Long-term effects of concussion on relevancy-based modulation of somatosensory-evoked potentials

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Conflict of Interest
The authors declare that they have no conflict of interest.

Highlights

- Concussions impair sensory processing at early cortical processing stages
- These effects appear to be chronic, lasting several years following the injury
- The behavioural cost is likely minimal, suggesting compensatory mechanisms

Abstract

Objective: The purpose of this investigation was to better understand the effects of concussions on the ability to selectively up or down-regulate incoming somatosensory information based on relevance.

Methods: Median nerve somatosensory-evoked potentials (SEPs) were elicited from electrical stimulation and recorded from scalp electrodes while participants completed tasks that altered the relevance of specific somatosensory information being conveyed along the stimulated nerve.

Results: Within the control group, SEP amplitudes for task-relevant somatosensory information were significantly greater than for non-relevant somatosensory information at the earliest cortical processing potentials (N20-P27). Alternatively, the concussion history group showed similar SEP amplitudes for all conditions at early processing potentials, however a pattern similar to controls emerged later in the processing stream (P100) where both movement-related gating and facilitation of task-relevant information were present.

Conclusions: Previously concussed participants demonstrated impairments in the ability to up-regulate relevant somatosensory information at early processing stages. These effects appear to be chronic, as this pattern was observed on average several years after participants' most recent concussion.

Significance: Given the role of the prefrontal cortex in relevancy-based facilitation during movement-related gating, these findings lend support to the notion that this brain area may be particularly vulnerable to concussive forces.

Keywords

- Concussion
- Traumatic brain injury
- Somatosensory processing
- Movement-related gating
- Prefrontal cortex
- Somatosensory-evoked potential

Abbreviations: SEP, somatosensory evoked potential; cTBS, continuous theta burst stimulation; RMSE, root mean square error

1.0 Introduction

Concussions are the result of biomechanical forces acting on the brain, resulting in diffuse neural disruption and often producing symptoms associated with altered perceptual experiences. Despite widespread effects to the nervous system, an abundance of research over the past few decades suggests that the prefrontal cortex may be particularly sensitive to concussive forces (Belanger et al., 2010). Several meta-analyses propose that the cognitive domains linked with prefrontal functioning, such as working memory and attention, are specifically impaired following a concussion (Belanger et al., 2005, 2010; Frencham et al., 2005; Rohling et al., 2011; Zakzanis et al., 1999). Imaging work has supported this hypothesis: functional magnetic resonance imaging research has shown disruptions in dorsolateral prefrontal cortex (DLPFC) activity post-concussion (Gosselin et al., 2010; Mayer et al., 2015; Shin et al., 2017) and diffusion tensor imaging studies have identified post-concussive damage to frontal white-matter tracts (Chong and Schwedt, 2015; Eierud et al., 2014).

The prefrontal cortex also plays a critical role in modulation of incoming afferent information. Movement-related gating, a form of sensory gating in which somatosensory information reaching the cortex is reduced during active or passive movement, has cortical, subcortical, presynaptic, and peripheral contributions (Jones et al., 1989; Cheron and Borenstein, 1991; Chapman, 1994; Brooke 2004; Morita et al., 1998, Nakata et al., 2003; Insola et al., 2004, 2010, 2015). Within, or in conjunction with, the gating system, incoming afferent information can be facilitated based on task-relevancy. Seminal work by Staines and colleagues (2000) demonstrated relevancy-based modulation of movement-related gating in the lower limbs by manipulating the relevancy of specific sources (sub-modalities) of sensory information from the lower limb by requiring participants to make ankle movements (of the non-stimulated limb) that were dictated by the 'cutaneous code' of stimuli applied to the dorsum of the foot, or by the direction of passive movement (proprioceptive) induced by the experimenters. Relative to movement-related gating that occurs during passive movement alone, the conditions where the sensory information (cutaneous / proprioceptive) was specifically relevant for the subsequent motor task resulted in an enhancement of cortical activity in the primary somatosensory cortex (SI), measured using somatosensory-evoked potentials (SEPs) elicited by different peripheral nerves representing the relevant sensory information. Importantly, while the stimulation itself was not informative, focus on somatosensory information in the pathways that would be impacted by sensation was enough to drive the facilitatory effect. Support for the role of the prefrontal cortex in modulating somatosensory information during movement-related gating comes from research employing a brain stimulation pattern known as continuous theta burst stimulation (cTBS) to transiently inhibit the DLPFC in healthy human subjects. Brown et al. (2015) had participants complete conditions with relevant and non-relevant passive wrist movements similar to those employed in the lower limb in the aforementioned work by Staines and colleagues. Compared to participants' baseline measures, cTBS over DLPFC resulted in significantly attenuated SEPs during relevant movement, suggesting an important role of the prefrontal cortex in modulating relevancy-based facilitation during movement-related gating.

Given the role of the prefrontal cortex in modulating sensory information, in combination with its link to concussion symptoms, it is possible that filtering of irrelevant information through sensory or movement-related gating and relevancy-based facilitation of afferent information is also impaired post-concussion (Adams et al., 2019, 2020). In 2005, Kumar and colleagues investigated sensory gating function following concussions using subjective methods (Kumar et al., 2005). Results from the Structured Interview for Assessing Perceptual Anomalies

(SIAPA) (Bunney et al., 1999), a 15-item structured interview assessing perceptual anomalies in each of the five senses, indicate that the majority of their sample were experiencing perceptual anomalies, which was interpreted as deficits in sensory gating; however, this study did not objectively test any physiological markers of sensory gating and did not explore the effects of task-relevancy. In the auditory domain, there is some indication that individuals with varying severities of chronic traumatic brain injury (TBI) demonstrate impairments in the ability to upregulate novel information, as well as downregulate repetitive information. Despite these findings, the number of TBI participants was relatively small, varied widely in severity, and did not focus on individuals with mild TBIs that would be associated with concussion, particularly when broken down by injury severity. Nevertheless, these preliminary findings suggest that auditory gating may be impaired following a concussion, and thus it's important to determine the replicability of this effect, its existence in other sensory domains, and the driving mechanism(s) underpinning these deficits (Arciniegas et al., 2000).

