



**COGNITIVE ISSUES AND ABNORMAL BALANCE FOLLOWING CONCUSSION:
A CLINICAL PILOT STUDY USING EEG**

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ABSTRACT

Introduction: Concussion is a common injury across all ages and with varied causes, including car crashes, falls, combat and sports. Balance impairments are common and well-documented after concussion but less is known about what causes these impairments at the neural and kinematic level. The main aim of this study was to investigate the existence and magnitude of the N100 ERP in concussed versus healthy participants during perturbed walking, a Push and Release Task, and a reaction time test (Hockey Puck Task).

Methods: Ten participants, 5 healthy (23.8 ± 4.7 years) and 5 concussed (24.6 ± 5.2 years), were recruited, outfitted with mobile EEG and triaxial inertial sensors, and carried out a battery of tasks, including the Hockey Puck Task, Push and Release Task, 30-Second Sway, 2-Minute Walk, and expected and unexpected perturbations during walking.

Results: Within the Push and Release Task there was evidence of an N100 related to moment of release of the participant, and it appeared to be greater in concussed individuals, but this difference was not significant. Within the Hockey Puck Task, there was no evidence of an N100, but there was a reliable positive trending potential following the drop of the puck by the experimenter, which was maximal between 260 and 300 ms. This positive trending potential is consistent with a P300 ERP.

Discussion: We cannot make any definitive statements on the neurophysiology of concussion based on these data, but the results are useful to us as researchers and for future studies. The results suggest that we may be able to elicit ERPs with these tasks, but we will likely need many more trials and participants in order to reliably establish (1) the presence of the ERPs and (2) if the ERPs differ based on concussion.

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INTRODUCTION

Mild traumatic brain injury (mTBI), also known as concussion, has reached epidemic levels, with 1.6-3.8 million occurring in the US every year and an estimated 50-80% going underreported (Buckley et al., 2016). Data suggest that motor-vehicle collisions and falls are the main causes of concussion, but many also occur in sports and in combat (Cassidy et al., 2004). Balance problems are one of the most common symptoms following concussion and are well documented, but there is much less known about how concussion affects the postural response to external perturbations that underlie these balance problems (Klefflegard et al., 2012). This gap in our knowledge is an important problem, as humans constantly have to contend with external perturbations, whether it be fast-paced sport/combat settings or more mundane constraints in everyday life.

Poor balance control following concussion can also create a negative feedback loop that leads to further injury. For instance, a premature return to sports may contribute to the high rate of musculoskeletal injuries in recently concussed athletes (Fino, 2016). These concussion symptoms, including balance problems, may subside within 3 weeks, but can persist for anywhere from 3 months to multiple years (Klefflegard et al., 2012). Deficits from concussion may last longer than reported by the patient and after return to unrestricted activities, which suggests that current clinical assessment tools may not be sensitive enough to functionally track recovery (Howell, Osternig, Donkelaar, et al., 2013). These concussed individuals may show deficits when performing multiple tasks (dual-task activities) at once, which includes responding to an external perturbation (Fino, 2016).

Concussion symptoms are often categorized as vestibular, ocular-motor, or cognitive and are well documented, but little is known about the connection between cognitive issues and balance deficits (Collins et al., 2014). The central nervous system is normally able to quickly shift attention to the task of balance recovery when required, but this ability is deficient in concussed individuals, which seems to degrade later phases of postural response to external perturbations (Maki & McIlroy, 2007). Those with concussion have been shown to struggle with maintaining and properly allocating attentional resources while performing one or more simultaneous tasks for at least two months post-concussion (Howell, Osternig, Donkelaar, et al., 2013). The interactions between sensory, cognitive, and motor processes in the control of balance are complex, so next I will briefly review the contributions of these different processes in successful balance control.

Overview of Sensory, Cognitive and Motor Processes in Balance Control:

Sensation and Perception. To achieve motor control, we regulate movements using sensory information about our environment, the state of our body, and the position of our body within our environment (Schmidt et al., 2018). Sensation and perception are how this information is taken in and interpreted. Sensation is a physical stimulus that is registered by specialized sensory organs in the body and transformed into neural signals that are sent to the brain (Schmidt et al., 2018). Perception is how the brain interprets a sensation; organizing and translating information into something we can rationalize (Schmidt et al., 2018). Some important examples of sensory information include proprioception, vision, hearing and touch.

Proprioception is the component of sensation and perception that provides information about the movement and orientation of body segments (Sarlegna & Sainburg, 2009). In order to control the body, the brain must be aware of the body's position in space and its surroundings so it can identify and respond to stimuli. There are specialized sensory neurons, known as proprioceptors, in the inner ear, skin, joints, muscles, tendons, and ligaments, which send neural signals to the brain (Schmidt et al., 2018). Vision is another major source of sensory information that aids in motor control. It provides extrinsic, spatial information about the environment and proprioception provides intrinsic information about muscle state, limb configuration and movement that aids in transforming a spatial plan into specific motor commands (Sarlegna & Sainburg, 2009).

