CONCUSSION AND AGE EFFECTS ON MISMATCH NEGATIVITY STABILITY

CONCUSSION AND AGE EFFECTS ON THE STABILITY OF THE MISMATCH NEGATIVITY BRAIN RESPONSE

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A Thesis Submitted to the School of Graduate Studies in Partial Fulfilment of the Requirements for the Degree of Master of Science

McMaster University

Master of Science (2024)

Hamilton, Ontario (Linguistics and Languages)

TITLE: Concussion and Age Effects on the Stability of the Mismatch Negativity Brain Response

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NUMBER OF PAGES: CIX, 109

Lay Abstract

Concussions are a growing public health concern affecting all ages. Impacts to the head and body can result in severe long-term symptoms and, in turn, lead to neurodegenerative conditions affecting a range of functions including motor and cognitive functioning. A brain imaging method called electroencephalography (EEG) records brain electrical activity through sensors attached to the scalp and has been proven useful in evaluating brain function. This thesis examined the stability of an EEG response known as the mismatch negativity (MMN) in concussed adolescents and retired Canadian Football League (rCFL) athletes. We found that the stability of the MMN, a response reflecting automatic attention, was significantly weaker in rCFL athletes compared to healthy individuals. There was also evidence indicating that the concussed adolescents were less sensitive to concussive symptoms compared to the older rCFL athletes. A stable MMN was achieved with 130 trials across all groups and stimuli.

Abstract

There is a large literature describing the effects of concussion on cognitive processes including attention and memory. Electroencephalography (EEG) is a neuroimaging tool that records brain electrical activity from the scalp using electrodes and has a distinguished history in medicine examining many neurological conditions such as epilepsy and sleep abnormalities. Derived from EEG, event-related potentials (ERPs) are neurophysiological responses that are differentially sensitive to specific cognitive processes. A much-investigated ERP component called the mismatch negativity (MMN) has been employed usefully in concussion research to assess changes in automatic attention. In the context of concussion, the stability of the MMN in a single test session and test-retest changes in the response have received little attention. The present thesis examined the internal consistency/reliability of the MMN component in four groups: concussed adolescents, retired Canadian Football League (rCFL) players, and respective groups of age-matched healthy controls. The number of trials necessary for the MMN to be elicited with a high degree of internal consistency was assessed for both amplitude and area under the curve (AUC) values. Cronbach's alpha was used as a measure of internal MMN consistency and changes in responses to deviant stimuli were employed in the oddball paradigm separately for each group. Data from each group revealed a significant effect of the number of trials on the reliability of the MMN. The concussed adolescents showed stronger MMN stability compared to the rCFL athletes in comparison to each groups' respective controls. The adolescent control group revealed lower response stability than the control group with the older adults. A stable MMN ($\alpha \geq 0.80$) was

achieved with 130 trials across all groups and stimuli. The findings demonstrate that the MMN is abnormal in rCFL athletes coping with post-concussion syndrome (PCS) whereas adolescents seem to have a reduced vulnerability to the symptoms of concussion.

Acknowledgements

I would like to thank my committee members, Drs. John F. Connolly and Elisabet Service for their guidance, patience, and support throughout my years in the Language, Memory and Brain Lab. I will always remember the plethora of stories shared.

I would also like to extend my gratitude to my external committee member, Dr. Daniel Schmidtke, for his time and helpfulness. Thank you for answering my statistics questions and giving me the opportunity to work with you in the MELD Research Lab.

A special thank you to Kiersten Mangold. Your problem-solving skills have saved me the countless times that I would encounter issues with BVA.

Thank you to Dr. Victor Kuperman and Nadia Lana for being exceptionally supportive of me during my graduate study journey. I am so grateful for you both!

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List of Abbreviations and Symbols

Ag/AgCl: Silver/Silver Chloride

ANCOVA: Analysis of Covariance

AUC: Area Under the Curve

BDI II: Beck Depression Inventory II

BVA: BrainVision Analyzer

CDI 2: Children's Depression Inventory 2

CEI: Cognitive Efficiency Index

CFL: Canadian Football League

CTE: Chronic Traumatic Encephalopathy

dB: Decibels

df: Degrees of Freedom

DRL: Driven-Right Leg

DT: Duration Tone

EEG: Electroencephalography

EP: Evoked Potential

ERN: Error-Related Negativity

ERP: Event-Related Potential

FT: Frequency Tone

Fz: Fronto-Central

HiREB: Hamilton Integrated Research Ethics Board

Hz: Hertz

IC: Impulse Control

ImPACT: Immediate Post-Concussion Assessment and Cognitive Testing

ISI: Interstimulus interval

IT: Intensity Tone

MEG: Magnetoencephalography

MMN: Mismatch Negativity

MS: Motor Speed

ms: Milliseconds

mTBI: Mild Traumatic Brain Injury

NMDAR: N-Methyl-D-Aspartate Receptor

oct: Octave

PCS: Post-Concussion Syndrome

PCSS: Post-Concussion Symptom Scale

Pe: Error Positivity

rCFL: Retired Canadian Football League

RT: Reaction Time

SD: Standard Deviation

SF-36: Short-Form Health Survey 36

SNR: Signal-to-Noise Ratio

SPL: Sound Pressure Level

ST: Standard Tone

VBM: Verbal Memory

VEP: Visual Evoked Potential

VIM: Visual Memory

μV: Microvolts

Declaration of Academic Achievement

I am the primary author of this thesis. I wrote, prepared, and revised it with feedback received from Dr. John F. Connolly, Dr. Elisabet Service, and Dr. Daniel Schmidtke. I conducted the literature reviews, designed the studies, and analyzed all the data.

The following individuals' roles in my work are outlined in the parentheses:

Dr. John F. Connolly (study design, revisions)

Dr. Elisabet Service (revisions)

Dr. Daniel Schmidtke (revisions, analysis)

Kiersten Mangold (study design, analysis)

Dr. Kyle Ruiter (data collection, analysis)

Dr. Rober Boshra (data collection, analysis)

Carol DeMatteo (participant collection)

Chapter 1

In Canada, it has been estimated that 200,000 to 250,000 concussions occur annually (SCSC, 2019). Approximately 150,000 Ontario residents alone received a diagnosis of concussion between 2008 and 2016 (Langer et al., 2020). Concussions have become a major public health concern in the United States as well, having been described as a "silent epidemic" by the Centers for Disease Control and Prevention (Broglio et al., 2017; Langlois et al., 2004). Considering the global impact of concussions, it is necessary to advance a tool that can better detect neurophysiological markers of concussive symptoms and measure post-injury changes. It has been argued that behavioural measures are unavoidably subjective and thus cannot be considered anything more than rough estimates that have no reliable ground truth characteristics (Alsalaheen et al., 2016; Broglio et al., 2017; Fischer et al., 2010; Rawlins et al., 2020; Ruiter et al., 2020).

What is a Concussion?

A concussion, also described by some as a mild traumatic brain injury (mTBI), is an injury caused by a direct impact to the head or body where a substantial amount of external force is transferred to the head, resulting in a disruption of brain function (Ruiter et al., 2019; Zuckerman et al., 2012). Some individuals may even experience a brief loss of consciousness immediately after a sustained concussion which, the Centers for Disease Control acknowledged, occurs in less than 10% of concussions (Grady, 2010; Zhang et al., 2016). Concussion assessment and management can become difficult for clinicians and researchers as individuals experience a combination of various symptoms such as

headaches, nausea, dizziness, sleep problems, and memory and attention problems (Kontos et al., 2012b). Many behavioural concussion symptoms typically resolve with time (Yeates et al., 2009). A study (McKeon et al., 2013) found that 85-90% of cases resolve within seven to 14 days. It is only in a small number of cases that symptoms last from weeks to months. Another study (Zuckerman, 2012) found that within one month, 90% of participants returned to their baseline neurocognitive and symptom scores. However, there is also evidence of a recovery trend which begins within a 21-day window, but symptoms are not yet resolved up to 58 days later (Ruiter et al., 2020). In other cases, concussed individuals might endure prolonged periods of recovery and symptoms along with permanent injury, as later described in Chapter 3. It is fair to say that the great disparity amongst studies regarding symptom resolution is attributable to the use of behavioural assessments that are subjective and have far lower test-retest reliability values compared to neurophysiological measures such as event-related potentials (Alsalaheen et al., 2016; Broglio et al., 2017; Grady, 2010; McKeon et al., 2013; Ruiter et al., 2019 & 2020).

As noted in the preceding paragraph, assessment of concussion is traditionally done with behaviourally based methods that are subjective and inherently have significant variability. An example of this type of assessment is the computerized Immediate Post-Concussion Assessment and Cognitive Testing Tool (ImPACT). The ImPACT is the most used concussion evaluation tool in both research and clinical practice (Alsaheen et al., 2016; Iverson et al., 2003). Additionally, there are self-report evaluations such as the Post-Concussion Symptom Scale (PCSS) and depression scales, such as the Beck

Depression Inventory II (BDI II)/Children's Depression Inventory 2 (CDI 2) (Beck et al., 1961; Kovacs, 2011; Lovell & Collins, 1998). The PCSS is a cognitive test battery whose content validity has been demonstrated in concussion assessment. Validity was obtained by correlating the PCSS's measures with other assessments from the cognitive test battery CogSport, developed by CogState Ltd (Melbourne, Australia). Regression analyses revealed that the performance on several CogSport subtests was predicted by the PCSS score (Chen et al, 2007). The BDI II and CDI 2 are also commonly used in psychiatric contexts. They provide insight on how concussion affects levels of depression (Ruiter et al., 2019 & 2020). Evidently, there are many behavioural measures used to assess concussion that should be supported by more objective measures.

Electroencephalography (EEG) is a technique that records neural signals from the scalp. Event-related potentials or ERPs are derived from EEG by signal averaging temporally aligned to stimulus or behaviour onset. They reflect activity from many different neural sources and do so with high temporal resolution. They can capture changes in neural responses reflecting cognitive functioning with millisecond resolution (Luck, 2014). EEG is one of two functional brain imaging methods that can record real-time evoked brain activity, the other being magnetoencephalography (MEG) (Wendel et al., 2009). The use of EEG and particularly ERPs has become increasingly prevalent in clinical settings and has demonstrated tremendous potential for brain injury research (Duncan et al., 2009). ERPs can measure specific neurophysiological manifestations of cognitive processes and dysfunctions. They include neural responses specific to cognitive, sensory, and motor stimuli or events. These neural responses are extracted from EEG using time-locked

averaging techniques and other sophisticated analyses. ERPs are characterized by amplitude (signal strength), polarity (either positive or negative), and latency (the time delay from the eliciting stimulus at which the peak manifests) (Luck, 2014). ERPs have proven to be a more objective assessment tool in concussion and recovery by acting as indices of cognitive decline or improvement (Brooks & Dickey, 2016; De Beaumont, 2007 & 2009; Ruiter et al., 2019). The P300 and MMN are two extensively studied ERP components in concussion research. They reflect processes such as stimulus classification and automatic auditory change detection, respectively (Cohen & Polich 1997; Näätänen et al., 2011). In the present thesis, we will focus exclusively on the MMN.

Mismatch Negativity (MMN)

The Mismatch Negativity (MMN) has a negative deflection of about 5 μV (microvolts), typically seen from 150-250 ms after the onset of an unexpected auditory stimulus. It is distributed in the fronto-central (Fz) and fronto-temporal electrodes across the scalp (Garrido et al. 2009; Luck, 2014). Some researchers have been considered the MMN to reflect the behaviour of the auditory perceptual N100 component as the two ERPs tend to overlap temporally and spatially (Tavakoli et al., 2021). Many researchers (e.g., Escera et al., 2003; Rinne et al., 2000) agree that the frontal MMN sources are associated with early involuntary attention switching to deviant auditory stimuli, whereas the temporal lobe sources reflect change detection. Lately, researchers have suggested that the MMN is a predictive coding response (Friston, 2012; Garrido et al., 2009). Predictive coding proposes that the brain constantly generates predictions about incoming sensory information based on prior knowledge and experience. When sensory input matches these

predictions, minimal neural activity occurs. However, when there is a mismatch between the predicted and actual input, the brain generates an MMN.

An oddball paradigm is commonly applied in MMN experiments. In this paradigm, a steady stream of repeating (referred to as "standard") auditory stimuli or stimulus patterns is presented. This is interrupted by an infrequently presented different (called the *deviant* or "oddball") auditory stimulus. The participant must be in a conscious state (although not necessarily consciously aware) but does not need to attend to these stimuli and is traditionally prevented from doing so. Brain responses to the standard and oddball stimuli are recorded. The averaged response to the standard stimuli is subtracted from the response to the oddball stimuli to create difference (also called subtraction) waveforms (Garrido et al., 2009). Most researchers have agreed that the MMN reflects a memory trace of the standard tones in comparison to each current deviant stimulus (Näätänen & Kreegipuu, 2012). The MMN has been recorded to deviant types with tones varying in different ways such as frequency, duration, or intensity (Todd et al., 2008).

The MMN has been widely applied in clinical research studies involving areas such as coma, schizophrenia, Alzheimer's disease, and autism spectrum disorder (Armanfard et al., 2018; Cecchi et al., 2015; Connolly et al., 2019; Duncan et al., 2009; Fischer et al., 2010). One of the most common concerns when using the MMN in clinical studies is the required amount of time to obtain data that will exhibit an identifiable response. The typical protocol (containing a single type of deviant stimuli) can be quite time consuming as the deviant stimulus is presented only 10-20% of the time. The use of multiple-deviant-type paradigms for tones can reduce the total time required to collect adequate data

(Näätänen et al., 2012). Also, more recent machine learning methods have enabled identification of the MMN response with significantly fewer trial numbers, resulting in a reduction in testing time (Armanfard et al., 2018; Herera-Diaz et al., 2023). For clinical purposes, it is important to know how few trials suffice to produce reliable data when using different MMN paradigms and analysis methods. The present study explores this in the context of mild brain trauma, i.e., concussion.

A number of brain injury studies (Baugh et al., 2012; Bernstein, 2002; Boshra et al., 2019; De Beaumont, 2009; Duncan et al., 2009; Dupuis et al., 2000; Ruiter et al., 2019) have validated the neurophysiological deficits associated with concussions using the MMN and other ERP components. Brain injury has been linked to various dysfunctions in the N-methyl-D-aspartate receptor (NMDAR) system of the brain which is related to memory functions (Javitt et al., 1996). A recent investigation of retired Canadian football players found the MMN amplitude to be significantly reduced. This was interpreted to demonstrate an abnormality in early automatic attention (Ruiter et al., 2019). The finding appears to reflect a long-term abnormality associated with automatic attention in as much as the retired football players had not sustained any concussions for decades. This result and the link to the NMDAR system suggests an interesting biomarker role for the MMN indicating permanent injury to one neural substrate of memory. It also contrasts very well with the absence of “permanent” MMN abnormalities in concussed younger populations (Ruiter et al., 2020).

Reliability Measures

The reliability of EEG recordings must be considered with clinical populations in mind. ERP studies examining cognitive functioning tend to compare specific patient participants to healthy controls. The use of such neurophysiological measures must be deemed reliable for both populations alike. Researchers have observed that patients have an inherently abnormal EEG which would require more or longer testing sessions to obtain reliable data (Duncan et al., 2009). For example, McCarley et al. (1993) found that patients with schizophrenia tend to have abnormal (reduced) P300 amplitudes to auditory stimuli. Few studies have examined the reliability of ERPs in clinical populations to determine the conditions of which they can be used in brain health assessments. Accurate estimates of ERP reliability are essential for obtaining useful data, yet the number of existing studies examining reliability are surprisingly limited (Huffmeijer et al., 2014). It is important to examine how ERP components change over time since they may do so differentially by factors such as age, injury, recovery, and decline. There are existing ERP studies which demonstrate how reduced reliability can reflect patient pathology rather than the invalidity of a test or measure. Due to variability in cognitive function, it may be difficult to record consistent ERPs in patients who suffer from a lack of consciousness, attention, or perception of stimuli. For example, studies with comatose patients found that there are cycles of MMN presence and absence throughout a single recording session (Armanfard et al., 2018; Connolly et al., 2019). When these MMN responses are averaged, they can result in an attenuated waveform due to the patient's pathology rather than reliability issues. Since ERPs have been found to be a promising tool in the

assessment, diagnosis, and recovery tracking of concussion, it is crucial to examine the effects of concussion on the stability of ERPs and determine how many trials are necessary to achieve *good* or *excellent* stability. The MMN technique has often yielded excellent results in groups, but further research is necessary before it can be reliably used to assess individual patients (Näätänen et al., 2011).

The test-retest method is a standard method in reliability research. The participants are tested at different times and the results are compared to assess the reliability of the measure or the experimental protocol. A study by Sinha et al (1992) examined the test-retest reliability of ERPs (i.e. the N1, N2 and P3) in participants with chronic alcoholism and healthy controls. They found that both groups, retested after about 14 months, produced similar correlation consistencies for visual and auditory ERP measures, suggesting that the long-term reliability of patients and controls was not any different. In previous research, the MMN has been measured with an overall acceptable reliability (ICC $\geq$ 0.60) across two test occasions with the retest session performed after a delay of at least two days, and up to two months (Lew et al., 2007). Specifically, the test-retest reliability was found to be stable and moderately to highly correlated across the wide range of time intervals (i.e. anywhere from two days to two months). The oddball paradigm that elicits the MMN can simultaneously contain different kinds of deviants such as stimuli differing from the standard stimulus in frequency, duration, and intensity. A study performed on the differences of these deviants found that the duration oddball elicited the most replicable amplitude and latency from stimulus onset (Tervaniemi et al., 1999). The same result was also reported by Kathmann et al. (1999), where the MMN

amplitudes were larger, and replicability was better for duration compared to frequency deviants. The reliability of duration deviants has now been replicated in many studies (Boshra et al., 2020; Ruiter et al., 2019; Todd et al., 2008). The present study used a multi-deviant MMN paradigm that included duration, frequency, and intensity deviants.

Reliability can also be studied within a single recording session. Previous studies have examined the internal consistency reliability of other ERP components than the MMN, such as the P300, the error-related negativity (ERN), the error positivity (Pe), and the N200, by comparing data across trials within a test. Cohen & Polich (1997) used both auditory and visual oddball paradigms to examine the internal consistency reliability of the P300 component that is associated with attention. They found that its amplitude stabilizes within 20 target trials and its peak latency hardly changes. Studies observing the ERN and Pe (Olvet & Hajcak, 2009; Pontifex et al., 2010) found that these components can be quantified using a minimum of six to eight error trials. In addition, Rietdijk et al. (2014) concluded that the N200 and P300 are internally consistent after 20 and 14 trials, respectively, have been included in the averages. Despite its importance in studying a range of pathological conditions (Näätänen et al., 2012), the MMN has yet to be studied using internal consistency reliability measures. The matter of how many trials is necessary for the MMN to achieve stability is essential to determine to allow investigation of the convergent effects of concussion and age.