The objective of this investigation was to identify the effects of concussive brain injuries on relevancy-based facilitation during movement-related gating in the somatosensory system at early cortical processing stages, while addressing the limitations of previous work on this topic. Briefly, this was achieved by delivering median nerve stimulation to elicit SEPs, while the relevancy of sensory information was altered at rest and during movement. SEP amplitudes under the experimental conditions were compared between a healthy control group and a group with a history of concussion.

Based on previous work (Brown et al., 2015; Staines et al., 2000), it was hypothesized that the control group would demonstrate smaller SEP amplitudes during movement than at rest, with SEPs quantified during task-irrelevant movement also being significantly smaller than those quantified during task-relevant movement. This would be reflective of typical movement-related gating and appropriate relevancy-based modulation. Within the concussion history group, it was hypothesized that sustaining previous head injuries would disrupt the appropriate relevancy-based gating modulations at early stages of cortical processing. This would be reflected by an impaired ability to facilitate relevant information and would be evident in early latency SEP amplitudes (N20-P27). It was also predicted that the post-concussion disruptions in movement-related gating would result in behavioural consequences. More specifically, it was hypothesized that the concussion history group would demonstrate poorer performance on a task that required the integration of sensory feedback to make an accurate response.

2.0 Methods

2.1 Participants

Participants in this study comprised two groups: a group with a history of previous concussion(s) and a control group. A total of 28 participants were recruited from the University of Waterloo, with half in each group. Inclusion criteria for the concussion history group consisted of sustaining at least one medically diagnosed concussion throughout life. Furthermore, subjects must have been clinically cleared to return to both physical and cognitive activities and been symptom-free at the time of testing. Apart from their concussion(s), participants must not have sustained any other central or upper limb peripheral nervous system injuries. Subjects in the control group must not have sustained or suspected to have sustained a previous concussion and must similarly have been free from any additional decrements to the nervous system. All subjects were required to be between the ages of 17 and 40, right hand dominant, and fluent in English. All experimental procedures received ethics clearance from the

Office of Research ethics at the University of Waterloo and comprised the Master's thesis of the lead author (Tennant, 2018).

Subjects completed a modified version of the University of Waterloo Health History Questionnaire, which has previously been used to gather participant characteristics following concussion (Tapper et al., 2016). This questionnaire collects information regarding previous head injuries, such as total number of concussions, time since last concussion, as well as current symptoms and their severity.

2.2 Experimental Design

To measure the degree of movement-related gating and relevancy-based facilitation, a protocol based on Brown et al. (2015) was employed. SEPs were generated by stimulating participants' left median nerve via a bar electrode placed on the wrist. A square wave pulse (0.5 ms) was delivered (Grass SD9 Stimulator, West Warrick, RI, USA) at an intensity of motor threshold (the intensity required to evoke a just visible twitch in the abductor pollicis brevis). The interstimulus interval (ISI) was randomly generated between 500 and 1000 ms to ensure that stimulation onset was not predictable. For conditions involving wrist movement, a custom device that allows for near frictionless movement within a 60° range was used. The medial aspects of bilateral forearms were supported on a desk with elbows flexed to 90° and shoulders in forward flexion ~0-10°. Flexion and extension of the wrist occurred in the horizontal plane. Participants grasped two separate handles of a custom-made device that was placed on a table. The handles of the device pivoted in clockwise and counter-clockwise directions and were linked to two separate potentiometers (sampled at 100 Hz) within the device structure.

Experimental conditions were designed to allow for comparison of the effects of task-relevancy at rest, and during movement. Given that task-relevancy manipulations alter SEP amplitudes during movement conditions, including similar attentional manipulations at rest during SEP collection provided a contrast to inform whether task-relevancy was particularly related to the movement-related gating system itself, and potentially driven by convergent systems. Establishing neurophysiological patterns seen in response to attentional manipulations at rest and during movement in controls then allowed for investigation into the impact of concussion on these systems. Therefore, there were two components to manipulate: attention and movement. All subjects underwent four different experimental conditions designed to alter the relevance of sensory information: 1) Attend Rest: participants maintained a neutral wrist position while mentally counting the number of nerve stimuli received to increase focus on afference quantified with the SEP without concurrent movement-related gating occurring, 2) Distract Rest: participants maintained a neutral wrist position while mentally counting backwards by seven from a given starting number to distract attention away from the afferent information, 3) Distract Move: participants' stimulated (left) wrist was passively moved through a series of flexion and extension movements (within 60°), while they mentally counted backwards by seven from a given starting number; designed to induce movement-related gating without directing attention to associated somatosensory feedback and 4) Attend Move: participants' stimulated (left) wrist was passively moved through a series of flexion and extension movements (within 60°) for seven seconds, participants then used their non-stimulated wrist to re-create the passive movements delivered to the stimulated wrist; designed to drive attentional focus onto afferent information during movement and therefore assess the impact of task-relevancy and attention during movement-related gating. This comprised one block, which was repeated seven times with a different pattern of movement presented in each block. Median nerve stimulation occurred during the passive movements only. The order of the four conditions was counter-balanced, and in all cases, participants' eyes remained closed.

A custom LabView (National Instruments, Austin, Texas, USA) program was used to generate the waveforms that guided the experimenter during the delivery of passive wrist movements. In each condition, over 100 nerve stimuli were delivered, although the exact number differed for each condition and participant due to the random ISI. In pilot data, and in previous work (Brown et al., 2015; Brown and Staines, 2016), we determined 100 to be a suitable number of stimuli to generate reproducible SEP waveforms, while maintaining a short enough period of time to expect participants to attend to the task.

