
- ◯ Right Parietal (top)
- ◯ Left Jaw
- ◯ Right Jaw
- ◯ Neck
- ◯ Face
- ◯ Other body part
- ◯ Indirect force
- ◯ Other [ ]

If other, please indicate.

When you sustained your most recent concussion, did you lose consciousness? *

Only answer this question if the following conditions are met:
Answer was NOT '0' at question '45 [NOCs]' (What is the total number of concussions you have sustained to date? If you have sustained more than 6, please indicate how many in the "other" section.) *and* Answer was 'Concussion 1' *or* 'Concussion 2' *or* 'Concussion 3' *or* 'Concussion 4' *or* 'Concussion 5' *or* 'Concussion 6+' at question '2 [Testing]' (What is the purpose of today's testing?)

❗ Choose one of the following answers
Please choose **only one** of the following:

- ◯ Yes
- ◯ No

Was your most recent concussion diagnosed by a health care professional/provider? *

Only answer this question if the following conditions are met:
Answer was NOT '0' at question '45 [NOCs]' (What is the total number of concussions you have sustained to date? If you have sustained more than 6, please indicate how many in the "other" section.) *and* Answer was 'Concussion 1' *or* 'Concussion 2' *or* 'Concussion 3' *or* 'Concussion 4' *or* 'Concussion 5' *or* 'Concussion 6+' at question '2 [Testing]' (What is the purpose of today's testing?)

Choose one of the following answers
Please choose **only one** of the following:

- ◯ Yes
- ◯ No

If you are currently experiencing any of the following symptoms, please indicate the severity of each. (0 = no, 3 = moderate, 6 = severe) *

Please choose the appropriate response for each item:

	0	1	2	3	4	5	6
Headache	○	○	○	○	○	○	○
Nausea	○	○	○	○	○	○	○
Vomiting	○	○	○	○	○	○	○
Balance Problems	○	○	○	○	○	○	○
Dizziness	○	○	○	○	○	○	○
Fatigue	○	○	○	○	○	○	○
Trouble Falling Asleep	○	○	○	○	○	○	○
Excessive Sleep	○	○	○	○	○	○	○
Loss of Sleep	○	○	○	○	○	○	○
Drowsiness	○	○	○	○	○	○	○
Light Sensitivity	○	○	○	○	○	○	○
Noise Sensitivity	○	○	○	○	○	○	○
Irritability	○	○	○	○	○	○	○
Sadness	○	○	○	○	○	○	○

	0	1	2	3	4	5	6
Nervousness	◯	◯	◯	◯	◯	◯	◯
More emotional	◯	◯	◯	◯	◯	◯	◯
Numbness	◯	◯	◯	◯	◯	◯	◯
Feeling "Slow"	◯	◯	◯	◯	◯	◯	◯
Feeling "Foggy"	◯	◯	◯	◯	◯	◯	◯
Difficulty Concentrating	◯	◯	◯	◯	◯	◯	◯
Difficulty Remembering	◯	◯	◯	◯	◯	◯	◯
Visual Problems	◯	◯	◯	◯	◯	◯	◯

Sports Injury

What is your primary sport? If you are on a varsity sports team, please select the corresponding sport.

Only answer this question if the following conditions are met:
Answer was NOT '0' at question '45 [NOCs]' (What is the total number of concussions you have sustained to date? If you have sustained more than 6, please indicate how many in the "other" section.) *and* Answer was 'Concussion 1' *or* 'Concussion 2' *or* 'Concussion 3' *or* 'Concussion 4' *or* 'Concussion 5' *or* 'Concussion 6+' at question '2 [Testing]' (What is the purpose of today's testing?)

Choose one of the following answers
Please choose **only one** of the following:

- ◯ Football
- ◯ Rugby
- ◯ Hockey
- ◯ Soccer
- ◯ Basketball
- ◯ Baseball/Softball
- ◯ Ski/Snowboarding
- ◯ Skating
- ◯ Bicycling
- ◯ Horseback Riding
- ◯ Skateboarding/Rollerblading
- ◯ Running
- ◯ Swimming
- ◯ Other

What position do you play? *

Only answer this question if the following conditions are met:
Answer was 'Football' at question '52 [SportPlay]' (What is your primary sport? If you are on a varsity sports team, please select the corresponding sport.)

Choose one of the following answers
Please choose **only one** of the following:

- ◯ Quarterback
- ◯ Wide receiver
- ◯ Defensive back
- ◯ Running back
- ◯ Linebacker
- ◯ Offensive lineman
- ◯ Defensive lineman
- ◯ Special teams
- ◯ Other

How many years have you spent playing your primary sport?

*

Choose one of the following answers
Please choose **only one** of the following:

- ◯ Less than 1 year
- ◯ 1 - 2 years
- ◯ 2 - 4 years
- ◯ 4 - 6 years
- ◯ 6 - 8 years
- ◯ 8 - 10 years
- ◯ 10 + years
- ◯ N/A

How many years in total have you spent playing contact sports? (e.g. basketball, soccer, rugby etc.) *

Choose one of the following answers
Please choose **only one** of the following:

- ◯ None
- ◯ Less than 1 year
- ◯ 1 - 2 years
- ◯ 2 - 4 years
- ◯ 4 - 6 years
- ◯ 6 - 8 years
- ◯ 8 - 10 years
- ◯ 10 + years

Were you playing your primary sport at the time of your most recent concussion? *

Only answer this question if the following conditions are met:
Answer was NOT '0' at question '45 [NOCs]' (What is the total number of concussions you have sustained to date? If you have sustained more than 6, please indicate how many in the "other" section.) *and* Answer was 'Concussion 1' *or* 'Concussion 2' *or* 'Concussion 3' *or* 'Concussion 4' *or* 'Concussion 5' *or* 'Concussion 6+' at question '2 [Testing]' (What is the purpose of today's testing?)

Choose one of the following answers
Please choose **only one** of the following:

- ◯ Yes
- ◯ No

Please specify which sport/activity you were doing at the time of your most recent concussion. *

Only answer this question if the following conditions are met:
Answer was NOT '0' at question '45 [NOCs]' (What is the total number of concussions you have sustained to date? If you have sustained more than 6, please indicate how many in the "other" section.) *and* Answer was 'No' at question '56 [SportConc]' (Were you playing your primary sport at the time of your most recent concussion?)

Please write your answer here:

What are the total minutes of play you have had this season? *

Only answer this question if the following conditions are met:
Answer was 'Contact' at question '3 [Subject1]' (Do you play a contact or non-contact sport?) *and* Answer was NOT 'Baseline' at question '2 [Testing]' (What is the purpose of today's testing?)

Only numbers may be entered in this field.
Please write your answer here:

Thank you for taking this survey. Your answers are a valuable part of this research.
11.08.2019 – 14:02

Submit your survey.
Thank you for completing this survey.