Thesis Overview

The purpose of the present thesis was to explore the internal consistency reliability of the MMN brain response in healthy individuals and to then compare it with that in concussed adolescents and retired athletes. A three-deviant auditory oddball paradigm was used. The first study examined the MMN of concussed compared to non-concussed adolescents and the second study included retired professional football players and age-matched control participants. The research question asked whether there is an effect of age and concussion on the internal consistency of the MMN. We hypothesized firstly that concussed participants would require more trials to obtain a MMN with a high internal consistency reliability. Secondly, we hypothesized that older age at the time of testing would negatively influence internal consistency of the MMN; that is, older individuals would require more trials to achieve a stable MMN than younger people and this effect would interact with a history of concussion.

The main objectives of this thesis included the following:

1. To determine the number of trials necessary for the MMN to be elicited with a high (*good* or *excellent*) degree of internal consistency.
2. To investigate the effects of age and concussion on MMN stability.

Chapter 2

Study 1: MMN Response Stability in Concussed Adolescents vs. Controls

Introduction

Historically, adolescents have been underrepresented in the concussion literature. However, recently, they have drawn attention by showing the largest increase of concussion rates (Grady, 2010; Zhang et al., 2016). This fact is concerning since adolescence is a human growth period of immense brain and cognitive development (Blakemore & Choudhury, 2006). According to Zuckerman et al. (2012), adolescents have a longer resolution period of concussion symptoms than adults. One ERP study of concussion in adolescents examined working memory and symptom persistence (Baillargeon et al., 2012). It found deficits to be present at least 6 months following the concussion. The researchers also concluded that adolescents are more sensitive to concussive symptoms than adults. Another study (Ruiter et al., 2020) found that concussed adolescents displayed deficits in executive control and attention compared to controls. Additional research is necessary to better understand the neurophysiological effects of concussion in adolescents who are extremely susceptible to neurological damage.

The purpose of this study was to explore the reliability of MMN methodology in the study of consequences of concussive impacts in adolescents compared to healthy controls. The study investigated the internal consistency reliability of the MMN component. The

primary objective was to establish the number of trials needed to elicit the MMN with high stability in adolescence.

Methods

This study was approved by the Hamilton Integrated Research Ethics Board (HiREB), Hamilton, Ontario, Canada. In accordance with the Declaration of Helsinki, all participants provided informed consent prior to study participation.

Participants

26 (seven male) adolescents (mean age = 15.04, range = 13 – 17) with recently sustained concussions, clinically diagnosed using neurological and neuropsychological assessments, took part in this study. The diagnosis was done at the McMaster Children's Hospital. Age was reported by participants and/or their parent(s). The concussed group also provided information of the number of prior concussions, and number of days since the latest concussion before the day of EEG testing. A control group consisting of 28 (five male) healthy subjects (mean age = 19.3, range = 17 – 22), reporting no history of head injuries, were also recruited. All control participants informed investigators that they had no history of neurological or auditory problems.

Behavioural Assessments

The Immediate Post-Concussion Assessment and Cognitive Test (ImPACT), the Post-Concussion Symptom Scale (PCSS), and Children's Depression Inventory 2 (CDI 2) were administered to the concussed participant group prior to beginning the experiment. Scores for all three tests were assessed using descriptive statistics.

The ImPACT assessment offers five different composite scores, a symptomatology score, and a Cognitive Efficiency Index (CEI) score through six sub-tests. The composite scores include Verbal Memory (VBM), Visual Memory (VIM), Motor Speed (MS), Reaction Time (RT), and Impulse Control (IC). The higher scores in the VBM, VIM, and MS composite scores correspond to better levels of verbal and visual memory as well as faster processing speed. Conversely, the lower scores in the RT and IC composite scores represent faster response times and greater impulse control. The symptomatology score was used to characterize the participant's state at the time of testing. The higher CEI scores indicate a better level of cognitive function. These are measured from the Symbol Matching Test with an interaction between accuracy and speed (Iverson et al., 2003). The ImPACT also contains a symptom inventory (the PCSS) which evaluates how participants feel on a regular basis in relation to symptoms such as headache, balance problems, sadness, numbness or tingling, and visual problems. Using a 0-6 Likert-type scale, symptoms are rated on severity. Each symptoms' score is combined to equal the total PCSS score (Lovell & Collins, 1998). A systematic review of the ImPACT's construct validity revealed strong convergence validity among scores. However, evidence for discriminant validity was inconclusive (Alsalaheen et al., 2016).

The CDI 2 assesses depression symptomatology exclusively for children and adolescents ages seven to 17. It contains 28 items, each of which includes three statements. Each item is related to a particular scale (listed below) and each statement has an assigned score between 0-2. The participant is asked to select the statement in each item that best describes their feelings. The total raw score is calculated by adding the score associated

with each selected statement for all items. There are also two scale scores (Emotional Problems and Functional Problems), and four subscale scores (Negative Mood/Physical Symptoms, Negative Self-Esteem, Ineffectiveness, Interpersonal Problems) that are determined from the calculation. These raw scores are converted to T-scores using female and male profiles for specific age ranges (7-12, 13-17). The T-scores are then classified into Very Elevated, Elevated, High Average, and Average or Lower for each scale and subscale. The test-retest reliability of test scores was calculated based on a subgroup of 79 children from the standardization sample. They completed the CDI 2 twice within a two- to four-week time interval. The reliability estimates revealed excellent temporal stability (Kovacs, 2011).

EEG Experiment

MMN

ERPs were recorded during an auditory oddball paradigm (Ruiter et al., 2019; Todd et al., 2008) which consisted of a standard tone (ST) and three deviant tones: differing from the standard in frequency (MMNf), duration (MMNd), and intensity (MMNi). The standard tone (1000 Hz [hertz], 80 dB [decibel] SPL [sound pressure level], 50 ms duration) was presented 1968 times (82% of the stimuli). The frequency deviant tone (FT, 1200 Hz, 80 dB SPL, 50 ms), the duration deviant tone (DT, 1000 Hz, 80 dB SPL, 100 ms), and the intensity deviant tone (IT, 1000 Hz, 90 dB SPL, 50 ms) were presented 144 times each (18% [6% each] of the stimuli). The interstimulus interval (ISI) was 500 ms for all tones.

Procedure

All participants completed a pre-screening form regarding demographic information along with the Edinburgh Handedness Inventory (Oldfield, 1971) before EEG testing. The ImPACT, CDI 2 and PCSS were completed by only the concussed participants. In a sound attenuated room, participants sat in a chair facing a computer monitor wearing noise-cancelling headphones where the auditory stimuli played through. For the MMN experiment, participants were instructed to focus on the visually neutral silent nature film on the screen. They were told that the auditory tones were of no significance.

EEG Recording

64 Silver/Silver Chloride (Ag/AgCl) electrodes were placed in accordance with a version of the International 10/20 system (Jasper, 1958) called the Modified Combinatorial Nomenclature (Oostenveld & Praamstra, 2001) on participants using an electrode cap. Continuous EEG was collected using the ActiveTwo BioSemi system and digitized at 512 Hz with a bandpass filter of 0.01 – 100 Hz and notch filter of 60 Hz. As is typical when using an active system, the driven-right leg (DRL) was used as an online reference for data. These recording settings were also applied to all external electrodes. Two external electrodes were placed above and over the outer canthus of the left eye to record vertical and horizontal eye movements (electrooculography). Three other external electrodes were attached to the two mastoid processes and on the tip of the nose. Markers were automatically placed to identify the onset of stimulus presentation.

Data Preprocessing

BrainVision Analyzer 2.1 (BVA; Brain Products Inc.) was used to process the EEG data offline. Prior to the application of a 0.1 – 30 Hz bandpass filter (24 dB/oct [octave]), non-ocular artifacts were first manually removed. After, the data was re-referenced to the averaged mastoids to maximize Signal-to-Noise Ratio (SNR). Data were then segmented into 200 ms pre- to 600 ms post-stimulus intervals for the MMN task and averaged for each condition. Difference waves were calculated by subtracting standard condition ERPs from the deviant condition ERPs. Automatic peak detection (Barr et al., 1978) was performed on these difference waveforms of the MMN component within a 150 – 250 ms time window. Some time window boundaries were manually adjusted after inspection to accommodate slightly earlier or later peaks. Next, the area under the curve (AUC) and amplitude data were exported to R Software (RStudio, version 4.0.2) as single trials from the Fz electrode for the reliability analysis. We did not export data from any temporal electrodes since the MMN tends to be larger in amplitude frontally (Baldeweg et al., 1999; Näätänen et al., 2007). The exported amplitude values were the detected peak amplitudes within the designated time-window for the MMN. The AUC values were exported from a time window of -25 ms to +25 ms around the latency of the peak. The extracted value was based on the average of data points surrounding the peak latency to account for potential amplitude outliers.

Internal Consistency Analysis of EEG Data

The ERP data exported from Brain Vision Analyzer 2.1 was imported into R statistical software (RStudio, version 4.0.2). The *psych* package was loaded to calculate Cronbach's

alpha with the function *alpha*. Cronbach's alpha is an internal consistency measure associated with the inter-relatedness of items within a test. It is expressed by a number between 0 and 1, and this value is increased if test items are correlated to one another (Cronbach, 1951; Tavakol & Dennick, 2011). The number is also referred to as alpha coefficient, α. Table 1 shows ranges of alpha coefficient values and their corresponding verbal descriptors of internal consistency. Cronbach's alpha is expressed using the following formula:

$$a = \frac{k}{k-1}\left(1 - \frac{\sum S_i^2}{S_T^2}\right)$$

where k is the number of items, s^2_i is the variance of the i^{th} item and s^2_T is the variance of the total score formed by summing all the items (see Bland & Altman, 1997). In the present study, Cronbach's alpha was calculated from the first 130 trials collectively for both amplitude and AUC data. The alpha values were calculated separately for each Group (Concussed vs. Control) and Stimulus Type (Standard vs. three levels of Deviant: Frequency, Intensity, Duration). We calculated amplitude and AUC averages by averaging successive blocks of ten trials (1–10, 1–20, 1–30, etc.) up to 130 trials. We included both sequential and randomized order of the subset ERP averages in our dataset.[1]

[1] We found no difference of consequences when including Order Type as a fixed factor in the analyses.

Table 1

Descriptors of Cronbach's alpha values

Cronbach's alpha	Internal Consistency
$\alpha \geq 0.9$	Excellent
$0.8 \leq \alpha < 0.9$	Good
$0.7 \leq \alpha < 0.8$	Acceptable
$0.6 \leq \alpha < 0.7$	Questionable
$0.5 \leq \alpha < 0.6$	Poor
$\alpha < 0.5$	Unacceptable

Note. See (Cronbach, 1951; Caruana et al., 2023).

The statistical analysis was performed using analysis of covariance (ANCOVA) tests with an alpha level of $p < 0.05$. The continuous dependent variables were either amplitude or AUC alpha coefficient values. The categorical variable was Group (Concussed vs. Control). The continuous variable acting as a covariate was Number of Trials (blocks of ten trials up to 130 trials).

Results

Demographic Data

The average age and number of days since last concussion on the date of EEG testing, the number of previous concussions, and the summary of demographic data for both concussed and control adolescent participants can be found in Table 2. The data show that control participants were on average 19.3 years old whereas concussed participants had an average age of 15.04. Concussed adolescents had an average of 1.88 previous concussions (range 0-6) and last sustained a concussion on average 20.15 days prior to EEG testing. Participants consisted of both males and females.

Table 2

Concussed and control adolescent participants' demographic data

	Concussed Adolescents (N = 26)			**Controls (N = 28)**
	Age	***# of Previous Concussions***	***# of Days Since Last Concussion***	***Age***
Mean (SD)	15.04 (1.53)	1.88 (1.63)	20.15 (13.35)	19.3 (1.22)

Behavioural Assessments

All participants completed the ImPACT, PCSS, and CDI 2 after providing consent. Participants' average behavioural assessment (ImPACT) scores are presented in Table 3. The mean score for the concussive symptomatology (PCSS) was 55.08 (SD = 24.92). The mean score for the depressive symptomatology (CDI 2) was 56.07 (SD = 10.29).

Table 3

Concussed adolescent participants' ImPACT behavioural scores compared to normative data (Iverson et al., 2003)

	Female Scores (N = 19)		**Male Scores (N = 7)**	
	Mean (SD)	***Comparison to ImPACT Normative Data***	***Mean (SD)***	***Comparison to ImPACT Normative Data***
VBM	79.00 (13.75)	Low-Average	81 (14.75)	Average
VIM	64.11 (13.78)	Low-Average	78.14 (15.11)	Average
MS	32.23 (5.89)	Low-Average	29.06 (7.48)	Low-Average
RT	0.71 (0.10)	Borderline	0.75 (0.09)	Borderline
IC	7.16 (5.69)	Norms Unavailable	5.71 (3.95)	Norms Unavailable
CEI	0.30 (0.13)	Norms Unavailable	0.22 (0.17)	Norms Unavailable

Note. VBM: Verbal memory, VIM: Visual memory, MS: Motor speed, RT: Reaction time, IC: Impulse control, CEI: Cognitive efficiency index.

In comparison to ImPACT normative data, the female concussed adolescents had "Low-Average" scores in Verbal Memory, Visual Memory, and Motor Speed. They also scored "Borderline" (almost "Impaired") in Reaction Time (Table 3). The male concussed adolescents scored "Average" in Verbal Memory and Visual Memory, "Low-Average" in Motor Speed, and "Borderline" in Reaction Time (Table 3). There were no available normative values for Impulse Control and CEI scores. The PCSS score of 55.08 and CDI 2 score of 56.07 showed higher levels of concussion symptoms and "Slightly above average" levels of depression.

Frequency Deviant (MMNf) Data

The results for the MMNf data are shown in Figures 1 and 2. An ANCOVA was performed with the Cronbach's alpha value for MMN amplitude as the dependent variable. The categorical variable was Group, and the covariate was Number of Trials. The main effect of Group on alpha was non-significant ($F(1, 49) = 1.2$, $p = 0.28$), indicating that reliability across trials was not different for the MMN amplitude of the two groups ($M\ \alpha = 0.81$ for concussed group, $M\ \alpha = 0.84$ for control group). The Number of Trials was found to have a significant effect on amplitude alpha coefficient values ($F(1,49) = 77.06$, $p < 0.001$). The interaction between Group and Number of Trials was not statistically significant ($F(1, 48) = 0$, $p = 0.99$), indicating that the impact of one fixed factor did not significantly differ based on the other. Thus, the effect of number of trials on reliability was not significantly different for the two groups.

A second ANCOVA was carried out with alpha values for the AUC as the dependent variable, Group as the categorical variable, and Number of Trials as the covariate. There was a marginally non-significant main effect of Group ($F(1, 49) = 3.92$, $p = 0.05$), indicating that the concussed group had somewhat lower MMN reliability ($M\ \alpha = 0.73$ for concussed group, $M\ \alpha = 0.78$ for control group) over the different numbers of trials. A significant main effect of Number of Trials was also observed ($F(1, 49) = 104.27$, $p < 0.001$), showing that reliability got better with increased number of trials. The interaction effect between Group and Number of Trials was not statistically significant ($F(1, 48) = 0.14$, $p = 0.71$). Thus, the effect of number of trials on reliability was similar for concussed and control groups.

Figure 1

Interaction between Group and Number of Trials on alpha coefficient values for the MMN amplitude in the frequency deviant condition