2.3 Data Acquisition

EEG was collected throughout the experiment using a 32-channel cap (Quik-Cap, Compumedics Neuroscan, NC, USA), with the main electrode of interest being CP4 (according to the International 10-20 system), which rested on the scalp directly above the somatosensory cortex contralateral to the nerve stimulation and produced the largest amplitude early SEP components. SEPs recorded at FCz were used to examine the P20-N30 component in order to determine if concussion impacts on movement-related gating and task-relevancy patterns were similar when measured over frontal and parietal electrode sites. Electrodes were referenced to linked mastoids, with all channel impedances less than 5 kΩ. A linked mastoid reference was chosen rather than a frontal reference as it is more suitable for quantifying longer latency components of the SEP and components such as the N30 that are thought to have frontal generators. The data was digitized at 1000 Hz and low-pass filtered at 200 Hz.

In addition to the electrophysiological data, behavioural data was also collected during the matching component of the Attend Move condition. Participants' accuracy was acquired via a custom LabView program, which recorded voltages from potentiometers embedded in each handle of the wrist movement device at a rate of 100 Hz.

2.4 Data Analysis

EEG data was analyzed using Neuroscan software (Compumedics, Charlotte, NC). Continuous data files were epoched from -100 to 500 ms of each nerve stimulus, band-pass filtered (1-200 Hz) and baseline corrected to the 100 ms pre-stimulus activity. All epochs were manually inspected for noise and artifacts. Epochs were then averaged within each condition for each participant, before extracting values in microvolts (μV) for all potentials of interest. Based on previous research (Brown et al., 2015; Cheron and Borenstein, 1987, 1991; Cohen and Starr, 1987; Jones et al., 1989; Starr and Cohen, 1985; Yamaguchi and Knight, 1990) and pilot data, peak amplitudes were extracted for the following potentials: Central-parietal – N20 (17-23 ms), P27 (24-31 ms), P50 (40-60 ms), N70 (60-80 ms), and P100 (80-120 ms); Frontocentral – N30 (28-36 ms).

Since the amplitude of a given cortical potential can be influenced by the preceding potential, peak-to-peak amplitudes were used for analysis (i.e. CP4 – N20-P27, P50-N70, and N70-P100; FCz – P20-N30). Peak-to-peak amplitudes were determined by calculating the absolute value of the difference in amplitude between the two adjacent potentials. SEP waveforms from the two groups are shown in Figure 1, with each potential of interest identified.

**** Figure 1 near here ****

Participant behavioural data for the task-relevant condition was analyzed using a custom LabView program. The root mean square error (RMSE) was calculated by comparing the target movement pattern provided by the experimenter to the participants' response, for each block. Movement patterns for a single block of the task-relevant condition from a single participant can be seen in Figure 2.

**** Figure 2 near here ****

For the SEP data, a 2x4 mixed factorial Analysis of Variance (ANOVA) with group (control, concussion history) as the between-subjects factor, condition (Attend Rest, Distract Rest, Attend Move, Distract Move) as the within-subjects factor, and SEP amplitude (in µV) as the dependent variable was conducted for each peak-to-peak potential of interest (CP4: N20-P27, P50-N70, N70-P100; FCz: P20-N30). At potentials where significant interactions between group and condition were revealed, one-way repeated measures ANOVAs with condition as the factor and SEP amplitude as the dependent variable were conducted within each group. Pre-planned contrasts were conducted to test the specific hypotheses on the difference between the Attend Rest and the Distract Move Condition and between the Distract Move and Attend Move conditions for the N20-P27 component, specifically. *Post-hoc* Tukey analyses were used to elucidate any additional significant differences identified from the ANOVAs. Prior to computation of the ANOVAs, residual errors were plotted and inspected to ensure that the data met the assumptions of normality and homogeneity of variances that are inherent to this type of analysis.

Similar 2x4 mixed factorial ANOVAs were conducted with group (control, concussion history) as the between-subjects factor, condition as the within-subjects factor, and SEP latency (in ms) as the dependent variable for each potential of interest.

The behavioural data was analyzed using an independent samples *t*-test to determine the effect of group on overall RMSE values. A *post-hoc* analysis compared the difference in RMSE between block one and block seven across the groups.

3.0 Results

3.1 Participant Characteristics

Participant demographics are summarized in Table 1. The control group consisted of 14 participants (9 female) with a mean age of 22.29 years (*SD* = 2.61). On the current symptom intensity checklist of the health history questionnaire, control participants received an average score of 1.21 (*SD* = 1.19) out of a possible 132. The concussion history group also consisted of 14 participants (11 female) with a mean age of 23.36 years (*SD* = 3.61). On the current symptom intensity checklist of the health history questionnaire, previously concussed participants received an average score of 1.50 (*SD* = 1.61). Concussion history participants also reported a mean of 1.64 medically diagnosed concussions (*SD* = 0.63) and a mean recovery time of 32.86 months (*SD* = 29.28) since their most recent concussion. A total of eight participants indicated losing consciousness at least once as a result of a head injury. Independent samples t-tests revealed no significant differences in age (t_{26} = 0.90, p = 0.377) or symptom score (t_{26} = 0.54, p = 0.597) between the groups.

**** Table 1 near here ****

3.2 SEP Amplitude Analyses

Table 2 displays mean SEP amplitudes and standard deviations, separated by potential, group, and condition.

3.2.1 N20-P27. For the N20-P27, a main effect of condition emerged ($F_{3, 71} = 14.77$, $p < 0.001$, $\eta^2_{partial} = 0.38$) in addition to a significant interaction between group and condition ($F_{3, 71} = 3.19$, $p = 0.029$, $\eta^2_{partial} = 0.12$). Mean amplitudes for each group and condition at the N20-P27 can be seen in Figure 3.