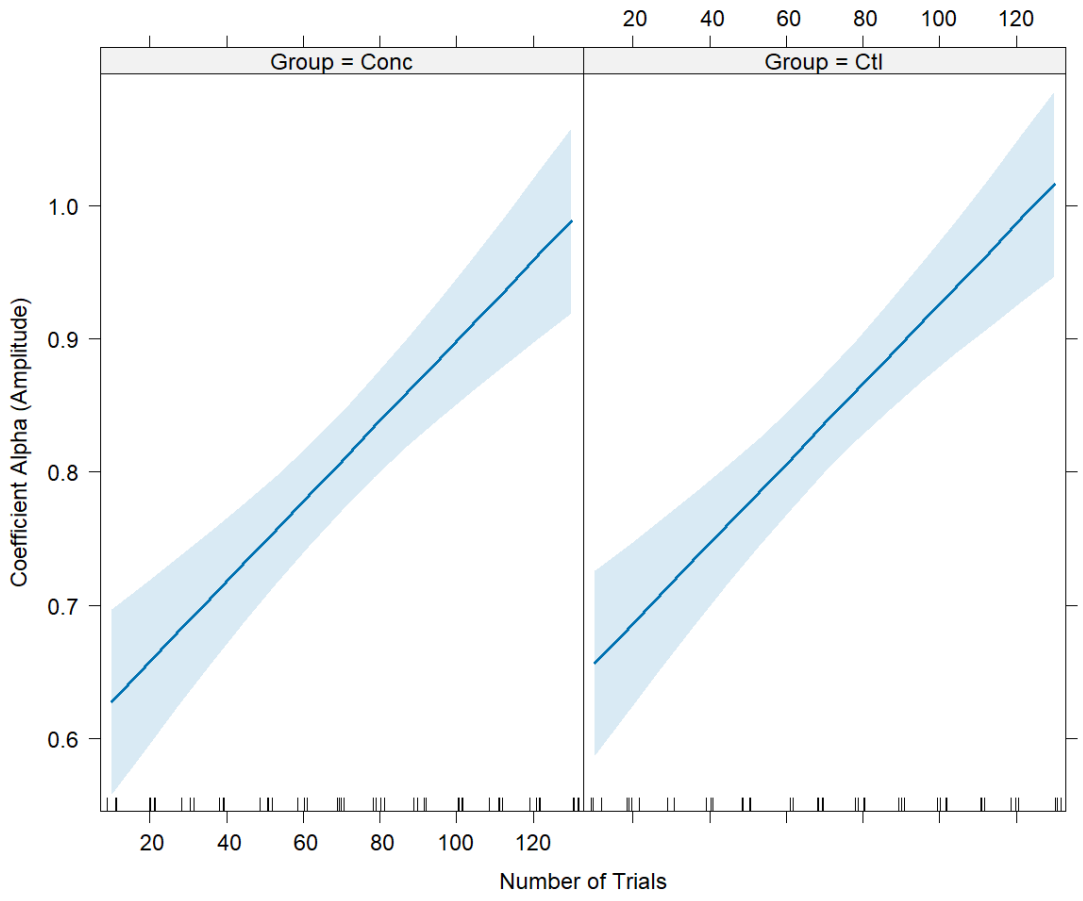
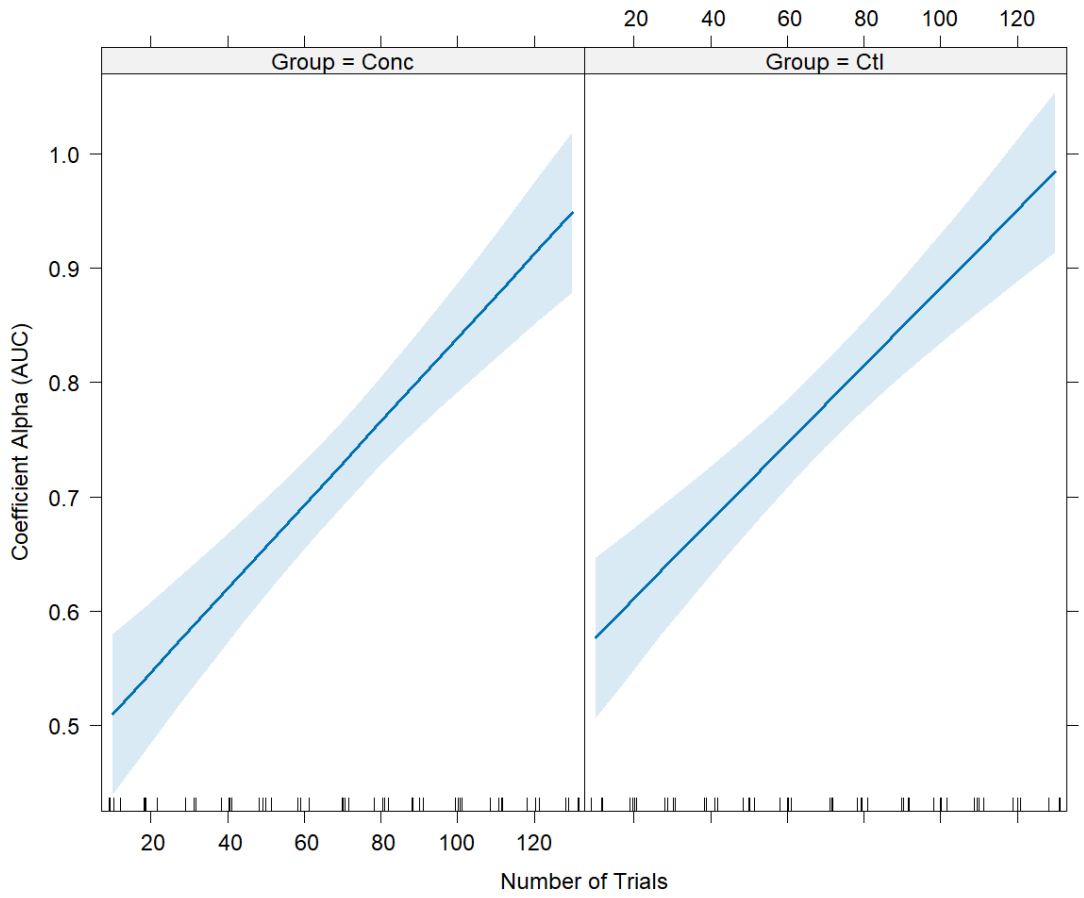


Figure 2

Interaction between Group and Number of Trials on alpha coefficient values for the MMN AUC in the frequency deviant condition



Cronbach's alpha was further studied as a function of increasing trial numbers to detect the minimum number of trials needed to reach *good* or *excellent* criterion levels (see Table 1) of MMN reliability to frequency deviants. These results are shown in Tables 4 and 5. We first studied sequential trials. Controls required 70 sequential trials to achieve *excellent* internal consistency ($\alpha = 0.9$) whereas concussed participants needed 100 trials to achieve *excellent* internal consistency ($\alpha = 0.91$) for MMN amplitude. For AUC,

controls required 110 sequential trials to achieve *excellent* internal consistency (α = 0.9). The concussed group did not reach *excellent* internal consistency for AUC even with the inclusion of all trials (up to 130) in this condition. The concussed participants needed 80 trials to achieve *good* internal consistency (α = 0.8) for AUC.

As high numbers of sequential trials with no artefacts cannot always be acquired, we also studied the number of trials needed for criterion internal consistency based on randomized trial order. Controls required 80 randomized trials to achieve *excellent* internal consistency (α = 0.92) whereas concussed participants needed 100 trials to achieve *excellent* internal consistency (α = 0.91) for MMN amplitude. For MMN AUC, controls required 120 randomized trials to achieve *excellent* internal consistency (α = 0.9). The concussed group did not achieve *excellent* internal consistency with the inclusion of all trials in this condition. They needed 90 trials to achieve *good* internal consistency (α = 0.82) for AUC.

Table 4

Concussed adolescent and control participants' results for good and excellent internal consistency in the frequency deviant condition (MMN amplitude)

Internal Consistency	**Order of Trials**	**Control Group**		**Concussed Group**	
		Cronbach's alpha	*Number of Trials*	*Cronbach's alpha*	*Number of Trials*
Excellent	Sequential	0.9	70	0.91	100
	Random	0.92	80	0.9	100
Good	Sequential	0.82	30	0.83	60
	Random	0.85	40	0.81	40

Table 5

Concussed adolescent and control participants' results for good and excellent internal consistency in the frequency deviant condition (MMN AUC)

Internal Consistency	Order of Trials	Control Group		Concussed Group	
		Cronbach's alpha	*Number of Trials*	*Cronbach's alpha*	*Number of Trials*
Excellent	Sequential	0.9	110	N/A	N/A
	Random	0.9	120	N/A	N/A
Good	Sequential	0.81	50	0.8	80
	Random	0.82	60	0.8	60

Duration Deviant (MMNd) Data

The results for the duration deviant MMN are shown in Figures 3 and 4. An ANCOVA was performed with the alpha coefficient values for MMN amplitude as the dependent variable, Group as the categorical variable, and Number of Trials as the covariate. The main effect of Group on alpha coefficient values for MMN amplitude was not statistically significant ($F(1, 49) = 2.22$, $p = 0.14$, $M\ \alpha = 0.81$ for concussed group, $M\ \alpha = 0.84$ for control group). There was a significant main effect of Number of Trials on the alpha coefficient values for MMN amplitude ($F(1, 49) = 117.25$, $p < 0.001$), indicating greater alpha values for higher numbers of trials. The interaction effect between Number of Trials and Group on MMN amplitude was not statistically significant ($F(1, 48) = 0.72$, $p = 0.4$). Thus, the effect of Number of Trials on the reliability of the MMN amplitude was not significantly different for the two groups.

A second ANCOVA was performed with alpha coefficient values for the MMN AUC as the dependent variable, Group as the categorical variable, and Number of Trials as the

covariate. There was no significant main effect of Group on alpha coefficient values for MMN AUC ($F(1, 49) = 2.43$, $p = 0.13$, $M\ \alpha = 0.73$ for concussed group, $M\ \alpha = 0.77$ for control group). There was a significant main effect of Number of Trials on the alpha coefficient values for the MMN AUC ($F(1, 49) = 155.11$, $p < 0.001$), indicating higher alpha coefficients when more trials were included. The interaction effect between Group and Trials was not statistically significant ($F(1, 48) = 0.15$, $p = 0.7$), suggesting that the effect of number of trials on alpha was not different between groups.

Figure 3

Interaction between Group and Number of Trials on alpha coefficient values for the MMN amplitude in the duration deviant condition

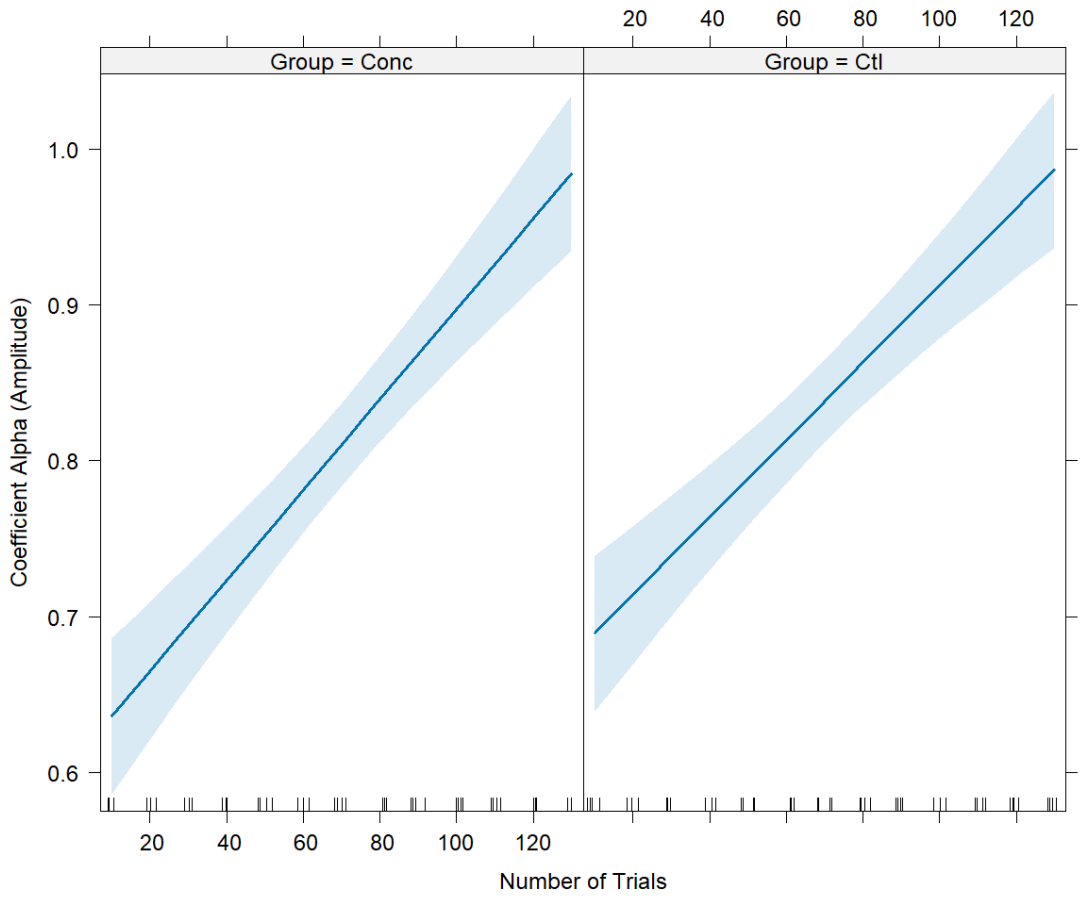
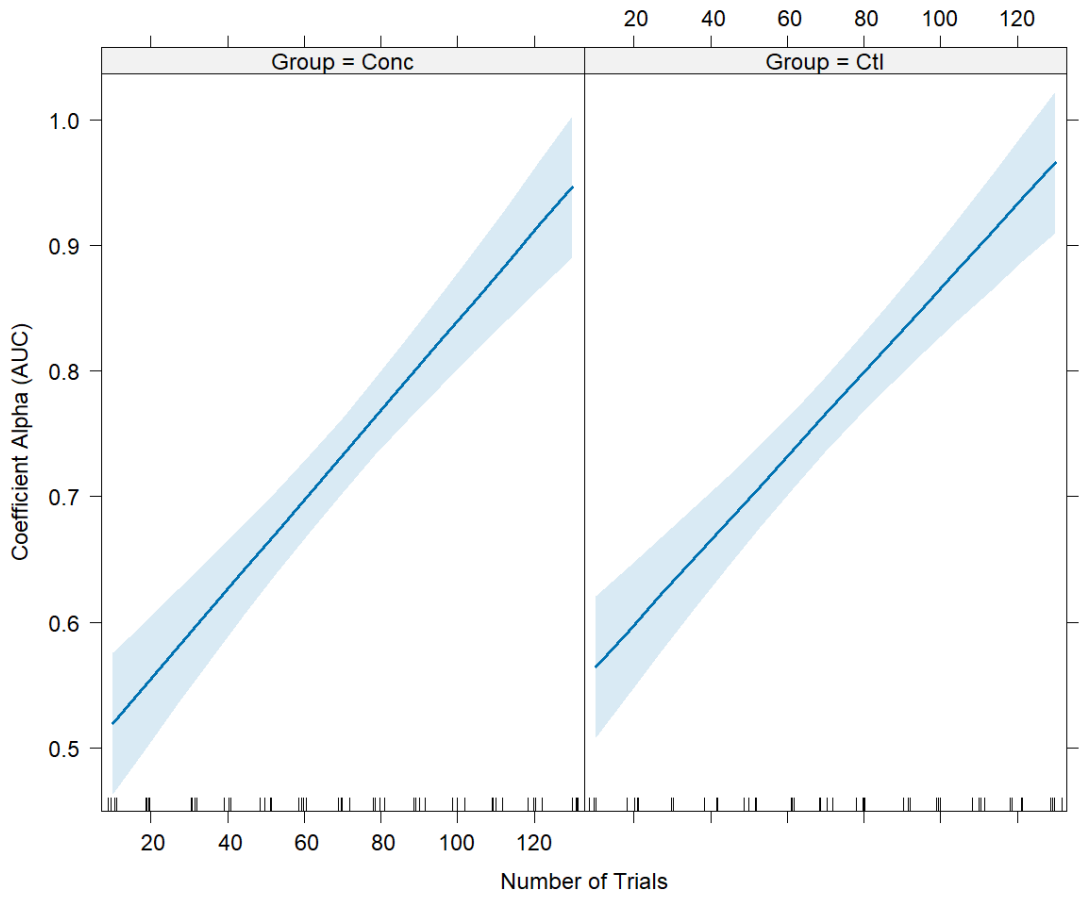


Figure 4

Interaction between Group and Number of Trials on alpha coefficient values for the MMN AUC in the duration deviant condition



An analysis of number of sequential trials needed for criterion levels of alpha were analyzed first. The following results are summarized in Tables 6 and 7. Controls required 90 sequential trials to achieve *excellent* internal consistency ($\alpha = 0.9$) whereas concussed participants needed 130 trials to achieve *excellent* internal consistency ($\alpha = 0.9$) for amplitude. Controls required 130 sequential trials to achieve *excellent* internal

consistency (α = 0.9). The concussed group did not reach *excellent* internal consistency even with the inclusion of all trials (up to 130) in this condition. Concussed participants needed 80 trials to achieve *good* internal consistency (α = 0.8) for the MMN AUC.

Number of trials in randomized order was analyzed next. For the MMN amplitude peak, controls required 90 randomized trials to achieve *excellent* internal consistency (α = 0.92) and concussed participants also needed 90 trials to achieve *excellent* internal consistency (α = 0.9). For MMN AUC, controls required 110 randomized trials to achieve *excellent* internal consistency (α = 0.9). The concussed group did not achieve *excellent* internal consistency even with the inclusion of all trials in this condition. Concussed participants needed 90 trials to achieve *good* internal consistency (α = 0.82) for AUC.

Table 6

Concussed adolescent and control participants' results for good and excellent internal consistency in the duration deviant condition (MMN amplitude)

Internal Consistency	**Order of Trials**	**Control Group**		**Concussed Group**	
		Cronbach's alpha	*Number of Trials*	*Cronbach's alpha*	*Number of Trials*
Excellent	Sequential	0.9	90	0.91	100
	Random	0.92	90	0.9	90
Good	Sequential	0.83	50	0.83	60
	Random	0.82	30	0.81	50

Table 7

Concussed adolescent and control participants' results for good and excellent internal consistency in the duration deviant condition (MMN AUC)

Internal Consistency	**Order of Trials**	**Control Group**		**Concussed Group**	
		Cronbach's alpha	*Number of Trials*	*Cronbach's alpha*	*Number of Trials*
Excellent	Sequential	0.9	130	N/A	N/A
	Random	0.9	110	N/A	N/A
Good	Sequential	0.82	80	0.8	80
	Random	0.81	50	0.83	70

Intensity (MMNi) Data

The results for the intensity deviant MMNs are shown in Figures 5 and 6. An ANCOVA was performed with alpha coefficient values for MMN amplitude as the dependent variable, Group as the categorical variable, and Number of Trials as the covariate. There was a marginally non-significant main effect of Group on alpha values ($F(1, 49) = 3.74$, $p = 0.06$), suggesting that reliability might be better for the concussed group ($M\ \alpha = 0.87$ for concussed group, $M\ \alpha = 0.82$ for control group). There was a significant main effect of Number of Trials ($F(1, 49) = 74.27$, $p < 0.001$). The interaction effect between Number of Trials and Group was not statistically significant ($F(1, 48) = 1.74$, $p = 0.19$). Thus, the effect of Number of Trials did not affect the two groups differently.

A second ANCOVA was performed with Cronbach's alpha for MMN AUC as the dependent variable, Group as the categorical variable, and Number of Trials as the covariate. There was a significant main effect of Group ($F(1, 49) = 20.62$, $p < 0.001$), reflecting the result that the concussed group had higher alpha values for MMN AUC

than the control group (M α = 0.86 for concussed group, M α = 0.76 for control group). There was also a significant main effect of Number of Trials ($F(1, 49) = 89.65$, $p < 0.001$), indicating that alpha got higher with more included trials. Lastly, there was a significant interaction effect between Group and Number of Trials, indicating that the impact of Number of Trials on alpha values for MMN AUC differed significantly based on the Group ($F(1, 48) = 8.42$, $p = 0.006$). Figure 6 shows this interaction with a steeper slope, and therefore, a larger effect of Number of Trials for the control group.