Within the control group, a one-way repeated measures ANOVA with condition as the within-subjects factor revealed a significant main effect of condition ($F_{3, 35} = 13.61$, $p < 0.001$, $\eta^2_{partial} = 0.54$). *A priori* contrasts revealed larger amplitudes in the rest conditions relative to the Distract Move condition ($F_{1, 35} = 40.71$, $p < 0.001$) and larger amplitudes in the Attend Move condition compared to the Distract Move condition ($F_{1, 35} = 10.82$, $p = 0.002$). A *post-hoc* Tukey analysis revealed no other significant differences.

Within the concussion history group, a one-way repeated measures ANOVA with condition as the within-subjects factor revealed a significant main effect of condition ($F_{3, 36} = 7.35$, $p < 0.001$, $\eta^2_{partial} = 0.37$). *A priori* contrasts revealed larger amplitudes in the rest conditions relative to the Distract Move condition ($F_{1, 36} = 7.24$, $p = 0.011$), but no significant difference between the Attend Move and Distract Move conditions ($F_{1, 36} = 1.93$, $p = 0.174$). A *post-hoc* Tukey test also revealed significantly smaller amplitudes in the Attend Move condition relative to both rest conditions (ps < 0.050).

*** *Figure 3 near here* ***

3.2.2 P50-N70. In this analysis, both main effects and the interaction between group and condition failed to reach significance (all *p*s ≥ 0.283). Figure 4 displays the mean SEP amplitudes at this potential.

**** Figure 4 near here ****

3.2.3 N70-P100. This analysis revealed a significant main effect of condition ($F_{3, 74}$ = 4.27, p = 0.008, $\eta^2_{partial}$ = 0.15) and a significant interaction between group and condition ($F_{3, 74}$ = 3.37, p = 0.023, $\eta^2_{partial}$ = 0.12). Figure 5 displays mean SEP amplitudes for each condition and group at this potential.

Within the control group, a one-way repeated measures ANOVA with condition as the within-subjects factor revealed no significant main effect of condition ($F_{3, 38}$ = 1.58, p = 0.210, $\eta^2_{partial}$ = 0.11).

Within the concussion history group, a one-way repeated measures ANOVA with condition as the within-subjects factor revealed a significant main effect of condition ($F_{3, 36}$ = 6.44, p = 0.001, $\eta^2_{partial}$ = 0.35). A Tukey *post-hoc* analysis revealed that amplitudes in the Distract Move condition were significantly less than all other conditions, $p < 0.050$. No other significant differences emerged.

**** Table 2 near here ****

**** Figure 5 near here ****

3.2.4 P20-N30. This analysis revealed a significant main effect of condition ($F_{3, 72} = 3.82$, $p = 0.014$). A Tukey's *post hoc* analysis showed significant differences between both movement conditions (Attend Move, Distract Move) and the Attend Rest condition, $p < 0.050$, where N30 amplitudes were lower in the movement tasks. Generally, the concussed group had larger P20-N30 amplitudes than the control group ($F_{1, 26} = 4.22$, $p = 0.050$, $\eta^2_{partial} = 0.19$).

3.3 SEP Latency Analysis

Separate 2x4 mixed factorial ANOVAs were conducted for the latency each potential (N20, P27, P50, N70, P100) with group (control, concussion history) as the between-subjects factor and condition (Attend Rest, Distract Rest, Attend Move, Distract Move) as the within-subjects factor. No significant main effects or interactions emerged from these analyses (all ps ≥ 0.199).

3.4 Behavioural Analyses

Mean behavioural scores, separated by group and block can be seen in Figure 6 and Table 3. An independent samples *t*-test revealed no significant difference in overall behavioural performance (RMSE) between the control and concussion history groups ($t_{26} = 0.21$, $p = 0.835$, d=0.08). A *post-hoc* analysis on the difference scores between block one and block seven demonstrated a significantly greater improvement in performance within the concussion history group relative to controls ($t_{26} = 2.29$, $p = 0.031$, d=0.86).

4.0 Discussion

The results of this experiment revealed that concussions have the potential to disrupt relevancy-based modulation of somatosensory information during movement-related gating. Of greater concern is that previously concussed participants were clinically recovered and asymptomatic with an average of over 29 months since their most recent injury, suggesting chronic effects.

Consistent with our hypotheses, the control group demonstrated efficient movement-related gating at the N20-P27. *A priori* contrasts revealed that SEP amplitudes in the Distract Move condition were significantly less than those at rest, as well as those in the Attend Move condition. These results suggest that the non-injured controls effectively gated non-relevant sensory information, while selectively facilitating relevant sensory information. This pattern of modulation has been shown previously (Brown et al., 2015; Staines et al., 2000) and our results serve to replicate these findings. The N20 and P27 are potentials generated by the arrival of somatosensory information to Brodmann areas (BAs) 3b and 1 within SI (Allison et al., 1989, 1991; Wood et al., 1985; Yamaguchi and Knight, 1990). However, since the N20 and P27 were the earliest cortical potentials measured, it remains uncertain exactly where the modulation of somatosensory information occurred. Past research suggests that the prefrontal cortex may be involved in this process via interaction with inhibitory interneurons connected to both the thalamus (Cao et al., 2008; Pandya and Barnes, 1987; Skinner and Yingling, 1976, 1977) and the somatosensory cortex (Jones et al., 1978; Pandya and Barnes, 1987; Vogt and Pandya, 1978; Yamaguchi and Knight, 1990; Knight et al., 1999).

The concussion history group also demonstrated results consistent with our hypotheses at the N20-P27. Here, an *a priori* contrast revealed significantly decreased amplitudes in the Distract Move condition relative to rest, indicating efficient gating of non-relevant sensory afferents. However, no significant difference between the Distract Move and Attend Move conditions indicates a potential impairment in the selective facilitation of relevant sensory information at the earliest level of modality-specific somatosensory processing. The prefrontal cortex has been the subject of an abundance of concussion research, which has consistently demonstrated both cognitive and neurophysiological disruptions as a result of head injuries (Belanger et al., 2010; Belanger and Vanderploeg, 2005; Broglio et al., 2011; Churchill et al., 2016; Dimou and Lagopoulos, 2014; Shin et al., 2017). Given the role of the prefrontal cortex in the upregulation of relevant sensory information during movement-related gating (Brown et al., 2015; Staines et al., 2002), this finding supports the notion that concussions may be particularly detrimental to prefrontal function.