Figure 5

Interaction between Group and Number of Trials on alpha coefficient values for MMN amplitude in the intensity deviant condition

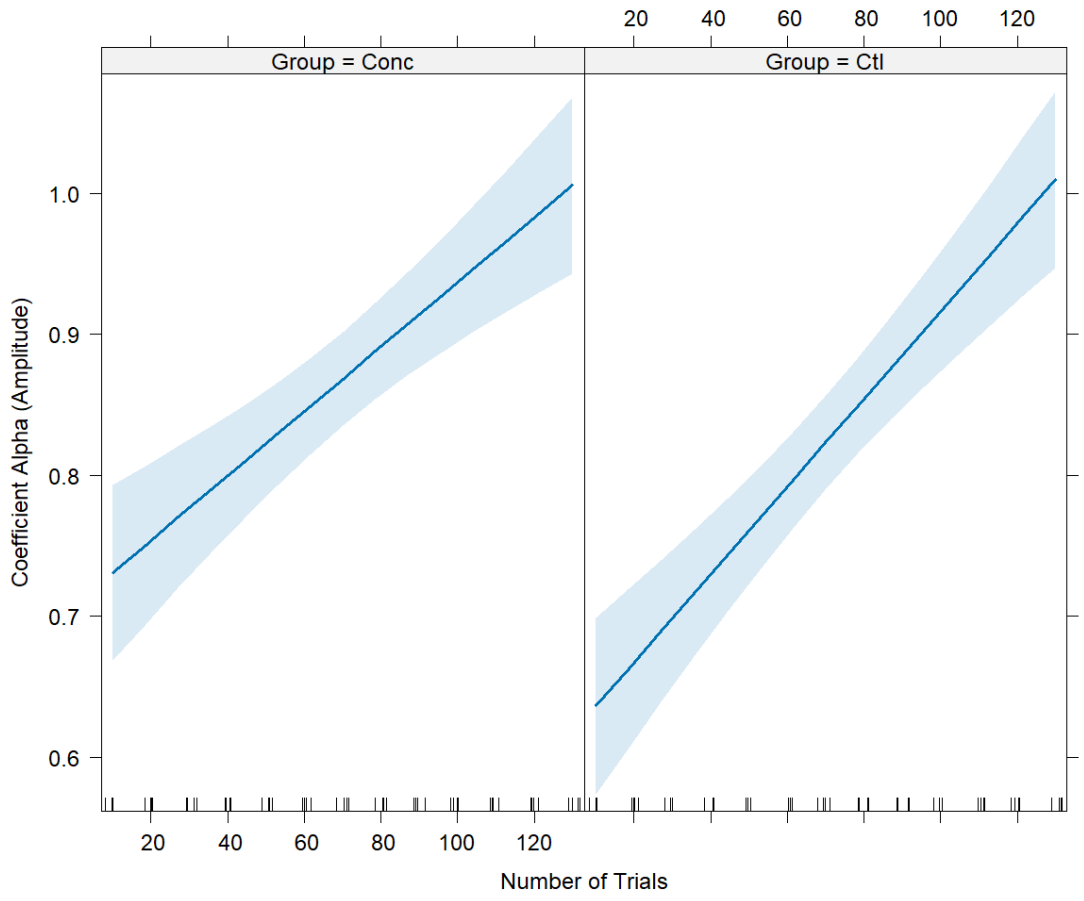
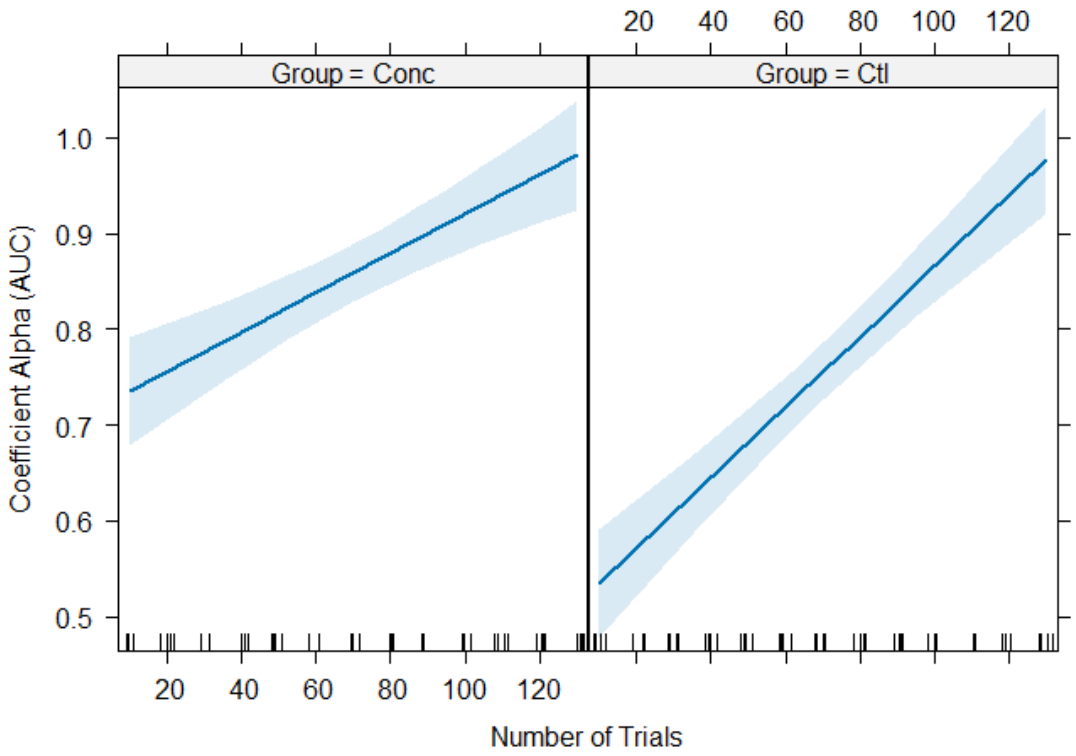


Figure 6

Interaction between Group and Number of Trials on alpha coefficient values for MMN AUC in the intensity deviant condition



Next, the number of trials required to reach criterion levels for Cronbach's alpha was investigated (summarized in Tables 8 and 9). When sequential trials were considered for MMN amplitude, the controls required 90 trials to achieve *excellent* internal consistency ($\alpha = 0.9$) whereas the concussed participants needed 70 trials ($\alpha = 0.91$). When the reliability for MMN AUC was observed, controls required 130 sequential trials to achieve *excellent* internal consistency ($\alpha = 0.9$) and concussed participants needed 80 trials.

When trials were considered in randomized order, controls required 80 trials to achieve *excellent* internal consistency (α = 0.9) whereas concussed participants needed 70 trials for MMN amplitude. For MMN AUC, controls required 130 randomized trials to achieve *excellent* internal consistency (α = 0.9) and concussed participants needed 80 trials.

Table 8

Concussed adolescent and control participants' results for good and excellent internal consistency in the intensity deviant condition (MMN amplitude)

Internal Consistency	**Order of Trials**	**Control Group**		**Concussed Group**	
		Cronbach's alpha	*Number of Trials*	*Cronbach's alpha*	*Number of Trials*
Excellent	Sequential	0.9	90	0.91	70
	Random	0.9	80	0.91	70
Good	Sequential	0.83	50	0.84	30
	Random	0.87	40	0.83	30

Table 9

Concussed adolescent and control participants' results for good and excellent internal consistency in the intensity deviant condition (MMN AUC)

Internal Consistency	**Order of Trials**	**Control Group**		**Concussed Group**	
		Cronbach's alpha	*Number of Trials*	*Cronbach's alpha*	*Number of Trials*
Excellent	Sequential	0.9	130	0.9	80
	Random	0.9	130	0.9	80
Good	Sequential	0.82	80	0.82	30
	Random	0.81	70	0.83	30

Discussion

Study 1 examined the reliability of the MMN component in concussed adolescents and respective controls by analyzing the number of trials necessary to elicit a stable response.

We hypothesized that the adolescents' MMN stability would be affected by concussion since they are more sensitive to concussive symptoms and typically require longer resolution periods than children or adults (Baillargeon et al., 2012; McCrory et al., 2013). Our findings suggested that the stability of the MMN is unaffected by concussions sustained in adolescence. The reliability of both the MMN amplitude and AUC got significantly better with the inclusion of additional trials for all deviant types. For concussed adolescents, we analyzed Cronbach's alpha for the MMN response obtained from up to 130 trials in increments of 10 trials and found that the brain response can be elicited with a *good* or an *excellent* degree of internal consistency by a minimum of 70 to 130 trials (for MMN amplitude) and 80 to 90 trials (for MMN AUC) depending on deviant type. In comparison, controls required a minimum of 70 to 90 trials (MMN amplitude) and 110 to 130 trials (MMN AUC) to achieve *excellent* internal consistency. Under certain conditions, the AUC values did not reach an *excellent* internal consistency even with the inclusion of all 130 trials.

The behavioural assessments (ImPACT, PCSS and CDI 2) completed by the concussed adolescents (N = 26) showed varying results. The ImPACT results were weak as the participants performed at low-average in nearly all categories. This meant that their scores were not low enough to show impairment nor high enough to be superior. The male participants (N = 7) scored Average in Verbal Memory and Visual Memory while the females (N = 19) scored Low-Average in these measures. Another behavioural category (i.e. Motor Speed) was also unaffected for both males and females, revealing Low-Average scores. These findings could be due to certain post-concussion

neurocognitive symptoms returning to baseline performance within a month (Zuckerman et al., 2012). The concussed adolescents had Borderline scores, meaning an increased score of 0.01 (for males) or 0.03 (for females) in Reaction Time (Table 3) would have shown impairment. This may be reflective of how individuals with post concussive impairments tend to have slower reaction times (Grady, 2010; Kontos et al., 2012a; Lempke et al., 2021).

The PCSS scores revealed that the concussed adolescents experienced numerous symptoms with elevated levels of symptom severity. The common symptoms reported were headaches, sadness, difficulty concentrating, difficulty remembering, sensitivity to light and noise, and feelings of emotional instability. These results demonstrate the mental and physical repercussions experienced by adolescents in the aftermath of sustaining a concussion (Covassin et al., 2013; Gornall et al., 2020; Grady, 2010; Ryan & Warden, 2003).

The concussed adolescents had higher levels of depressive symptomology than the controls as reported through the CDI 2. Studies have consistently found above average depression scores in adolescent and other age-group populations following concussion (Fish et al., 2023; Garden & Sullivan, 2010; Ho et al., 2020; Kontos et al., 2012a; Strain et al., 2013; Vargas et al., 2015).

Our results showed that Number of Trials was a significant factor for both the amplitude and AUC alpha coefficient values across all three MMN deviants. The number of trials required to attain an internally consistent MMN for concussed adolescents was higher

(range 90-130) than healthy controls (range 70-90) for amplitude alpha coefficient values in frequency and duration deviants. These findings were aligned with our assumption that concussed adolescents would need more trials to reach a high internal consistency in comparison to healthy controls. On the contrary, concussed participants required less (70) trials than control participants who required 80-90 trials for the intensity deviant.

Regarding the AUC values, concussed participants did not reach *excellent* internal consistency with the inclusion of up to 130 trials whereas controls required 110-130 trials for the frequency and duration deviants. For the intensity deviant, concussed participants required more (80) trials to achieve *excellent* internal consistency whereas controls required 130 trials. Interestingly, for both amplitude and AUC values, the intensity deviant produced results in opposition to what we had postulated: the concussed adolescents required less trials than their respective controls to achieve *excellent* internal consistency and, in some cases, did not reach it with even the inclusion of 130 trials. An explanation could be that the elicited MMNs in the intensity deviant condition (1000 Hz, 90 dB SPL, 50 ms) act similarly to evoked potentials (EPs). EPs are produced by the central nervous system and create a bioelectric signal when triggered by an explicit external event. The visual evoked potential (VEP) is a type of EP that can be generated by visual stimuli such as unpatterned flashing lights or a patterned checkerboard (Kothari et al., 2016). Stimuli like this (i.e. louder or brighter) can be intense enough to cause muscle reflexes in the body, resulting in noisier waveforms and thereby creating the need for more trials. Research has confirmed that VEPs with flash stimuli are less consistent than with the patterned stimuli (Pojda-Wilczek et al., 2019). Considering that young adults

show strong MMNs even at a small level of deviance, it may be that stimuli of elevated intensity caused noisier MMNs (Gaeta et al., 1998). It is possible that the concussed adolescents were unphased by this effect due to their delayed reaction times (as observed by their "Borderline" ImPACT scores) compared to healthy controls.

Furthermore, we only found group differences and an interaction effect between Group and Number of Trials when attaining an internally consistent MMN for the intensity deviant using AUC alpha coefficient values. As seen in Figure 6, the control group shows a steeper curve indicating the stability of the MMN rapidly changes as more trials are included whereas the concussed group seems to begin with greater stability including a smaller number of trials which slowly increases with the inclusion of more trials. This effect can also be attributed to the beforementioned phenomenon of the intensity deviant creating an involuntary muscle reflex for healthy participants while the concussed participants remain relatively unaffected by the stimuli. In addition, the concussed group is likely to have more variability between participants, specifically in severity of concussions, than the control group which is what may have caused an interaction effect. Future research should also consider the individual differences of participants for alpha values and the slope of alpha as a function of number of trials. The lack of interaction effects between Group and Number of Trials for all other conditions demonstrates that the concussed participants and the control participants had similar consistencies in their MMN stability. This is aligned with research that examined a clinical population (chronic, recently detoxified alcoholics) and healthy controls where both groups showed good reliability in ERP measures (Sinha et al., 1992).

Limitations

One of the limitations of this study was that the two groups differed in approximately 5 years of age: the control participants were 17-22 years old whereas concussed participants were 13-17 years old. Research investigating concussion in high school and collegiate athletes has found significant differences in the average number of days to recover in neurocognitive measures and their overall symptoms (as measured by the PCSS). Specifically, 13–16-year-old athletes required a greater average number of days to return to baseline than 18–22-year-olds on the following: verbal memory, visual memory, reaction time and PCSS score (Zuckerman et al., 2012). It should be noted that high school and collegiate athletes may have different motivations in claiming recovery since those at the collegiate level could have professional career aspirations. With that said, the subjectivity of scores retrieved from self-report tests must be considered.

Females have proved to be more honest in reporting their injuries than males which can result in reporting biases (for a review see Dick, 2009). Based on neuropsychological (self-report) testing, female athletes have reported to be more susceptible to concussions than males, showing different baseline and post-concussion results. These outcomes are worse for various measures such as poor memory, impaired concentration, and anxiety and depression. Self-report measures tend to reveal subjectivity and personal distortion. This further highlights the need for standardized approaches, such as ERP analysis, to account for potential reporting bias.

Another limitation was the small sample size of males in both the concussed adolescent group (N = 26, 7 males) and the control group (N = 28, 5 males). We were unable to recruit more males to participate in this study. As mentioned later in Chapter 4, this was a shortcoming since we compare the results of the male and female adolescents with those of older male adults. If females were excluded to create a more comparative group, our sample size would have been too small to show true effects.

Conclusion

The present study explored the internal consistency reliability of the MMN in the study of consequences of concussive impacts in adolescents compared to healthy controls. The primary objective was to establish the number of trials needed to elicit the MMN with high stability. We found that 130 trials were enough for a stable MMN response to emerge in both groups for all deviant types, supporting the use the MMN as an indicator of brain recovery after brain traumas varying in severity with this number of trials.

Chapter 3

Study 2: MMN Response Stability in Retired Canadian Football League (rCFL) Athletes vs. Controls

Introduction

Most athletic concussions occur in contact sports, such as football and ice hockey (Kelly et al., 1991). A single football player can receive up to 1400 head impacts during a season with the average number sustained per game being about three times greater compared to practice sessions (Crisco et al., 2010). Many athletes suffer from a collection of persisting physical, cognitive, emotional, and behavioural symptoms following concussion/mTBI, which has been termed Post-Concussion Syndrome (PCS). Although many cases resolve within weeks, studies have shown PCS symptoms being experienced months and years post-injury (Ryan & Warden, 2003). There are no scientifically established metrics for identifying what constitutes a resolution(s) of these symptoms (Willer & Leddy, 2006). De Beaumont et al. (2009) found that former athletes who sustained a concussion more than 30 years ago showed slowed execution of motor functions and tasks. Furthermore, the development of a neurodegenerative disease called chronic traumatic encephalopathy (CTE) has become increasingly concerning for professional football athletes as it has been linked with concussions and repetitive head collisions (Stern et al., 2019). Studies that investigated the neuropathology of deceased National Football League players found evidence suggesting that CTE may be related to these repeated head traumas from football (Mez et al., 2017; Omalu et al., 2005). The research has demonstrated that

athletes' exposure to repetitive concussions can pose devastating repercussions. There is a desperate need for an objective assessment tool that can successfully track functional recovery from such head impacts.

The purpose of this study was to investigate the stability of the MMN brain response component – a demonstrated functional biomarker for brain injury – in retired football players who have a history of concussion as compared to healthy controls. The primary goal was to establish the number of trials needed to elicit the MMN with high internal consistency.

Methods

This study was approved by the Hamilton Integrated Research Ethics Board (HiREB), Hamilton, Ontario, Canada. In accordance with the Declaration of Helsinki, all participants provided informed consent prior to study participation.

Participants

19 retired Canadian Football League (rCFL) athletes (all males; *M* age = 57.63, range = 45 – 66) with histories of concussions (*M* number of concussions = 4.05) were recruited. The mean number of years since their last concussion was 28.11 and the mean number of years spent playing professional football was 7.84. 20 healthy age-matched control subjects (all males; *M* age = 53.63, range = 45 – 61) were also recruited. All participants were native English speakers. They were recruited through the local newspaper, personal connections, and McMaster University. No participants had reported hearing issues, and none were on psychoactive medications.

The rCFL participants self-reported information regarding the number of sustained concussions and the number of years since their last reported concussion. No official medical records exist since concussion protocols and even references to brain injury were non-existent during the period that the rCFL players were active in their football careers.

Behavioural Assessments

The following neuropsychological assessments were completed by the former CFL players: ImPACT, PCSS, Beck Depression Inventory II (BDI II), and Short Form Health Survey (SF-36) (Beck et al., 1961; Iverson et al., 2003; Lovell & Collins, 1998; Ware & Sherbourne, 1992). The control group completed the ImPACT, BDI II and SF-36 but did not complete the PCSS. The statistical analyses of the ImPACT, SF-36, PCSS and BDI II were all performed using R Software (RStudio, Version 4.0.2). The results of the PCSS and BDI II were analyzed using descriptive statistics and two-tailed t-tests with an alpha level of 0.05. The ImPACT and SF-36 scores were analyzed using descriptive statistics and Bonferroni-corrected two-tailed t-tests. Both two-tailed t-tests had significance thresholds of $p = 0.008$ (0.05/6) for the ImPACT and $p < 0.006$ (0.05/8) for the SF-36.

The ImPACT and PCSS were identical to those used in Study 1. There were no ImPACT normative data available for this age group (older adults) at the time of testing which is why the scores were examined statistically with the age-matched healthy control group.