Alterations in relevancy-based modulation of electrophysiological responses have recently been reported in individuals with a history of concussion, even after they are considered recovered from their injury (Adams et al., 2020). Using a sensory guided motor task in which participants had to perform a graded motor response dependent on the amplitude of an attended target stimulus in the presence of a distractor, Adams et al. (2020) showed that the early event-related potentials (ERPs) were modulated by task relevance in the control group but not in those with a history of concussion. Furthermore, there was a greater cost to task accuracy in the motor response when the target stimulus was presented in the presence of a distractor in those with a history of concussion. This pattern of a loss of relevancy-based modulation in early ERPs and behavioural cost is similar to what is observed in the same task following continuous theta burst stimulation applied to the DLPFC (Adams et al., 2019).

Despite impairments in the gating process at the N20-P27, the concussion history group did demonstrate regulation of sensory information at the N70-P100. *Post-hoc* analyses revealed significantly reduced SEP amplitudes in the Distract Move case compared to both rest and Attend Move. Thus, previously concussed participants demonstrated the same modulation pattern at the N70-P100 as control participants demonstrated earlier at the N20-P27. The notion of delayed sensory gating has been discussed previously within the literature. Gaetz and Weinberg (2000) demonstrated a prolonged visual P1 latency in response to a reversing checkerboard paradigm for previously concussed participants relative to controls. In their review, Broglio et al. (2011) interpreted this finding to suggest the possibility of a delay in sensory gating and preferential attention processes, although the authors did not elaborate on this interpretation. As previously mentioned, the N20-P27 SEP component is thought to reflect early somatosensory processing occurring in SI, whereas the later potentials are associated with secondary somatosensory processing. In accordance with the proposed delay in sensory gating following concussion, it's possible that movement-related gating and relevancy-based facilitation are also delayed and no longer seen in primary processing but occur later in the processing pipeline in individuals with concussion.

The exact mechanism(s) driving the observed results remains uncertain. Previous research has shown that attention is specifically affected by concussions (Belanger et al., 2005, 2010; Frencham et al., 2005; Rohling et al., 2011; Zakzanis et al., 1999), presenting the possibility of delays in the ability to decipher relevant versus non-relevant sensory information. Given that the output of the prefrontal cortex is generally modulatory (Miller and Cohen, 2001), the default response may be to vastly inhibit large amounts of incoming information until the specific relevancy can be determined. This may explain why SEP amplitudes for the concussion history group in both the Distract Move and Attend Move conditions were similarly inhibited at the N20-P27, and the specific disinhibition of relevant information was not apparent until the N70-P100.

Another possibility is that the concussive effects may reflect a down-regulation of cortical activity in the prefrontal cortex. A previous study by Brown et al. (2015) measured peak-to-peak N20-P27 amplitudes in neurologically intact participants before and after cTBS was applied to the DLPFC. A similar modulation pattern was present in their pre-stimulation group as control participants in the current investigation. Critically, their post-stimulation effects showed a strikingly similar pattern of disruption to movement-related gating and the associated effects of task-relevancy as the concussion history group in the current study. Given that cTBS results in a transient down-regulation of cortical activity in the targeted area, it is plausible that concussions may result in similar effects, albeit for a much longer period of time.

While this discussion provides potential cortical areas and mechanisms that might drive concussion-related differences in relevancy-based facilitation during movement related gating, it is important to remember that concussion is a diffuse injury that likely affects a number of cortical areas and networks that may contribute to these results. Similarly, the prefrontal cTBS employed by Brown and colleagues (2015) that provided the inspiration for the current work could have had network-level implications rather than being localized to the prefrontal cortex. Therefore, while the primary somatosensory cortex and prefrontal cortex are likely contributors to these deficits, future work should consider broad network-level changes and the potential implications for these changes on gating and attention in all sensory domains.

Although not the primary intent of this study, we expanded analysis from the parietal cortex to examine the P20-N30, measured from a frontal-central electrode site (FCz). With this analysis we found that there was movement-related gating of the P20-N30, but there was not a facilitation of the component amplitude in the Attend Move condition in either group. Additionally, the amplitudes of the P20-N30 were larger in the concussed group than in controls.

In order to interpret these findings, it is important to understand that there is disagreement in the literature about the generator of the P20-N30. A variety of experimental approaches provide evidence supporting the hypothesis that the N30 represents afferent information arriving at motor planning areas, such as the supplementary motor area or premotor cortex (Rossini et al., 1999; Mauguière and Desmedt, 1991; Cebolla et al., 2014; Kaňovský et al., 2003). However, there is also evidence from intracerebral recordings and dipole modelling that suggests the N30 is generated in the somatosensory cortex and thus provides overlapping information with the parietal SEP components (ie. N20-P27 – Valeriani et al., 1998, 2000; Barba et al., 2003, 2005).

The current results show different patterns in the parietal N20-P27 and the frontal P20-N30, with relevancy-based facilitation occurring in controls at the parietal electrode site, but not the frontal site, which may support different generators for these components. Further, analysis of the P20-N30 component also revealed that these amplitudes were greater in the concussion group, as compared to the controls, and this was not the case in the N20-P27 component. Together these would indicate that gating patterns in the premotor/supplementary motor areas are not disrupted by concussion; however, there may be disruption of tonic inhibition exerted onto these areas by the prefrontal cortex, as has been seen in other neurological injury (Yamaguchi and Knight, 1990). At this point that theory is speculative but warrants further investigation. In addition, we cannot discount the possibility that the P20-N30 is generated in the somatosensory cortex and any analysis of results should take this into consideration.