The BDI II assesses depression symptomatology through 21 groups of statements in a questionnaire. Participants choose the statement which applies to them out of four options. Statements are scored from 0-3 and totaled: a higher total score is indicative of a

higher level of depression (Beck et al., 1961). The utility of this inventory has been demonstrated by many studies (Garden & Sullivan, 2010; Kontos et al., 2012a; Ruiter et al., 2019; Stern et al., 2019; Strain et al., 2013; Vargas et al., 2015).

The SF-36 evaluates general health on a day-to-day basis through criteria such as social activities, physical health problems, and energy and emotions. Each category of questions is scored out of 100, with 100 representing the top score for health (Ware & Sherbourne, 1992). A study analysing the criterion validity and reliability of this questionnaire found evidence for its usefulness in subjects between 18-64 years old with varying states of health (Jenkinson et al., 1994).

EEG Experiment

MMN

The present study used the auditory oddball paradigm adapted from Ruiter et al. (2019; Todd et al., 2008). A standard tone and three deviant tones (frequency, duration, and intensity) were presented. This was the same paradigm as in the first study with adolescent participants. Participants watched a visually neutral silent nature film, presented on a computer screen in front of them. They were instructed to ignore the tones.

Procedure

Participants first completed their respective demographic and self-report questionnaires. A computer monitor was positioned 90-cm away from where participants were comfortably seated. They were asked to focus on the film while stimuli played binaurally through sound-isolating headphones in a sound-attenuated room.

EEG Data: Recording, Preprocessing and Internal Consistency Analysis

The EEG recording procedures, data preprocessing methodology and internal consistency analysis were all identical to those used in Study 1.

Participants wore an electrode cap with 64 Ag/AgCl electrodes placed in accordance with the Modified Combinatorial Nomenclature version (Oostenveld & Praamstra, 2001) of the International 10/20 system (Jasper, 1958). Five external electrodes were placed above and over the outer canthus of the left eye, on the two mastoids, and on the tip of the nose.

EEG data were first preprocessed offline using BVA to manually remove non-ocular artifacts. A 0.1 – 30 Hz bandpass filter (24 dB/oct) was then applied. Data were segmented corresponding to stimulus type after being re-referenced to the averaged mastoids to maximize SNR. The analysed epochs had a duration span of 800 ms, starting 200 ms before stimulus onset. Automatic peak detection (Barr et al., 1978) was performed on the difference waveforms of the MMN component. Some peaks were adjusted manually after inspection. Lastly, the amplitude and AUC data were exported as single trials from the Fz electrode.

R Software (RStudio, version 4.0.2) was used to calculate Cronbach's alpha on the exported ERP data. Cronbach's alpha was calculated with the first 130 trials collectively for both MMN amplitude and MMN AUC data. The alpha coefficient values were calculated for each Group (Concussed vs. Control) and Stimulus Type (Standard vs. Deviant and its three levels).

The statistical analysis was performed using analysis of covariance (ANCOVA) tests with an alpha level of $p < 0.05$. The continuous dependent variables were alpha coefficient values for either MMN amplitude or MMN AUC. The categorical variable was Group (Concussed vs. Control). The covariate was Number of Trials in cumulative 10-trial bins up to 130 trials. We included both sequential and randomized ordering of trial blocks in the dataset.

Results

Demographic Data

The rCFL participants were on average 57.6 years old. Over an average career length of 7.84 years, participants had sustained an average of 4.05 reported concussions (range 1-11) with an average of 28.11 years since their last concussion. The control participants were age- and sex-matched.

Behavioural Assessments

All participants completed the ImPACT, SF-36, PCSS, and BDI II after providing consent (scores for the ImPACT are recorded in Table 10). For the SF-36, the rCFL participants scored an average of 72.11 whereas the control participants scored an average of 79.72. The means for the concussive scores (PCSS) were 14.05 (SD = 12.20) for the rCFL players and 2.95 (SD = 5.55) for the control participants. For the depressive symptom scores (BDI II), the means were 8.53 (SD = 7.20) for the rCFL players and 2.26 (SD = 2.75) for the controls.

Table 10

Concussed rCFL and control participants' ImPACT behavioural scores

	rCFL Players	**Controls**
	Mean (SD)	***Mean (SD)***
VBM	77.42 (10.43)	82.4 (10.31)
VIM	63.32 (12.73)	62.55 (14.33)
MS	30.74 (4.80)	34.15 (6.66)
RT	0.79 (0.16)	0.76 (0.14)
IC	1.89 (1.52)	1.6 (1.43)
CEI	0.03 (0.24)	0.14 (0.17)

Note. VBM: Verbal memory, VIM: Visual memory, MS: Motor speed, RT: Reaction time, IC: Impulse control, CEI: Cognitive efficiency index. Normative data for this age group was unavailable for comparison.

Analysis of the ImPACT scores revealed no significant differences between control and rCFL participants (Table 11). Overall, the rCFL group did show slightly weaker performance in Verbal Memory, Visual Memory, Motor Speed, and Cognitive Efficiency. As well, their higher averaged scores in Reaction Time and Impulse Control reflect slower response times and higher levels of impulsivity. The PCSS and BDI II scores demonstrated significance between groups, indicating more depressive and concussion-related symptoms (Table 11). The SF-36 health survey scores for Social Function and Pain were significantly different between groups, indicating better social functioning and less pain in the control group (Table 11).

Table 11

Results of ImPACT, PCSS, BDI II, and SF-36 scores for rCFL and control groups

Assessment	***Subtests***	**Control Mean (SD)**	**rCFL Mean (SD)**	***t***	***p***
PCSS		3.11 (5.78)	14.05 (11.88)	3.45	< 0.01†
BDI II		2.39 (2.83)	8.53 (7.21)	3.37	< 0.01†
SF-36	*Physical Function*	81.94 (28.56)	78.15 (19.21)	0.47	> 0.00625
	Physical Health Limitations	98.61 (5.89)	88.15 (23.46)	1.79	> 0.00625
	Emotional Health Limitations	98.15 (7.86)	80.70 (36.38)	1.94	> 0.00625
	Energy & Fatigue	70.83 (11.79)	62.63 (20.22)	1.47	> 0.00625
	Emotional Well-being	86.89 (6.83)	77.68 (18.28)	1.96	> 0.00625
	Social Function	97.22 (5.35)	78.29 (23.59)	3.24	< 0.00625*
	Pain	83.89 (18.49)	61.45 (20.67)	3.42	< 0.00625*
	General Health	79.72 (12.77)	72.11 (16.08)	1.56	> 0.00625
ImPACT	*Verbal Memory*	82 (10.80)	77.42 (10.43)	1.31	> 0.00833
	Visual Memory	63.83 (14.46)	63.32 (12.38)	0.12	> 0.00833
	Motor Speed	34.19 (6.95)	30.74 (4.66)	1.77	> 0.00833
	Reaction Time	0.75 (0.15)	0.79 (0.16)	0.69	> 0.00833
	Impulse Control	1.44 (1.38)	1.89 (1.48)	0.94	> 0.00833
	Cognitive Efficiency Index	0.13 (1.17)	0.03 (0.23)	1.48	> 0.00833

Note. † Uncorrected *p*-values. All others given with Bonferroni correction (0.05/Number of Subtests). * Indicated Significance Between Groups < 0.05. All degrees of freedom (*df*) = 35.

Frequency Deviant (MMNf) Data

The results for the MMNf data are shown in Figures 7 and 8. An ANCOVA was conducted with Cronbach's alpha value for MMN amplitude as the dependent variable, Group as the categorical variable, and Number of Trials as the covariate. The main effect of Group on alpha was significant ($F(1, 49) = 35.59$, $p < 0.001$), indicating that the reliability was better for the MMN amplitude in the control group ($M\ \alpha = 0.88$) compared to the rCFL group ($M\ \alpha = 0.76$). The main effect of Number of Trials on alpha was also found to be significant ($F(1, 49) = 110.81$, $p < 0.001$), indicating better alpha with increasing trials. Importantly, the interaction between Group and Number of Trials was also statistically significant ($F(1, 48) = 7.76$, $p = 0.008$), revealing a trend where the impact of number of included trial blocks on alpha was greater and alpha grew more steeply in the rCFL Group.

A second ANCOVA was conducted with alpha values for the MMN AUC as the dependent variable, Group as the categorical variable, and Number of Trials as the covariate. There was a significant main effect of Group ($F(1, 49) = 14.37$, $p < 0.001$) indicating that the rCFL group had lower MMN reliability over the different numbers of trials ($M\ \alpha = 0.66$ for concussed group, $M\ \alpha = 0.8$ for control group). There was also a significant main effect of Number of Trials on alpha coefficient values for MMN AUC ($F(1, 49) = 74.01$, $p < 0.001$), showing that the reliability improved with an increased number of trials. The interaction between Group and Number of Trials reached significance ($F(1, 48) = 5.95$, $p = 0.02$), indicating a trend where the impact of Number of Trials on alpha coefficient values for MMN AUC was stronger for the rCFL Group.

Figure 7

Interaction between Group and Number of Trials on alpha coefficient values for MMN amplitude in the frequency deviant condition

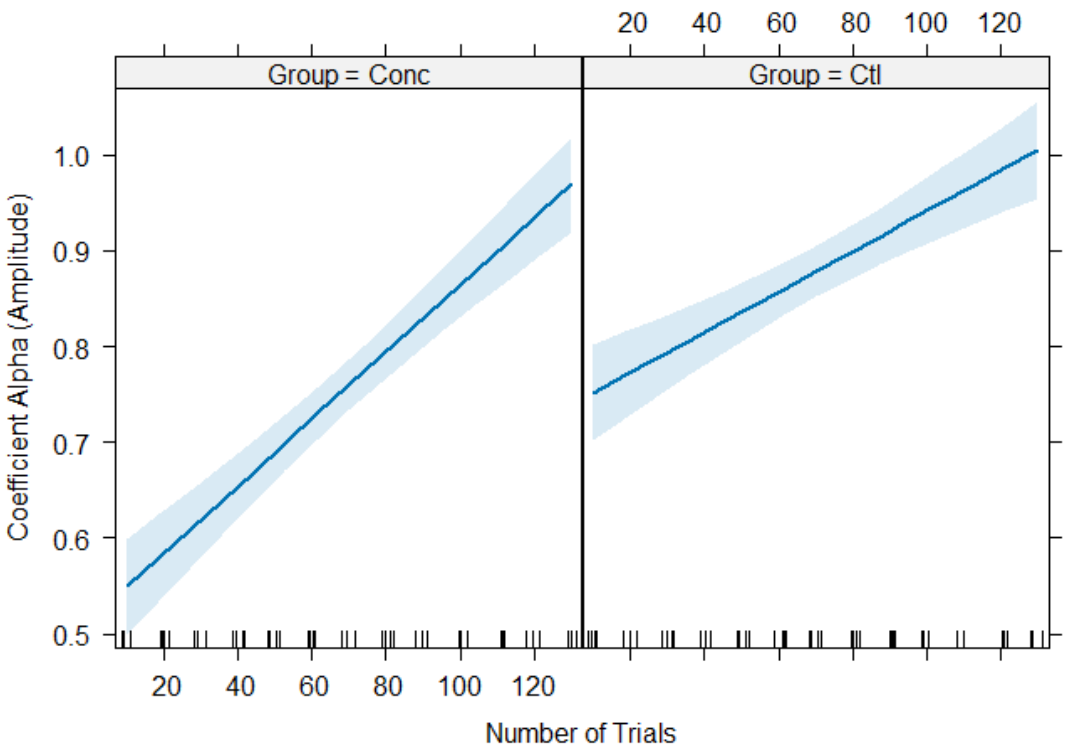
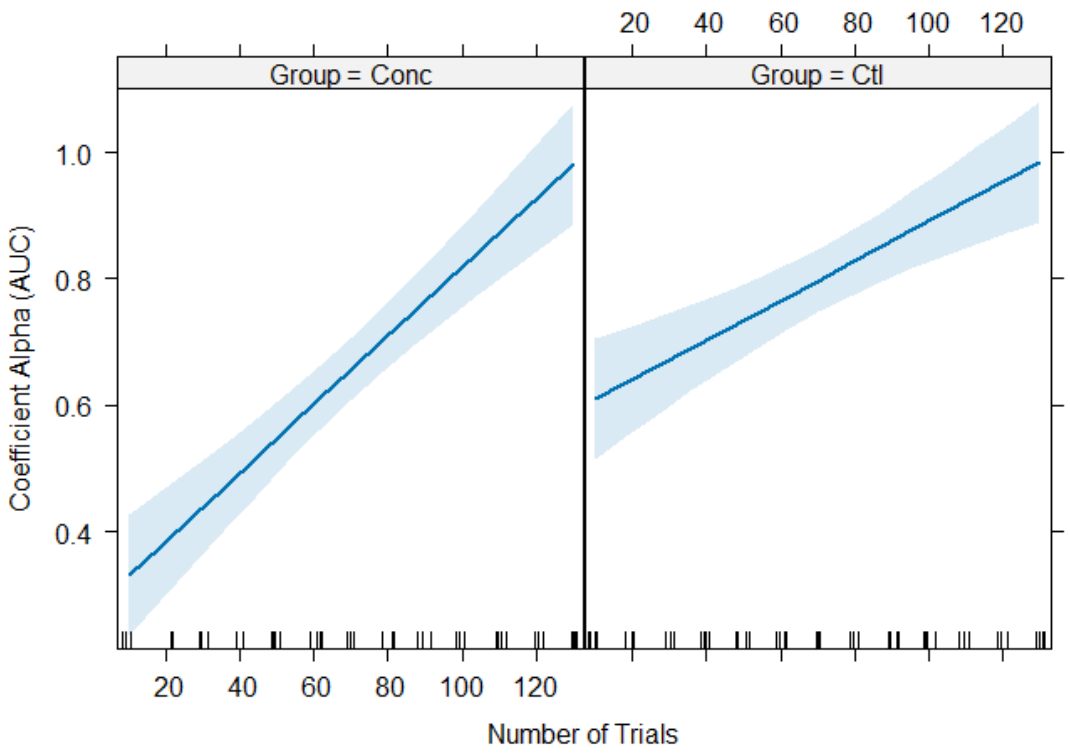


Figure 8

Interaction between Group and Number of Trials on alpha coefficient values for MMN AUC in the frequency deviant condition



Cronbach's alpha was further studied as a function of increasing trial numbers to detect the minimum number of trials needed to reach *good* or *excellent* criterion levels (Table 1) of reliability for the MMN. A summary of these results can be found in Tables 12 and 13. We first looked at sequential trials. Controls required 60 sequential trials to achieve *excellent* internal consistency ($\alpha = 0.9$) whereas rCFL participants needed 120 trials to achieve *excellent* internal consistency ($\alpha = 0.9$) for MMN amplitude. For MMN AUC, controls required 110 sequential trials to achieve *excellent* internal consistency ($\alpha = 0.9$)

and concussed participants needed 100 trials to achieve *good* internal consistency (α = 0.83). The concussed participants did not reach *excellent* internal consistency for AUC even with the inclusion of all trials (up to 130) in this condition.

We also studied the number of trials needed for criterion internal consistency based on trials in randomized order. Controls required only 50 randomized trials to achieve *excellent* internal consistency (α = 0.9) whereas rCFL participants needed 130 trials to achieve *excellent* internal consistency (α = 0.91) for MMN amplitude. For AUC, controls required 120 randomized trials to achieve *excellent* internal consistency (α = 0.9) and concussed participants needed 110 trials to achieve *good* internal consistency (α = 0.83). The concussed group did not achieve *excellent* internal consistency with all trials in this condition.

Table 12

Concussed (rCFL) and control participants' results for good and excellent internal consistency in the frequency deviant condition (MMN amplitude)

Internal Consistency	**Order of Trials**	**Control Group**		**Concussed Group**	
		Cronbach's alpha	*Number of Trials*	*Cronbach's alpha*	*Number of Trials*
Excellent	Sequential	0.9	60	0.9	120
	Random	0.9	50	0.9	130
Good	Sequential	0.82	30	0.81	70
	Random	0.8	30	0.84	70

Table 13

Concussed (rCFL) and control participants' results for good and excellent internal consistency in the frequency deviant condition (MMN AUC)

Internal Consistency	**Order of Trials**	**Control Group**		**Concussed Group**	
		Cronbach's alpha	*Number of Trials*	*Cronbach's alpha*	*Number of Trials*
Excellent	Sequential	0.9	110	N/A	N/A
	Random	0.9	120	N/A	N/A
Good	Sequential	0.84	50	0.83	100
	Random	0.8	60	0.82	70

Duration Deviant (MMNd) Data

The results for MMNd are shown in Figures 9 and 10. An ANCOVA was performed with the alpha coefficient values for MMN amplitude as the dependent variable, Group as the categorical variable, and Number of Trials as the covariate. The main effect of Group on alpha coefficient values ($F(1, 49) = 17.55$, $p < 0.001$) was significant, indicating that the concussed group had lower MMN reliability across the number of trials ($M\ \alpha = 0.79$ for concussed group, $M\ \alpha = 0.88$ for control group). There was also a significant main effect of Number of Trials on alpha ($F(1, 49) = 68.92$, $p < 0.001$), indicating stronger alpha values for an increased number of trials. The interaction effect between Group and Trials was not statistically significant ($F(1, 48) = 3.28$, $p = 0.08$). Thus, the effect of Number of Trials on the reliability of the MMN amplitude was not significantly different for the rCFL and control groups.

A second ANCOVA was performed with alpha coefficient values for MMN AUC as the dependent variable, Group as the categorical variable, and Number of Trials as the covariate. There was a significant main effect of Group on the alpha coefficient values ($F(1, 49) = 17.84$, $p < 0.001$), showing that the MMN AUC reliability was better for controls than rCFL players over all trial blocks (M α = 0.72 for concussed group, M α = 0.81 for control group). There was also a significant main effect of Number of Trials on alpha coefficient values for MMN AUC ($F(1, 49) = 101.19$, $p < 0.001$), showing that the MMN reliability improves with an increased number of trials. The interaction between Group and Trials was not statistically significant ($F(1, 48) = 1.45$, $p = 0.23$), indicating that the impact of Number of Trials does not significantly differ based on Group.

Figure 9

Interaction between Group and Number of Trials on alpha coefficient values for MMN amplitude in the duration deviant condition

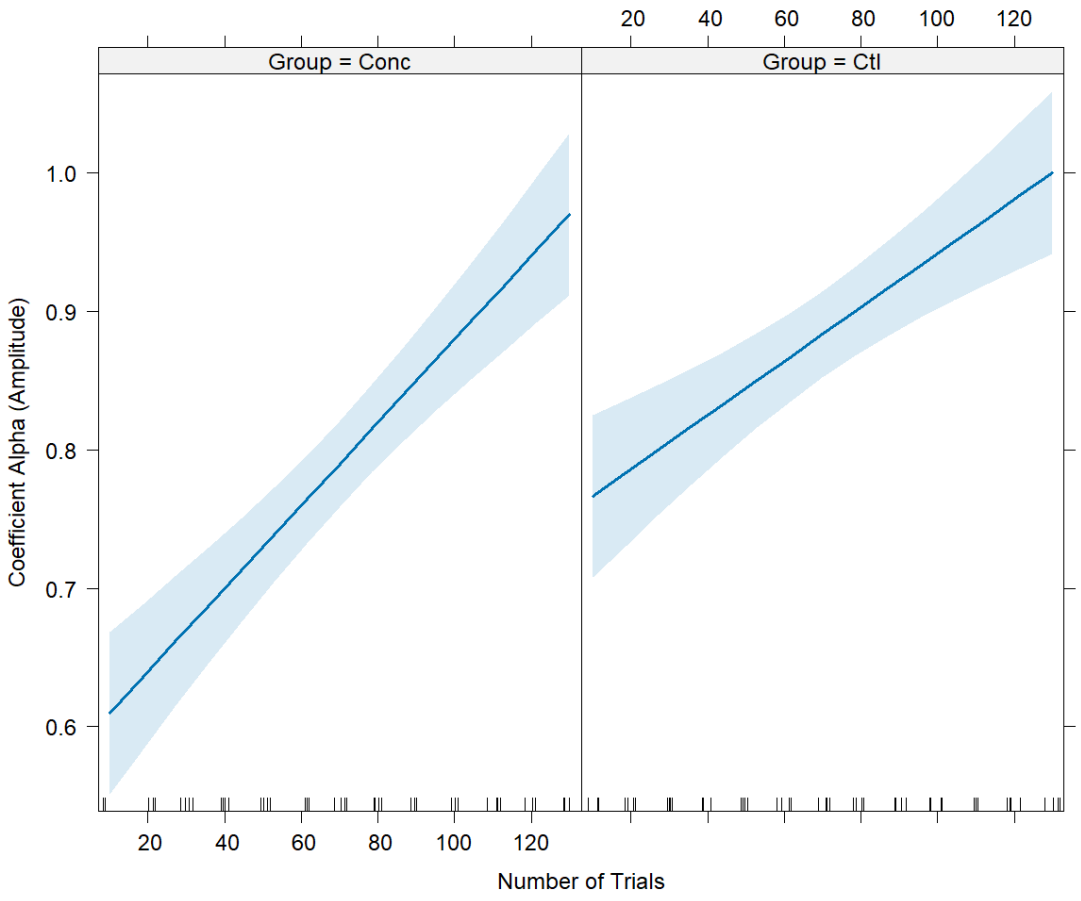
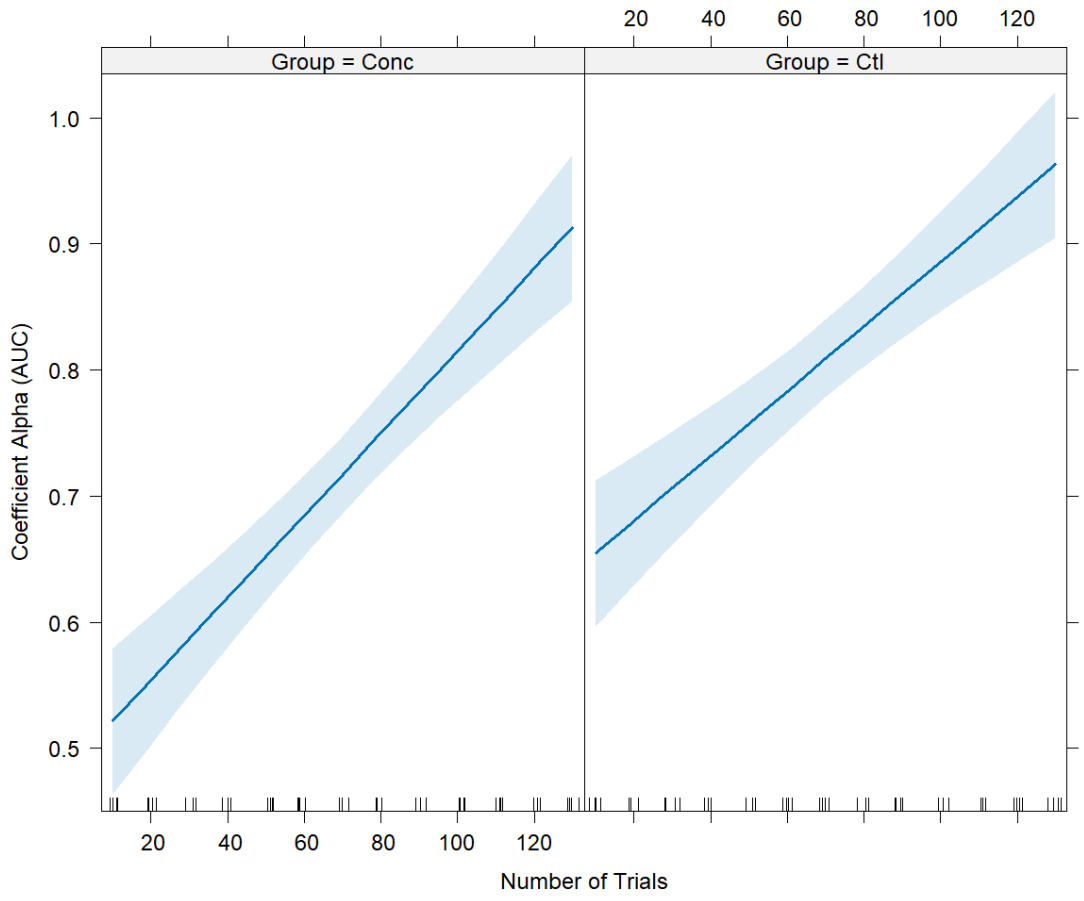


Figure 10

Interaction between Group and Number of Trials on alpha coefficient values for MMN AUC in the duration deviant condition



We then analyzed the number of sequential trials needed for criterion levels of alpha. The following results are summarized in Tables 14 and 15. Controls required only 60 sequential trials to achieve *excellent* internal consistency (α = 0.9) whereas rCFL participants needed 130 trials to achieve *excellent* internal consistency (α = 0.9) for MMN amplitude. Controls required 110 sequential trials to achieve *excellent* internal consistency (α = 0.9) and rCFL participants needed 70 trials to achieve *good* internal

consistency (α = 0.81) for MMN AUC. The concussed participants did not reach *excellent* internal consistency even with all trials in this condition.

We analyzed the number of trials in randomized order needed to reach the criterion levels next. For the MMN amplitude peak, controls required 50 randomized trials to achieve *excellent* internal consistency (α = 0.9) whereas rCFL participants needed 120 trials to achieve *excellent* internal consistency (α = 0.91). For MMN AUC, controls required 110 randomized trials to achieve *excellent* internal consistency (α = 0.9). Concussed participants needed 90 trials to achieve *good* internal consistency (α = 0.83). The concussed participants did not reach *excellent* internal consistency even after adding all trials in this condition.

Table 14

Concussed (rCFL) and control participants' results for good and excellent internal consistency in the duration deviant condition (MMN amplitude)

Internal Consistency	**Order of Trials**	**Control Group**		**Concussed Group**	
		Cronbach's alpha	*Number of Trials*	*Cronbach's alpha*	*Number of Trials*
Excellent	Sequential	0.9	60	0.9	130
	Random	0.9	50	0.9	120
Good	Sequential	0.82	30	0.81	40
	Random	0.8	30	0.83	60

Table 15

Concussed (rCFL) and control participants' results for good and excellent internal consistency in the duration deviant condition (MMN AUC)

Internal Consistency	Order of Trials	Control Group		Concussed Group	
		Cronbach's alpha	*Number of Trials*	*Cronbach's alpha*	*Number of Trials*
Excellent	Sequential	0.9	110	N/A	N/A
	Random	0.9	110	N/A	N/A
Good	Sequential	0.84	50	0.81	70
	Random	0.83	70	0.83	90

Intensity Deviant (MMNi) Data

The results for the MMNi are shown in Figures 11 and 12. An ANCOVA was performed with the alpha coefficient values for MMN amplitude as the dependent variable, Group as the categorical variable, and Number of Trials as the covariate. There was a significant main effect of Group on alpha coefficient values for MMN amplitude ($F(1, 49) = 63.35$, $p < 0.001$), indicating that the rCFL group ($M\ \alpha = 0.73$) had lower MMN reliability than the control group ($M\ \alpha = 0.87$). There was also a significant main effect of Number of Trials on alpha coefficient values for MMN amplitude ($F(1, 49) = 165.19$, $p < 0.001$), showing that the MMN amplitude reliability improves with the addition of trials. The interaction effect between Group and Trials was also statistically significant ($F(1, 48) = 9.07$, $p = 0.004$), showing that the impact of increased trial blocks differs based on Group, being stronger for the rCFL group.

A second ANCOVA was performed with Cronbach's alpha for MMN AUC as the dependent variable, Group as the categorical variable, and Number of Trials as the

covariate. There was a significant main effect of Group on alpha coefficient values for MMN AUC ($F(1, 49) = 38.89$, $p < 0.001$), reflecting the result that the control group (M α = 0.83) had higher alpha values than the rCFL group (M α = 0.53). There was also a significant main effect of Number of Trials ($F(1, 49) = 47.71$, $p < 0.001$), indicating that the alpha value increased when more trials were included. The interaction effect between Group and Number of Trials was also statistically significant ($F(1, 48) = 17.48$, $p < 0.001$), showing that the impact of Number of Trials on alpha values for MMN AUC differed significantly based on Group. This interaction is shown in Figure 12 where the concussed group has a steeper slope and consequently, a larger effect from the Number of Trials.

Figure 11

Interaction between Group and Number of Trials on alpha coefficient values for MMN amplitude in the intensity deviant condition

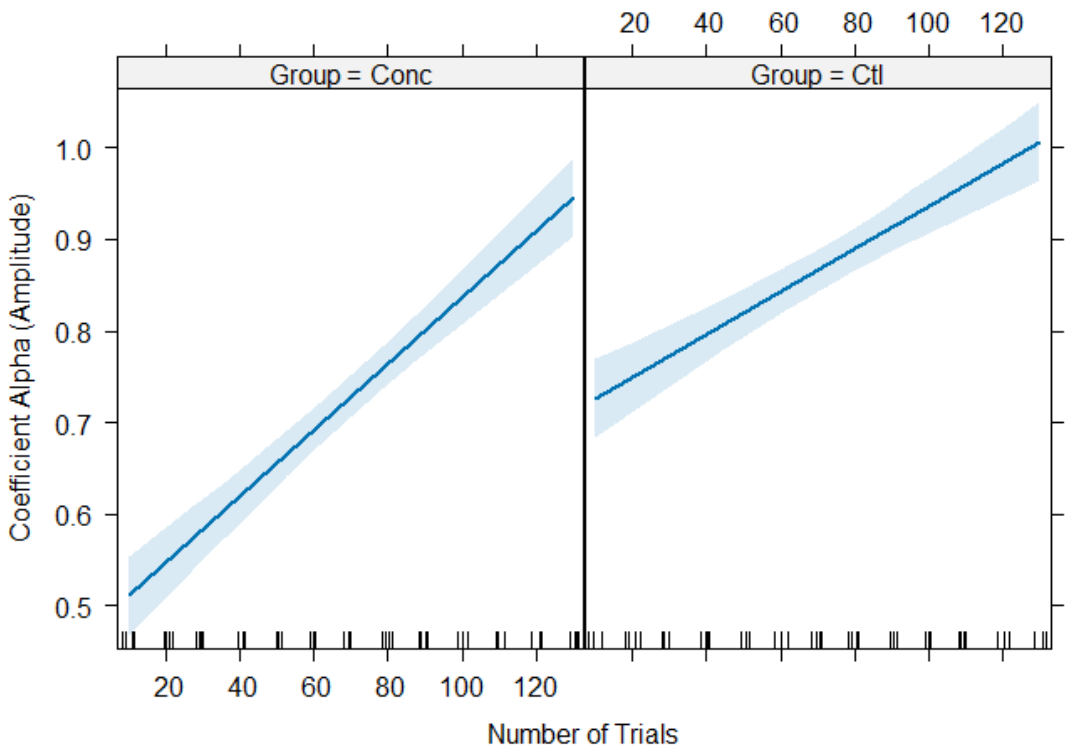
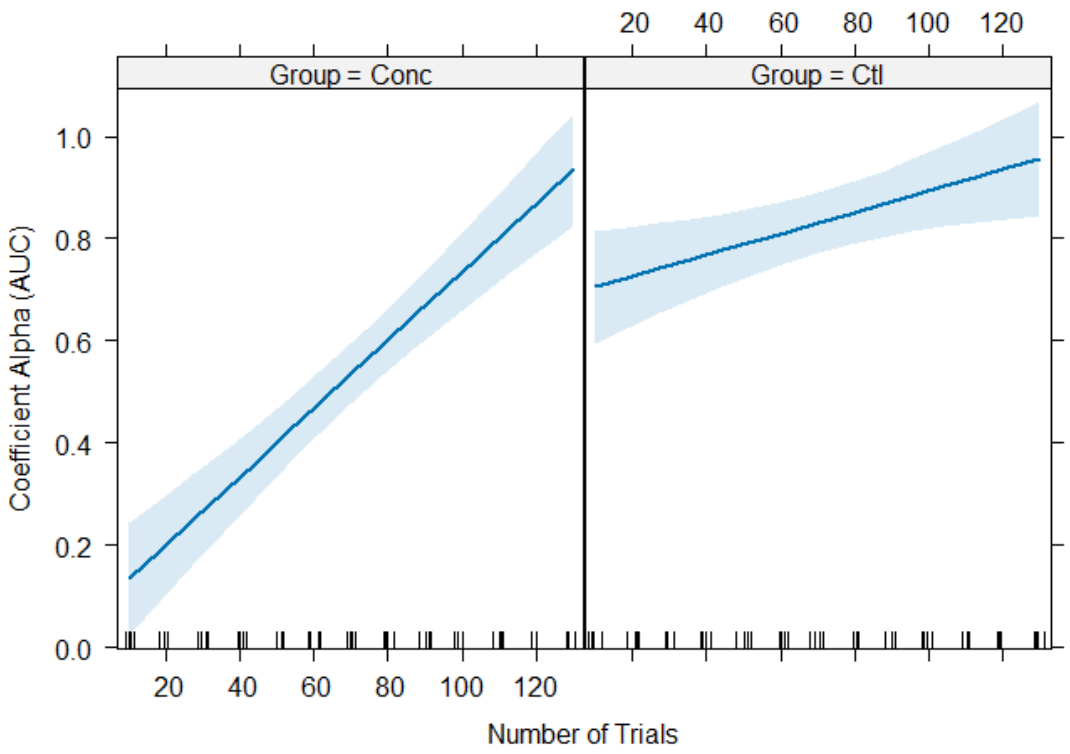


Figure 12

Interaction between Group and Number of Trials on alpha coefficient values for MMN AUC in the intensity deviant condition



We investigated the number of trials required to reach criterion levels for Cronbach's alpha next (summarized in Tables 16 and 17). When sequential trials were considered for MMN amplitude, controls required 70 trials to achieve *excellent* internal consistency (α = 0.9) whereas rCFL participants needed 90 trials to achieve *good* internal consistency (α = 0.81). The rCFL participants did not reach *excellent* internal consistency in this condition. When the reliability of MMN AUC was tested, controls required 110 sequential trials to achieve *excellent* internal consistency (α = 0.9) and rCFL participants needed 130 trials to

achieve *good* internal consistency (α = 0.81). Again, the concussed participants did not reach *excellent* internal consistency with the inclusion of all trials.

When trials were considered in randomized order, controls required 60 trials to achieve *excellent* internal consistency (α = 0.91) whereas rCFL participants needed 70 trials to achieve *good* internal consistency (α = 0.8) for MMN amplitude. The rCFL participants did not reach *excellent* internal consistency in this condition. For MMN AUC, controls required 100 randomized trials to achieve *excellent* internal consistency (α = 0.9) and rCFL participants needed 120 trials to achieve *good* internal consistency (α = 0.82). Again, the rCFL participants did not reach *excellent* internal consistency even when all trials were included.

Table 16

Concussed (rCFL) and control participants' results for good and excellent internal consistency in the intensity deviant condition (MMN amplitude)

Internal Consistency	**Order of Trials**	**Control Group**		**Concussed Group**	
		Cronbach's alpha	*Number of Trials*	*Cronbach's alpha*	*Number of Trials*
Excellent	Sequential	0.9	70	N/A	N/A
	Random	0.91	60	N/A	N/A
Good	Sequential	0.81	40	0.81	90
	Random	0.83	30	0.8	70

Table 17

Concussed (rCFL) and control participants' results for good and excellent internal consistency in the intensity deviant condition (MMN AUC)

Internal Consistency	Order of Trials	Control Group		Concussed Group	
		Cronbach's alpha	*Number of Trials*	*Cronbach's alpha*	*Number of Trials*
Excellent	Sequential	0.9	110	N/A	N/A
	Random	0.9	100	N/A	N/A
Good	Sequential	0.83	60	0.81	130
	Random	0.81	30	0.82	120

Discussion

Study 2 examined the reliability of the MMN component in retired Canadian Football League players and age-matched controls by analyzing the number of trials necessary to elicit a stable response. We hypothesized that the rCFL group with a history of concussions would demonstrate the need for more trials due to long-term effects of concussion as supported by an overwhelming amount of existing research (De Beaumont et al., 2009; Ruiter et al., 2019; Ryan & Warden, 2003). Our findings suggested that the stability of the MMN amplitude and AUC, derived from frequency and intensity deviants, are especially affected by multiple concussions over the years in rCFL players. As can be expected, both the MMN amplitude and AUC values were significantly affected by the number of trials for all deviant types. We observed the degree of similarity of the MMN averaged over different numbers of bins of 10 trials up to 130 trials (all 13 bins). For the rCFL players, we found that the MMN can be elicited with a *good* or *excellent* degree of internal consistency by a minimum of 70 to 130 trials (both MMN amplitude and AUC)

depending on deviant type. In comparison, controls required a minimum of only 50 to 70 trials (MMN amplitude) and 100 to 120 trials (MMN AUC) to achieve *excellent* internal consistency. Under certain conditions, the MMN amplitude and AUC values did not reach an *excellent* internal consistency even with the inclusion of all 130 trials for the rCFL group.