Results from the behavioural task suggest the possibility of compensatory mechanisms to preserve performance. The task required participants to integrate somatosensory feedback generated by experimenter induced passive wrist movements, in order to mirror those movements with the opposite limb. Overall RMSE values were not statistically different between groups, indicating that control and previously concussed participants completed the task with a similar degree of accuracy. However, a follow-up analysis revealed that the difference between the first and last block was larger for previously concussed participants than controls. As seen in Figure 6, the concussion history group had worse performance on the first block but maintained similar performance to controls on the remaining blocks. The delayed upregulation of relevant sensory information following concussion may be responsible for the initial discrepancy in performance at block one. However, the appropriate upregulation of relevant sensory information later in the processing stream may be capable of preserving overall performance.

Our results also suggest that attention does not have a significant effect on SEP amplitudes at rest, consistent with previous reports (Desmedt and Tomberg, 1989). We found no significant differences between the Attend Rest and Distract Rest conditions at any of the potentials measured. Thus, it appears that task-relevancy effects are specifically linked to the movement-related gated system.

Changes in SEP amplitude as a result of movement of the stimulating electrode cannot be entirely ruled out. However, the experimental setup used in the current investigation was modeled after the one employed by Brown et al. (2015), who monitored M-wave activity following stimulation using EMG and found that the movements induced during the experiment did not significantly change the muscular response to the stimulation. Since the diameter of efferent nerve fibres are approximately the same size as the large-diameter fibres transmitting the afferent signal, this method can provide useful information with regard to changes in stimulation intensity. Furthermore, in the current study, participants' APB twitches were visually monitored throughout the collection to ensure stimulation at motor threshold was maintained.

The behavioural task employed in this study aimed to identify the potential post-concussive consequences of altered sensory gating. Although the efficient gathering of appropriate sensory information is a necessary process to accurately complete the task, other neural processes are likely to contribute to performance. Specifically, working memory, which has consistently shown post-concussive deficits, would be critically involved and may have contributed to the behavioural results obtained.

4.3 Conclusions

This study sought to understand the effects of sustaining a concussion on the ability to filter incoming sensory information. Consistent with our hypotheses, previously concussed participants showed an impaired ability to disinhibit relevant sensory information at the earliest modality specific cortical processing stages. Further results, however, indicate that this ability is not lost following concussion, but rather occurs later in the processing stream relative to healthy non-injured controls. Overall, previously concussed participants performed equivalent to controls on a matching task requiring the integration of specific sensory feedback to guide performance. However, a follow-up analysis revealed a greater improvement from the first to last block within the concussion history group relative to controls. Although we were unable to directly link the neurophysiological and behavioural data, it remains possible that the early performance deficits in the concussion history group may be a result of the belabored sensory gating function, however the system is capable of adapting quickly to preserve overall performance. The mechanism contributing to these effects following a head injury is currently unknown, however an abundance of research has shown that the prefrontal cortex may be particularly vulnerable to concussive forces. The prefrontal cortex is also heavily involved in the selective inhibition of incoming sensory information, lending further support for this hypothesis. Further research should aim to better understand the mechanism producing this effect, as well as the clinical implications of these results.

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Figure Captions:

Figure 1. Grand average waveforms during Rest (Distract / Attend together), Distract Move and Attend Move conditions for (A) the concussion history group and (B) the control group, showing all potentials of interest, recorded from electrode CP4.

Figure 2. Waveforms representing the target and response movement patterns, as well as the difference between the two, for a single block of the Attend Move condition from an individual participant. Positive values indicate wrist flexion, while negative values indicate extension. RMSE values for the behavioural analysis were calculated using the difference waveform.

Figure 3. Mean N20-P27 SEP amplitudes (μV) for each condition separated by group (Control – solid bars; Concussion History – hatched bars) recorded from electrode CP4. Error bars represent ± 1 *SEM*. * denotes $p < 0.05$.

Figure 4. Mean P50-N70 SEP amplitudes (μV) for each condition separated by group (Control – solid bars; Concussion History – hatched bars) recorded from electrode CP4. Error bars represent ± 1 *SEM*.

Figure 5. Mean N70-P100 SEP amplitudes (μV) for each condition separated by group (Control – solid bars; Concussion History – hatched bars) recorded from electrode CP4. Error bars represent ± 1 *SEM*. * denotes $p < 0.05$.

Figure 6. Mean RMSE values for each block, separated by group (Control – black line; Concussion History – grey line) Error bars represent ± 1 *SEM*.

Table 1
Participant Characteristics.

Demographic	Control Mean	Control *SD*	Concussion history Mean	Concussion history *SD*
Age (years)	22.29	2.61	23.36	3.61
Symptom score	1.21	1.19	1.50	1.61
Medically diagnosed concussions	-	-	1.64	0.63
Recovery time (months)	-	-	32.86	29.28

Note. *SD* = standard deviation.

Table 2
Mean SEP Amplitudes (μV) and Standard Deviations for Each Potential, Each Group, and Each Condition.

	N20-P27				P50-N70				N70-P100			
	Control		Concussion history		Control		Concussion history		Control		Concussion history	
Condition	Mean	*SD*	Mean	*SD*	Mean	*SD*	Mean	*SD*	Mean	*SD*	Mean	*SD*
Attend Rest	3.95	2.55	4.42	2.26	3.94	2.60	4.77	3.19	6.52	1.85	7.27	3.45
Distract Rest	3.97	2.26	4.77	2.55	4.41	2.09	5.20	2.21	5.39	2.65	6.72	2.76
Distract Move	2.46	1.88	3.65	2.22	4.69	2.46	5.44	2.81	5.58	2.74	4.65	2.83
Attend Move	3.46	2.10	3.10	2.09	4.40	3.87	5.71	2.27	5.13	3.67	7.06	2.69

Note. *SD* = standard deviation.