As a group, the rCFL participants showed signs of neurophysiological dysfunction in terms of the stability of their elicited MMN component. Evidence of cognitive and behavioural problems in their self-reports (SF-36, ImPACT, PCSS and BDI II) indicated more social, emotional, physical, and psychological health issues.

The overall general health of rCFL players was poorer compared to controls as reported in the SF-36 assessment. They revealed lower scores in each category, though Social Function and Pain categories were significantly different between groups (as found in Ruiter et al., 2019).

Group differences were not seen in the ImPACT (The Immediate Post-Concussion Assessment and Cognitive Test) results. This is not surprising, given that the concussions were sustained years prior to the current experiment. Impulse Control scores were very strong for both groups in comparison to the “normal” in the ImPACT normative data (Iverson et al., 2003). This may be attributable to participants being apprehensive to accuracy of their responses rather than reaction time. Both groups had below-average CEI scores which is likely because several participants were over 59 years old which was outside the ImPACT normative data age range at the time of testing (Iverson et al., 2003).

These results can only be considered suggestive because of the inadequate norms. Overall, the two groups did not significantly differ for ImPACT scores. However, a trend of slightly poorer performance was exhibited by the rCFL group in each category.

Next, the PCSS, asking about symptoms such as headache, balance problems, sadness, numbness or tingling, and visual problems, revealed significant differences between the scores of rCFL players and controls. This suggests that sports-related concussions may increase scores in symptomatology such as somatic depression (as seen in Chen et al., 2007; Kontos et al., 2012) even years after acute neurological trauma.

The depression inventory (BDI II) had been administered to examine the effects of concussion on emotional and psychological health. The results showed that rCFL players have higher levels of depressive symptoms. They scored nearly four times higher than the controls, further emphasizing the literature backing the PCSS results. Willer & Leddy (2006) have suggested that depression may be a predictor of PCS. As long-lived athletes, the rCFL players are likely suffering from PCS where symptoms can persist years after injury (Ryan & Warden, 2003). Although depressive symptomology scores were significantly different between the two groups, the rCFL group scores did not surpass the clinical cut-off for depression.

The ANCOVAs revealed a significant effect of Group and a significant effect of Number of Trials for both amplitude and AUC alpha coefficient values across all MMN deviants. Our results showed that a history of concussion affects the number of trials as well as the strength of the alpha coefficient needed to obtain an internally consistent MMN amplitude

and AUC. The rCFL athletes required a greater number of trials than controls to achieve a stable MMN. These findings are like other ERP studies in that neurophysiological dysfunction is exposed by event-related potentials and demonstrated in individuals with a history of concussions (De Beaumont et al., 2007 & 2009; Dupuis, 2000).

We found interaction effects (Group x Number of Trials) on both amplitude and AUC values in only the frequency and intensity deviants. The lack of an effect in the duration deviant suggests that the reliability was consistent between the rCFL and control groups. This inference is supported by research that examined the reliability of the MMN and found the duration deviant to be more dependable when eliciting MMNs in comparison to frequency and intensity deviants (Tervaniemi et al., 1999). As seen for frequency (Figures 7, 8) and intensity (Figures 11 and 12) deviants, the control groups' MMN stability was relatively high with a small number of trials whereas the concussed group' stability began low and steadily increased with more trials added.

Limitations

In this study, we had sex- and age-matched non-athletes as the control group for retired professional athletes with a history of concussions. The ideal control group would have consisted of non-concussed professional football players, but considering that football is a contact sport, this is simply not possible.

On average, rCFL participants remembered sustaining four concussions over almost eight years of playing professional football 28 years ago. Most of the concussions reported by the rCFL athletes were self-identified rather than clinically diagnosed. This makes it

difficult to know the precise number, severity, and occurrence of these concussions. In addition, many of the injuries went undiagnosed because concussion was not well understood during that time and people were unaware of how serious such injuries were. Moreover, the career length of participants varied, ranging from one year to 14 years. Although there were no significant correlations between the demographic data and the behavioural results, a longer career length could suggest a larger number of sustained concussions.

Another critical factor to consider is the football players' position when their concussions were sustained. Studies have shown that the frequency and severity of sustaining a concussion can differ based on position. Specifically, offensive positions (such as quarterbacks, running backs, and wide receivers) sustain a higher number of greater magnitude head impacts compared to others (Funk et al., 2012). The positions that receive the most severe head impacts are running backs and quarterbacks. There has also been evidence of how the location of impact on the helmet varies by player position. Quarterbacks receive the most impacts to the back of the helmet in comparison to all other player positions where the most impacts occur to the front (Crisco et al., 2011). Future studies could examine the effect of player position on the stability of the MMN.

Three participants in the rCFL group reported that their last concussion was sustained after they retired from professional football. It is not certain how these concussions occurred and their severity, but analyses excluding these three participants revealed that ERP and behavioural results remained the same.

Two rCFL players reported health comorbidities which could have affected the neuropsychological and EEG assessments. One had been diagnosed with chronic pain and depression, the other with rheumatoid arthritis and chronic pain. The participant who reported chronic pain and depression was prescribed to take Duloxetine which has been found to lower ERP amplitudes and prolong latency (Zhou et al., 2019). The other participant who reported rheumatoid arthritis and chronic pain was prescribed Amitriptyline which has been shown to have no effect on ERP amplitudes (Veldhuijzen et al., 2006). Other medications prescribed to participants in the rCFL group are not known to have an influence on ERP data.

Conclusion

This study investigated the stability of the MMN brain response component in retired football players who have a history of concussion compared to healthy controls. The primary goals were to establish the number of trials needed to elicit the MMN with high internal consistency and to investigate the effects of concussion on MMN stability. Our results revealed that 130 trials were enough to elicit a stable MMN response for all deviant types in both groups. This finding provides an accurate estimate of the number of trials needed to achieve an internally consistent MMN in an older concussed population. This is essential when assessing cognitive function and tracking recovery.

Chapter 4

General Discussion

This is the first study to date that examines the internal consistency reliability of the MMN component in concussed adolescents, retired professional athletes and their respective controls. It also gives new insights on the number of trials needed to obtain a stable MMN component for both amplitude and AUC alpha coefficient values contingent on age and history of concussions. For applicability to clinical assessment, both sequential and randomized trial order counts were considered in the data analysis. This study also describes the cognitive dysfunction caused by concussions using behavioural and neurophysiological measures. Participants completed various behavioural assessments to evaluate overall health, concussion history and symptoms, and depressive symptoms. Completion of these behavioural assessments was followed by an ERP assessment using the MMN in a 3-deviant oddball paradigm.

In the adolescent group, we found no significant effects of group on the MMN amplitude or AUC values whereas these effects were present for the older adult group, meaning that the concussed adolescents and their controls had similar consistencies to reach MMN stability. We can attribute these findings to the fact that rCFL athletes have sustained a greater amount and severity of concussions which is reflected in their MMN instability. This also supports previous findings by Ruiter et al. (2019; 2020) that revealed: 1) retired football players experiencing PCS have altered MMN responses compared to controls and

2) acutely concussed adolescents do not seem to be affected cognitively compared to their controls as observed in their elicited ERPs.

Across all groups and deviant types, the number of trials had a significant effect on both MMN amplitude and MMN AUC values. The range of number of trials for concussed adolescents was 90-130 trials and for healthy controls, 70-90 trials. The rcFL athletes had a range of 70-130 trials and for healthy controls, 50-120 trials. Overall, 130 trials were sufficient to obtain a high internal consistency under all conditions. Duncan et al. (2009) had suggested the use of at least 150 trials for eliciting the MMN. We conclude that the number of trial repetitions can be reduced by 20 trials and still produce a reliable MMN. This is beneficial especially when testing clinical populations where they may naturally need more breaks. The MMN requires a far greater number of trials to reach internal consistency compared to other ERP components such as the N200 or P300. Researchers found that the N200 and P300 were internally consistent after only 20 trials and 14-20 trials, respectively (Cohen & Polich, 1997; Rietdijk et al., 2014). The MMN can present itself as rather small in amplitude, especially if elicited by deviants with small discrimination (Schröger, 1998). To become distinguishable, the MMN requires a greater number of responses to be averaged, suggesting it would also need a greater number of trials to stabilize.

There was only an interaction effect for the MMN AUC in the intensity deviant for adolescents whereas effects were found for both MMN amplitude and AUC values in the frequency and intensity deviants for older adults. We observed differing trends for MMN AUC in the intensity deviant between the two populations. The adolescent controls and

the rCFL athletes showed steeper, faster growing slopes compared to their opposing group with the addition of more trials (see Figures 6 and 12). This would suggest that the effect was greater for the adolescent controls in comparison to the concussed adolescents and for the rCFL athletes in comparison to their healthy controls. In Chapter 2 (adolescents), we explained that the interaction effect could be due to the intensity deviant acting as an EP to control participants. They needed more trials to reach stability because of the noisier waveforms caused by involuntary muscle movements. On the contrary, older adults are less sensitive to stimuli deviance. It requires more vigor to capture their attention (Gaeta et al., 1998). With that being said, the intensity deviant likely did not act similarly to an EP for the older adults but instead revealed effects of PCS in rCFL athletes.

Cronbach's alpha as a measure of internal consistency reliability has been used in literature with varying acceptable ranges and different terminology describing such ranges (Moran et al., 2013; Olvet & Hajcak, 2009; Rietdijk et al., 2014; Thigpen et al., 2017). For example, some researchers consider $\alpha > 0.70$ to be satisfactory while others would describe a value between 0.70 and 0.90 as having high internal reliability (Olvet & Hajcak, 2009; Thigpen et al., 2017). For this study, we referenced our Cronbach's alpha scale (see Table 1) from a recent study on pediatric patients with varying levels of consciousness (Caruana et al., 2023). It is crucial that studies using coefficient alpha values report the precise criteria used so that there is a mutual understanding between authors and readers alike. In addition, it may be difficult to generalize the results of studies if they are using criteria differently to determine the minimum number of trials to

achieve an internally consistent ERP. Cronbach's alpha requires the MMN amplitude and AUC values to be exported at the single trial level since it calculates the similarity between items. There tends to be more variability in the MMN at the single trial level than with averaged responses. This means that more data and trials are required to achieve reliability compared to other ERPs. Regarding the types of alpha values, our results across all groups showed that the MMN required a greater number of trials to reach stability when derived from AUC values than amplitude values.

Our results revealed acceptable reliability of the MMN with a small number of trials granted we exported averages from a single electrode, Fz. Baldeweg et al. (1999) reported that the MMN is usually of maximal amplitude at the central frontal electrode, Fz, due to the tangential orientation of bilateral sources in the superior temporal gyrus (STG). Future studies may want to depict the MMN as a region of interest by including more electrodes. A study investigating the P3 component stated that ERP amplitudes across several electrodes yield more reliable measurements than relying on a single electrode (Huffmeijer et al., 2014).

Future studies of reliability should expand to other ERPs that are associated with health assessment and diagnosis in concussion. For example, the P300 component is a centro-parietal positive deflection linked to attention and memory processes and has been proven useful in assessing cognitive dysfunction (Duncan et al., 2009; Elting et al., 2005; Polich & Herbst, 2000). A common finding is that the P300 is delayed or weakened in traumatic brain injury (Bernstein, 2002; De Beaumont et al., 2007; Dupuis et al., 2000; Ruiter et al., 2019; 2020).

Conclusion

The present thesis builds on the growing area of research on how concussions, specifically repetitive traumatic impacts, can develop into a serious health concern. We sought to determine the number of trials necessary for the MMN to be elicited with a high (*good* or *excellent*) degree of internal consistency and to investigate the effects of age and concussion on MMN stability. By examining both concussed adolescents and rCFL athletes through statistical and ERP analyses, we found the stability of the MMN, reflecting automatic attention processing and early memory formation, to be considerably affected in retired athletes compared to their controls. The concussed adolescents did not show as significant of concussive effects on the stability of their elicited MMNs in comparison to rCFL athletes with respective control groups. Examining age, the healthy adolescents showed a generally lower MMN stability than the healthy older adults. Overall, 130 trials were enough to achieve internally consistent MMNs (both amplitude and AUC) for all deviant types. For future implications, 130 trials should be considered as an accurate estimate for obtaining a reliable MMN response in concussed and healthy individuals across adolescent and older adult populations.

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Appendices

Appendix A: Concussed and control adolescent participants' demographic data

Concussed Adolescents					**Controls**		
Participant	***Sex***	***Age***	***# of Previous Concussions***	***# of Days Since Last Concussion***	***Participant***	***Sex***	***Age***
1	F	17	6	36	1	F	19
2	F	16	0	20	2	F	20
3	F	13	1	5	3	F	19
4	M	14	2	23	4	F	19
5	M	13	2	30	5	F	21
6	M	16	2	7	6	F	21
7	F	17	2	14	7	F	20
8	F	16	6	8	8	F	19
9	F	15	1	17	9	M	19
10	F	15	1	9	10	F	19
11	F	17	1	17	11	F	19
12	M	13	5	14	12	F	21
13	F	15	1	13	13	F	21
14	F	17	4	15	14	M	22
15	F	17	3	30	15	F	20
16	F	13	0	7	16	F	20
17	F	13	1	8	17	F	19
18	M	15	2	19	18	M	19
19	F	17	1	12	19	M	19
20	M	14	1	58	20	F	17
21	F	14	0	30	21	M	19
22	F	17	2	39	22	F	19
23	F	16	2	26	23	F	18
24	F	14	1	6	24	F	17
25	M	13	1	13	25	F	17
26	F	14	1	48	26	F	19
					27	F	18
					28	F	20
Mean (SD)	**-**	**15.04 (1.53)**	**1.88 (1.63)**	**20.15 (13.35)**	**Mean (SD)**	**-**	**19.3 (1.22)**

Appendix B: Concussed adolescent participants' ImPACT behavioural scores compared to Normative Data (Iverson et al., 2003)

Table B1

Concussed female adolescent participants' ImPACT behavioural scores

Participant	**VBM**	**VIM**	**MS**	**RT**	**IC**	**CEI**
1	81	64	32.33	0.91	5	0.3
2	66	60	28.55	0.7	9	0.12
3	83	49	28.73	0.74	11	0.24
7	67	59	28.33	0.68	6	0.17
8	72	89	35.95	0.65	10	0.17
9	91	79	29.67	0.7	4	0.53
10	96	88	35.98	0.54	1	0.5
11	98	65	30.17	0.76	2	0.34
13	69	57	23.95	0.73	14	0.29
14	98	77	42.93	0.61	3	0.53
15	74	61	41.28	0.61	16	0.48
16	79	68	32.9	0.59	22	0.26
17	99	63	31.33	0.71	2	0.42
19	72	56	39.08	0.69	3	0.2
21	67	63	26.55	0.77	7	0.19
22	91	50	36.7	0.71	2	0.32
23	47	31	18.23	0.99	1	0.19
24	67	58	33.17	0.76	9	0.2
26	84	81	36.55	0.6	9	0.27
Mean (SD)	**79.00 (13.75)**	**64.11 (13.78)**	**32.23 (5.89)**	**0.71 (0.10)**	**7.16 (5.5)**	**0.30 (0.13)**
Comparison to ImPACT Normative Data	Low-Average	Low-Average	Low-Average	Borderline	Norms Unavailable	Norms Unavailable

Table B2

Concussed male adolescent participants' ImPACT behavioural scores

Participant	**VBM**	**VIM**	**MS**	**RT**	**IC**	**CEI**
4	91	82	26.85	0.66	12	0.3
5	51	55	20.9	0.91	0	0.14
6	84	84	28.38	0.67	5	0.26
12	89	88	24.8	0.72	4	0.39
18	99	95	42	0.66	2	0.42
20	70	55	22.13	0.82	7	0.12
25	83	88	38.33	0.84	10	-0.1
Mean (SD)	**81 (14.75)**	**78.14 (15.11)**	**29.06 (7.48)**	**0.75 (0.09)**	**5.71 (3.95)**	**0.22 (0.17)**
Comparison to ImPACT Normative Data	Average	Average	Low-Average	Borderline	Norms Unavailable	Norms Unavailable

Appendix C: Concussed adolescent participants' concussive and depressive symptom scores

Participant	**PCSS**	**CDI 2**
1	109	71
2	55	68
3	54	68
4	20	76
5	64	49
6	33	57
7	35	46
8	94	52
9	92	67
10	67	51
11	50	46
12	101	63
13	41	43
14	24	58
15	58	46
16	17	43
17	12	47
18	46	44
19	53	62
20	55	49
21	59	68
22	60	71
23	80	67
24	55	63
25	32	46
26	66	55
Mean (SD)	**55.08 (24.92)**	**56.07 (10.29)**

Appendix D: Concussed rCFL and control participants' demographic data

rCFL Players					**Controls**	
Participant	***Age***	***# of Concussions***	***Years Since Last Concussion***	***# of Years Played***	***Participant***	***Age***
1	62	7	14	12	1	56
2	45	1	13	13	2	46
3	60	2	32	13	3	51
4	59	2	36	11	4	53
5	54	4	7	1	5	58
6	48	2	27	3	6	58
7	63	11	31	10	7	59
8	63	3	36	14	8	49
9	57	2	33	5	9	56
10	48	8	2	5	10	58
11	64	6	38	4	11	55
12	61	2	37	3	12	50
13	47	3	16	9	13	56
14	64	3	36	11	14	56
15	66	4	39	6	15	62
16	53	2	31	5	16	48
17	57	3	34	1	17	61
18	66	1	45	11	18	61
19	58	11	27	12	19	45
					20	52
Mean (SD)	**57.63 (6.71)**	**4.05**	**28.11**	**7.84**	**Mean (SD)**	**54.63 (5.04)**

Appendix E: Concussed rCFL and control participants' ImPACT behavioural scores

Table E1

Concussed rCFL players' ImPACT behavioural scores

Participant	VBM	VIM	MS	RT	IC	CEI
1	88	67	28.7	0.96	1	-0.25
2	63	64	33.3	0.58	1	0.11
3	74	54	25.5	0.77	5	0.05
4	94	52	26.05	0.97	0	-0.42
5	56	68	31.03	0.89	3	0.06
6	81	79	39.05	0.66	3	0.2
7	70	66	26.45	0.76	1	0.05
8	66	77	25.8	0.66	4	0.07
9	79	71	38.13	1.03	1	-0.25
10	71	82	38.55	0.63	1	0.14
11	86	65	26	0.79	3	0.03
12	65	56	31.8	0.67	4	0.18
13	79	64	25.75	0.74	1	0.21
14	82	41	29.58	0.71	0	0.14
15	72	71	29.05	0.74	1	0.07
16	83	31	29.58	1.24	3	-0.6
17	89	60	34.88	0.64	1	0.37
18	91	75	37.47	0.78	0	0.24
19	82	60	27.4	0.75	3	0.13
Mean (SD)	**77.42 (10.43)**	**63.31 (12.73)**	**30.74 (4.80)**	**0.79 (0.16)**	**1.89 (1.52)**	**0.03 (0.24)**