Table 3
Mean Behavioural Scores (RMSE) for Each Group and Each Block.

Block	Control Mean	Control *SD*	Concussion history Mean	Concussion history *SD*
1	18.27	5.60	22.29	5.49
2	18.58	3.22	18.39	8.27
3	22.57	7.89	22.57	6.81
4	22.08	6.42	20.55	12.74
5	21.39	7.60	20.63	9.44
6	22.76	7.64	20.78	7.47
7	17.97	5.09	16.00	5.16
Overall	20.52	3.22	20.17	5.22

Note. RMSE = root mean square error, *SD* = standard deviation.

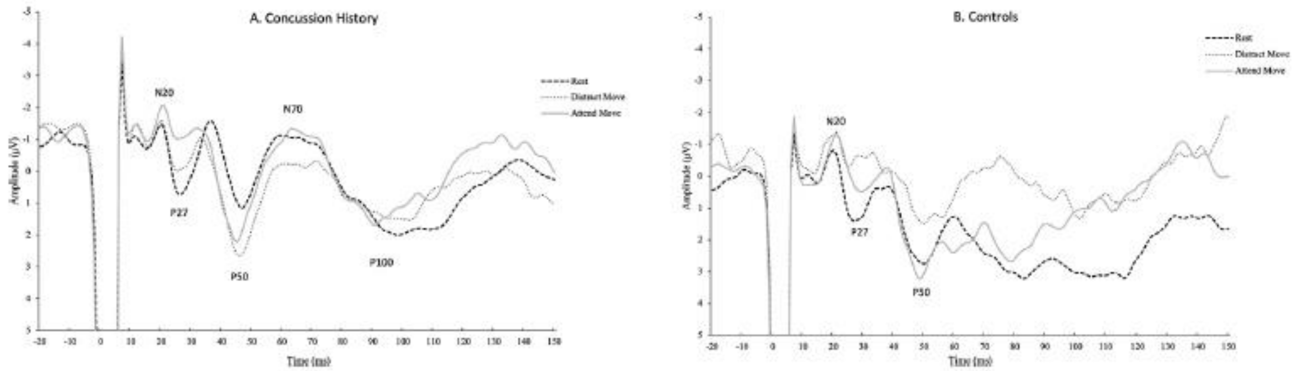

Figure 1. Grand average waveforms during Rest (Distract / Attend together), Distract Move and Attend Move conditions for (A) the concussion history group and (B) the control group, showing all potentials of interest, recorded from electrode CP4.

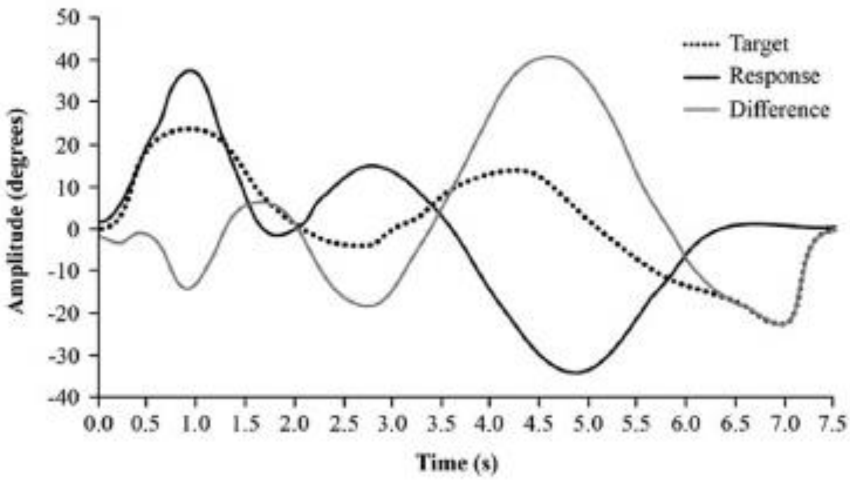

Figure 2. Waveforms representing the target and response movement patterns, as well as the difference between the two, for a single block of the Attend Move condition from an individual participant. Positive values indicate wrist flexion, while negative values indicate extension. RMSE values for the behavioural analysis were calculated using the difference waveform.

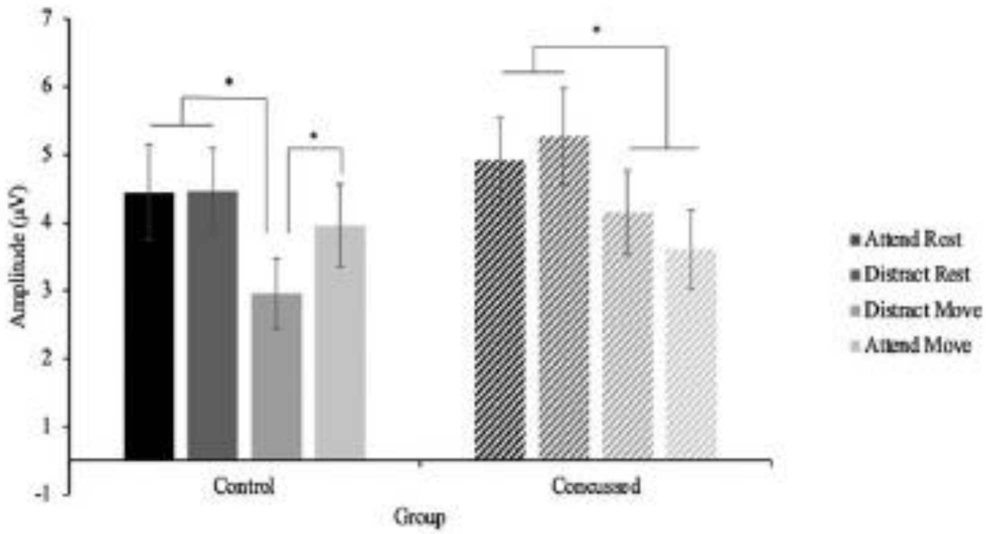

Figure 3. Mean N20-P27 SEP amplitudes (µV) for each condition separated by group (Control – solid bars; Concussion History – hatched bars) recorded from electrode CP4. Error bars represent ± 1 *SEM*. * denotes $p < 0.05$.

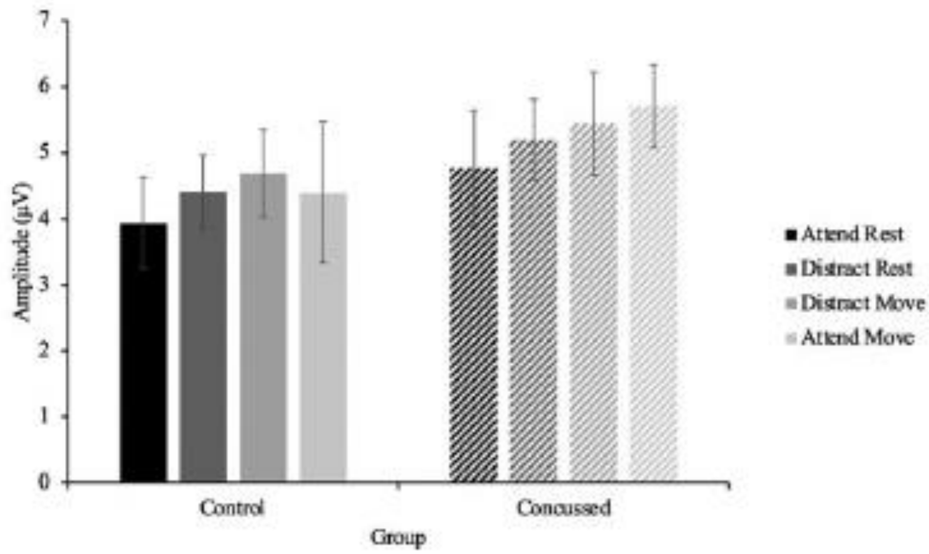

Figure 4. Mean P50-N70 SEP amplitudes (µV) for each condition separated by group (Control – solid bars; Concussion History – hatched bars) recorded from electrode CP4. Error bars represent ± 1 *SEM*.

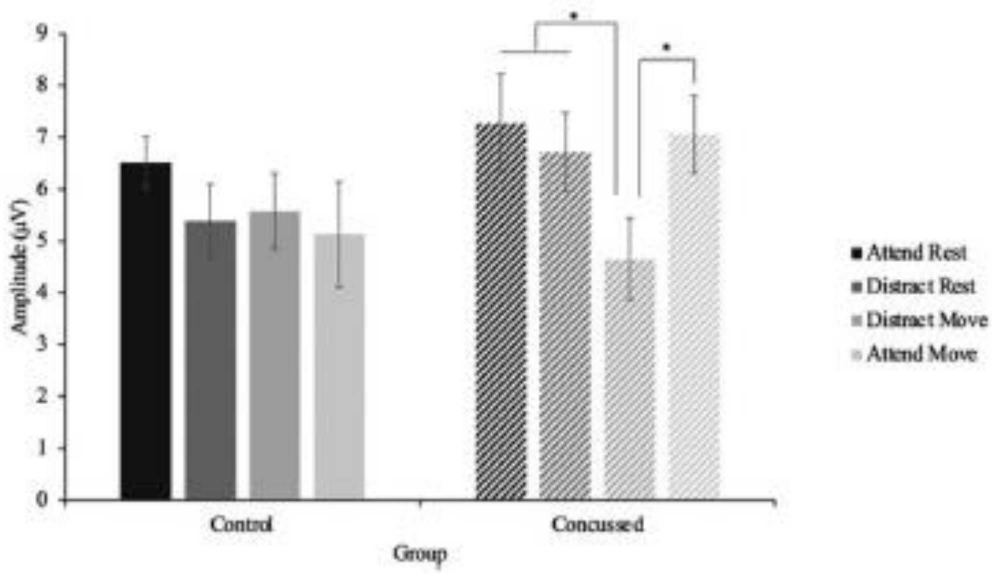

Figure 5. Mean N70-P100 SEP amplitudes (µV) for each condition separated by group (Control – solid bars; Concussion History – hatched bars) recorded from electrode CP4. Error bars represent ± 1 *SEM*. * denotes $p < 0.05$.

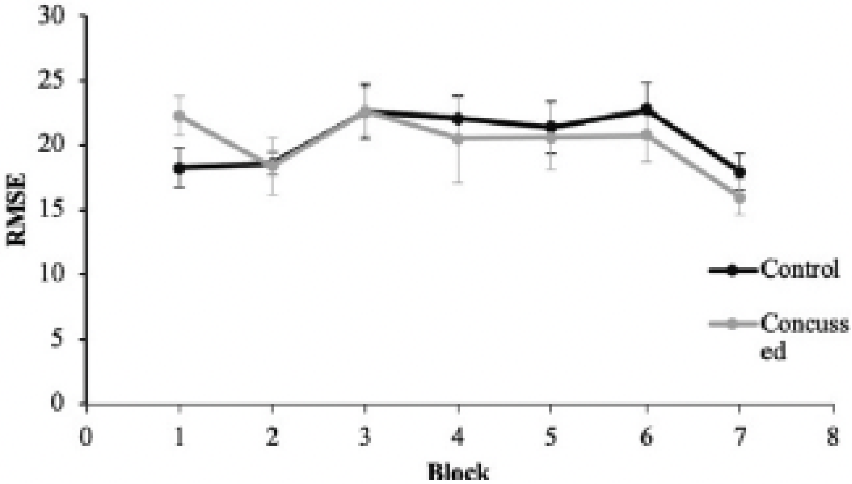

Figure 6. Mean RMSE values for each block, separated by group (Control – black line; Concussion History – grey line) Error bars represent ± 1 *SEM*.