Note. Normative data for this age group unavailable for comparison

Table E2

Control adult participants' ImPACT behavioural scores

Participant	VBM	VIM	MS	RT	IC	CEI
1	99	84	36.08	0.85	1	-0.2
2	93	89	50.8	0.6	1	0.43
3	79	48	32.7	0.73	0	0.11
4	71	64	36.92	0.63	0	0.1
5	72	47	25.48	0.83	2	0.03
6	80	56	25.33	1.09	2	-0.16
7	71	65	33.83	0.71	2	0.08
8	90	81	47.63	0.49	1	0.46
9	91	63	26.75	0.99	0	0
10	59	33	32.17	0.88	1	0.02
11	76	69	34.4	0.77	1	0.14
12	96	82	36.83	0.84	1	0.04
13	95	60	31.42	0.74	0	0.36
14	87	51	29.95	0.82	1	0.13
15	88	46	36.97	0.73	4	0.21
16	79	58	30.9	0.58	5	0.23
17	72	73	31.67	0.67	4	0.28
18	84	56	30.4	0.83	2	0.14
19	81	66	42.63	0.64	1	0.11
20	85	60	30.08	0.68	3	0.2
Mean (SD)	**82.4 (10.31)**	**62.55 (14.33)**	**34.15 (6.66)**	**0.76 (0.14)**	**1.6 (1.43)**	**0.14 (0.17)**

Note. Normative data for this age group unavailable for comparison

Appendix F: Concussed rCFL participants' SF-36 behavioural scores

rCFL Player	**SF-36 (General Health)**	**Control**	**SF-36 (General Health)**
1	65	1	60
2	75	2	55
3	80	3	100
4	100	4	90
5	70	5	80
6	50	6	75
7	75	7	90
8	70	8	80
9	70	9	80
10	40	10	100
11	60	11	80
12	95	12	90
13	90	13	75
14	45	14	65
15	65	15	95
16	95	16	90
17	85	17	75
18	70	18	90
19	70	19	85
		20	65
Mean (SD)	**72.11 (16.08)**	**Mean (SD)**	**79.72 (12.77)**

Appendix G: Concussed rCFL and control participants' concussive and depressive symptom scores

rCFL Players			**Controls**		
Participant	***PCSS***	***BDI II***	***Participant***	***PCSS***	***BDI II***
1	9	13	1	0	7
2	4	3	2	2	8
3	17	9	3	0	1
4	4	2	4	0	0
5	52	25	5	5	2
6	7	6	6	0	0
7	12	8	7	0	2
8	5	6	8	0	3
9	14	3	9	0	1
10	27	20	10	0	0
11	11	11	11	6	0
12	17	1	12	0	2
13	13	2	13	14	2
14	25	20	14	9	4
15	27	16	15	0	0
16	0	0	16	0	0
17	1	6	17	20	9
18	9	4	18	0	1
19	13	7	19	0	1
			20	0	1
Mean (SD)	**14.05 (12.20)**	**8.53 (7.21)**	**Mean (SD)**	**2.95 (5.55)**	**2.26 (2.75)**

Appendix H: Edinburgh Handedness Inventory

Edinburgh Handedness Inventory[1]

Please indicate with a check (✓) your preference in using your left or right hand in the following tasks.

Where the preference is so strong you would never use the other hand, unless absolutely forced to, put two checks (✓✓).

If you are indifferent, put one check in each column (✓ | ✓).

Some of the activities require both hands. In these cases, the part of the task or object for which hand preference is wanted is indicated in parentheses.

Task / Object	Left Hand	Right Hand
1. Writing		
2. Drawing		
3. Throwing		
4. Scissors		
5. Toothbrush		
6. Knife (without fork)		
7. Spoon		
8. Broom (upper hand)		
9. Striking a Match (match)		
10. Opening a Box (lid)		
Total checks:	LH =	RH =
Cumulative Total	CT = LH + RH =	
Difference	D = RH – LH =	
Result	R = (D / CT) × 100 =	
Interpretation: (Left Handed: R < -40) (Ambidextrous: -40 ≤ R ≤ +40) (Right Handed: R > +40)		

[1] Oldfield, R. C. (1971). The assessment and analysis of handedness: The Edinburgh inventory. *Neuropsycholologia*, *9*, 97-113.

Appendix I: Post-Concussion Symptom Scale

Name: _____ Age/DOB: _____ Date of Injury:_____

Post Concussion Symptom Scale

No symptoms"0"-------Moderate "3"---------Severe"6"

Time after Concussion

SYMPTOMS	Days/Hrs _____	Days/Hrs _____	Days/Hrs _____
Headache	0 1 2 3 4 5 6	0 1 2 3 4 5 6	0 1 2 3 4 5 6
Nausea	0 1 2 3 4 5 6	0 1 2 3 4 5 6	0 1 2 3 4 5 6
Vomiting	0 1 2 3 4 5 6	0 1 2 3 4 5 6	0 1 2 3 4 5 6
Balance problems	0 1 2 3 4 5 6	0 1 2 3 4 5 6	0 1 2 3 4 5 6
Dizziness	0 1 2 3 4 5 6	0 1 2 3 4 5 6	0 1 2 3 4 5 6
Fatigue	0 1 2 3 4 5 6	0 1 2 3 4 5 6	0 1 2 3 4 5 6
Trouble falling to sleep	0 1 2 3 4 5 6	0 1 2 3 4 5 6	0 1 2 3 4 5 6
Excessive sleep	0 1 2 3 4 5 6	0 1 2 3 4 5 6	0 1 2 3 4 5 6
Loss of sleep	0 1 2 3 4 5 6	0 1 2 3 4 5 6	0 1 2 3 4 5 6
Drowsiness	0 1 2 3 4 5 6	0 1 2 3 4 5 6	0 1 2 3 4 5 6
Light sensitivity	0 1 2 3 4 5 6	0 1 2 3 4 5 6	0 1 2 3 4 5 6
Noise sensitivity	0 1 2 3 4 5 6	0 1 2 3 4 5 6	0 1 2 3 4 5 6
Irritability	0 1 2 3 4 5 6	0 1 2 3 4 5 6	0 1 2 3 4 5 6
Sadness	0 1 2 3 4 5 6	0 1 2 3 4 5 6	0 1 2 3 4 5 6
Nervousness	0 1 2 3 4 5 6	0 1 2 3 4 5 6	0 1 2 3 4 5 6
More emotional	0 1 2 3 4 5 6	0 1 2 3 4 5 6	0 1 2 3 4 5 6
Numbness	0 1 2 3 4 5 6	0 1 2 3 4 5 6	0 1 2 3 4 5 6
Feeling "slow"	0 1 2 3 4 5 6	0 1 2 3 4 5 6	0 1 2 3 4 5 6
Feeling "foggy"	0 1 2 3 4 5 6	0 1 2 3 4 5 6	0 1 2 3 4 5 6
Difficulty concentrating	0 1 2 3 4 5 6	0 1 2 3 4 5 6	0 1 2 3 4 5 6
Difficulty remembering	0 1 2 3 4 5 6	0 1 2 3 4 5 6	0 1 2 3 4 5 6
Visual problems	0 1 2 3 4 5 6	0 1 2 3 4 5 6	0 1 2 3 4 5 6
TOTAL SCORE	_____	_____	_____

Use of the Post-Concussion Symptom Scale: The athlete should fill out the form, on his or her own, in order to give a subjective value for each symptom. This form can be used with each encounter to track the athlete's progress towards the resolution of symptoms. Many athletes may have some of these reported symptoms at a baseline, such as concentration difficulties in the patient with attention-deficit disorder or sadness in an athlete with underlying depression, and must be taken into consideration when interpreting the score. Athletes do not have to be at a total score of zero to return to play if they already have had some symptoms prior to their concussion.

Appendix J: Beck Depression Inventory II

Beck's Depression Inventory

This depression inventory can be self-scored. The scoring scale is at the end of the questionnaire.

1.
- 0 I do not feel sad.
- 1 I feel sad
- 2 I am sad all the time and I can't snap out of it.
- 3 I am so sad and unhappy that I can't stand it.

2.
- 0 I am not particularly discouraged about the future.
- 1 I feel discouraged about the future.
- 2 I feel I have nothing to look forward to.
- 3 I feel the future is hopeless and that things cannot improve.

3.
- 0 I do not feel like a failure.
- 1 I feel I have failed more than the average person.
- 2 As I look back on my life, all I can see is a lot of failures.
- 3 I feel I am a complete failure as a person.

4.
- 0 I get as much satisfaction out of things as I used to.
- 1 I don't enjoy things the way I used to.
- 2 I don't get real satisfaction out of anything anymore.
- 3 I am dissatisfied or bored with everything.

5.
- 0 I don't feel particularly guilty
- 1 I feel guilty a good part of the time.
- 2 I feel quite guilty most of the time.
- 3 I feel guilty all of the time.

6.
- 0 I don't feel I am being punished.
- 1 I feel I may be punished.
- 2 I expect to be punished.
- 3 I feel I am being punished.

7.
- 0 I don't feel disappointed in myself.
- 1 I am disappointed in myself.
- 2 I am disgusted with myself.
- 3 I hate myself.

8.
- 0 I don't feel I am any worse than anybody else.
- 1 I am critical of myself for my weaknesses or mistakes.
- 2 I blame myself all the time for my faults.
- 3 I blame myself for everything bad that happens.

9.
- 0 I don't have any thoughts of killing myself.
- 1 I have thoughts of killing myself, but I would not carry them out.
- 2 I would like to kill myself.
- 3 I would kill myself if I had the chance.

10.
- 0 I don't cry any more than usual.
- 1 I cry more now than I used to.
- 2 I cry all the time now.
- 3 I used to be able to cry, but now I can't cry even though I want to.

11.

0	I am no more irritated by things than I ever was.
1	I am slightly more irritated now than usual.
2	I am quite annoyed or irritated a good deal of the time.
3	I feel irritated all the time.

12.

0	I have not lost interest in other people.
1	I am less interested in other people than I used to be.
2	I have lost most of my interest in other people.
3	I have lost all of my interest in other people.

13.

0	I make decisions about as well as I ever could.
1	I put off making decisions more than I used to.
2	I have greater difficulty in making decisions more than I used to.
3	I can't make decisions at all anymore.

14.

0	I don't feel that I look any worse than I used to.
1	I am worried that I am looking old or unattractive.
2	I feel there are permanent changes in my appearance that make me look unattractive
3	I believe that I look ugly.

15.

0	I can work about as well as before.
1	It takes an extra effort to get started at doing something.
2	I have to push myself very hard to do anything.
3	I can't do any work at all.

16.

0	I can sleep as well as usual.
1	I don't sleep as well as I used to.
2	I wake up 1-2 hours earlier than usual and find it hard to get back to sleep.
3	I wake up several hours earlier than I used to and cannot get back to sleep.

17.

0	I don't get more tired than usual.
1	I get tired more easily than I used to.
2	I get tired from doing almost anything.
3	I am too tired to do anything.

18.

0	My appetite is no worse than usual.
1	My appetite is not as good as it used to be.
2	My appetite is much worse now.
3	I have no appetite at all anymore.

19.

0	I haven't lost much weight, if any, lately.
1	I have lost more than five pounds.
2	I have lost more than ten pounds.
3	I have lost more than fifteen pounds.

20.

0	I am no more worried about my health than usual.
1	I am worried about physical problems like aches, pains, upset stomach, or constipation.
2	I am very worried about physical problems and it's hard to think of much else.
3	I am so worried about my physical problems that I cannot think of anything else.

21.

0	I have not noticed any recent change in my interest in sex.
1	I am less interested in sex than I used to be.
2	I have almost no interest in sex.
3	I have lost interest in sex completely.

INTERPRETING THE BECK DEPRESSION INVENTORY

Now that you have completed the questionnaire, add up the score for each of the twenty-one questions by counting the number to the right of each question you marked. The highest possible total for the whole test would be sixty-three. This would mean you circled number three on all twenty-one questions. Since the lowest possible score for each question is zero, the lowest possible score for the test would be zero. This would mean you circles zero on each question. You can evaluate your depression according to the Table below.

Total Score	Levels of Depression
1-10	These ups and downs are considered normal
11-16	Mild mood disturbance
17-20	Borderline clinical depression
21-30	Moderate depression
31-40	Severe depression
over 40	Extreme depression

Appendix K: Children's Depression Inventory 2 Sample Items

Item 1
☐ I am sad once in a while.
☐ I am sad many times.
☐ I am sad all the time.

Item 2
☐ Nothing will ever work out for me.
☐ I am not sure if things will work out for me.
☐ Things will work out for me O.K.

Item 3
☐ I do most things O.K.
☐ I do many things wrong.
☐ I do everything wrong.

Item 4
☐ I have fun in many things.
☐ I have fun in some things.
☐ Nothing is fun at all.

Item 5
☐ I am important to my family.
☐ I am not sure if I am important to my family.
☐ My family is better off without me.

Item 6
☐ I hate myself.
☐ I do not like myself.
☐ I like myself.

Appendix L: SF-36 Health Survey

Your Health and Well-Being

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

For each of the following questions, please mark an ☒ in the one box that best describes your answer.

1. In general, would you say your health is:

Excellent	Very good	Good	Fair	Poor
☐ 1	☐ 2	☐ 3	☐ 4	☐ 5

2. <u>Compared to one year ago</u>, how would you rate your health in general <u>now</u>?

Much better now than one year ago	Somewhat better now than one year ago	About the same as one year ago	Somewhat worse now than one year ago	Much worse now than one year ago
☐ 1	☐ 2	☐ 3	☐ 4	☐ 5

3. 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?

	Yes, limited a lot	Yes, limited a little	No, not limited at all
a. Vigorous activities, such as running, lifting heavy objects, participating in strenuous sports	☐ 1	☐ 2	☐ 3
b. Moderate activities, such as moving a table, pushing a vacuum cleaner, bowling, or playing golf	☐ 1	☐ 2	☐ 3
c. Lifting or carrying groceries	☐ 1	☐ 2	☐ 3
d. Climbing several flights of stairs	☐ 1	☐ 2	☐ 3
e. Climbing one flight of stairs	☐ 1	☐ 2	☐ 3
f. Bending, kneeling, or stooping	☐ 1	☐ 2	☐ 3
g. Walking more than a kilometre	☐ 1	☐ 2	☐ 3
h. Walking several hundred metres	☐ 1	☐ 2	☐ 3
i. Walking one hundred metres	☐ 1	☐ 2	☐ 3
j. Bathing or dressing yourself	☐ 1	☐ 2	☐ 3

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

	All of the time	Most of the time	Some of the time	A little of the time	None of the time
a Cut down on the amount of time you spent on work or other activities	☐ 1	☐ 2	☐ 3	☐ 4	☐ 5
b Accomplished less than you would like	☐ 1	☐ 2	☐ 3	☐ 4	☐ 5
c Were limited in the kind of work or other activities	☐ 1	☐ 2	☐ 3	☐ 4	☐ 5
d Had difficulty performing the work or other activities (for example, it took extra effort)	☐ 1	☐ 2	☐ 3	☐ 4	☐ 5

5. During the past 4 weeks, how much of the time 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)?

	All of the time	Most of the time	Some of the time	A little of the time	None of the time
a Cut down on the amount of time you spent on work or other activities	☐ 1	☐ 2	☐ 3	☐ 4	☐ 5
b Accomplished less than you would like	☐ 1	☐ 2	☐ 3	☐ 4	☐ 5
c Did work or other activities less carefully than usual	☐ 1	☐ 2	☐ 3	☐ 4	☐ 5

6. During the <u>past 4 weeks</u>, to what extent has your physical health or emotional problems interfered with your normal social activities with family, friends, neighbours, or groups?

Not at all	Slightly	Moderately	Quite a bit	Extremely
☐ 1	☐ 2	☐ 3	☐ 4	☐ 5

7. How much <u>bodily</u> pain have you had during the <u>past 4 weeks</u>?

None	Very mild	Mild	Moderate	Severe	Very severe
☐ 1	☐ 2	☐ 3	☐ 4	☐ 5	☐ 6

8. During the <u>past 4 weeks</u>, how much did <u>pain</u> interfere with your normal work (including both work outside the home and housework)?

Not at all	A little bit	Moderately	Quite a bit	Extremely
☐ 1	☐ 2	☐ 3	☐ 4	☐ 5

9. 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…

	All of the time	Most of the time	Some of the time	A little of the time	None of the time
a. Did you feel full of life?	☐ 1	☐ 2	☐ 3	☐ 4	☐ 5
b. Have you been very nervous?	☐ 1	☐ 2	☐ 3	☐ 4	☐ 5
c. Have you felt so down in the dumps that nothing could cheer you up?	☐ 1	☐ 2	☐ 3	☐ 4	☐ 5
d. Have you felt calm and peaceful?	☐ 1	☐ 2	☐ 3	☐ 4	☐ 5
e. Did you have a lot of energy?	☐ 1	☐ 2	☐ 3	☐ 4	☐ 5
f. Have you felt downhearted and depressed?	☐ 1	☐ 2	☐ 3	☐ 4	☐ 5
g. Did you feel worn out?	☐ 1	☐ 2	☐ 3	☐ 4	☐ 5
h. Have you been happy?	☐ 1	☐ 2	☐ 3	☐ 4	☐ 5
i. Did you feel tired?	☐ 1	☐ 2	☐ 3	☐ 4	☐ 5

10. 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.)?

All of the time	Most of the time	Some of the time	A little of the time	None of the time
☐ 1	☐ 2	☐ 3	☐ 4	☐ 5

11. How TRUE or FALSE is <u>each</u> of the following statements for you?

	Definitely true	Mostly true	Don't know	Mostly false	Definitely false
a. I seem to get sick a little easier than other people	☐ 1	☐ 2	☐ 3	☐ 4	☐ 5
b. I am as healthy as anybody I know	☐ 1	☐ 2	☐ 3	☐ 4	☐ 5
c. I expect my health to get worse	☐ 1	☐ 2	☐ 3	☐ 4	☐ 5
d. My health is excellent	☐ 1	☐ 2	☐ 3	☐ 4	☐ 5

Thank you for completing these questions!