Cognitive Processes. Executive cognitive control is needed in order to maintain stability during walking and respond to perturbations in the environment. Executive control includes switching between tasks, updating and monitoring working memory, and inhibiting prepotent responses (Miyake et al., 2000). The cognitive demand of certain motor tasks can be measured using dual-task methodology, "where performance changes in either or both of the concurrent tasks indicate the extent of their cognitive demand" (Al-Yahya et al., 2011). Attentional resources are needed to carry out both tasks and it is not possible to do both at the same time without deficits (Hiraga et al., 2009). These deficits are greater when impairments exist in the brain, such as in those with a concussion (Howell, Osternig, and Chou, 2013).

Motor Control. Motor control is "how the nervous system interacts with other body parts and the environment to produce purposeful, coordinated movement" (Latash, 2012). It "involves the processing of sensory information (e.g., somatosensory, visual,

vestibular, and auditory) and coordination of motor output within the central nervous system” (Chmielewski et al., 2020). Motor control includes motor planning, which begins by taking in sensory cues and processing them to select an appropriate motor plan, and motor learning, which is the experience-dependent gain of a motor skill and how a motor skill adapts when task conditions change (Chmielewski et al., 2020). The brain communicates with muscles through electrical signals sent along motor neurons and sensory neurons. Neural and muscle cells are excitable cells that produce an electrical signal, a brief change in membrane potential, called an action potential, when a certain threshold membrane potential is reached (Latash, 2012). Once this happens the signal can propagate down the length of the neuron and muscle cell to carry out a certain action (Latash, 2012).

Event Related Potential (ERPs) in Balance Control:

The disruption in motor processes by concussion can be investigated using mobile electroencephalography (EEG), which measures and records the electrical activity of the brain conducted from the cerebral cortex (Conley et al., 2019). Historically, EEG has only been possible to be used in stationary tasks, but recent innovations have led to EEG with a wireless connection, so data can be collected during walking. Specifically, event related potentials (ERPs), which are voltage changes that arise when a specific operation is preformed, can be used to see how the brain is working at the neural level (Luck, 2014).

Studies have shown that unpredictable postural perturbations, which elicit a rapid balance-recovery reaction, trigger a cortical response that includes the N100 ERP (Maki & McIlroy, 2007). The N100 component appears as a negative deflection in the ERP

waveform between 125 and 200 milliseconds after the onset of a stimulus, which could be visual, auditory, or others (Krigolson et al., 2015). The N100 is generally elicited by an unpredicted stimulus in the absence of any other tasks demands (e.g., a person at rest might show an N100 following a loud noise or a disturbance to their balance) (Yppärilä et al., 2004; Maki & McIlroy, 2007). The N100 is sensitive to several different characteristics of a stimulus. Specifically, the N100 is larger for less frequent/less expected stimuli, larger for brighter/louder stimuli, and larger for sudden stimuli (Wunderlich & Cone-Wesson, 2001; Keidel & Spreng, 1965; Butler, 1968; Connolly, 1993).

Although largely thought to reflect subconscious processes, the N100 may reflect neural activity associated with advanced stages of visual processing, which “facilitates efficient motor control such as the detection of unexpected environmental change, the magnitude of the change, and/or the location of the change” (Krigolson et al., 2015). In this study we are looking at balance responses to unexpected environmental change, so we are expecting to observe the N100. Another hypothesis is that the N100 represents “engagement or orienting of attention to a task-relevant location,” so it could increase when an unexpected perturbation is presented and recognized (Luck et al., 1990). We are also interested in how the N100 is associated with reaction time because the N100 component could be associated with the updating of target location within visuomotor areas of cortex” (Krigolson et al., 2015).

In the current study, we recruited N=5 healthy control participants and N=5 concussed participants (4 males; 6 females; median age = 24y) and recorded EEG and inertial data during various tasks. Specifically, we were interested in the N100 ERP in

concussed versus healthy individuals during perturbation response, balance recovery and a reaction time task. The tests/tools we used were a special shoe that delivered expected and unexpected perturbations during walking, a Push and Release Task and a Hockey Puck Task. We generally expected the N100 to be smaller for people with concussion because their sensory processing is disrupted by the injury.

METHODS

Participants:

Ten participants were recruited for the study; five healthy control participants, 4 Female, 1 Male, age = 23.8 (4.7) years (as mean (SD)), and five recently concussed participants, 2 Female, 3 Male, age = 24.6 (5.2) years, following approval of the University Institutional Review Board. The inclusion criterion for concussed participants was a clinical diagnosis of a concussion by a physician. Inclusion criteria were the ability to walk unassisted and be willing and able to provide informed consent. This sample allows for a comparison between non-concussed and concussed participants.

After providing written, informed consent, participants filled out the Post-Concussion Symptom Scale (PCSS) and the Ohio State University Traumatic Brain Injury Identification (OSU TBI ID) Modified Form. The PCSS is a 22-item self-reported measure of symptom severity following a concussion and the OSU TBI ID Modified Form identifies the most recent, most severe, and frequency of TBI experience.

Tasks and Measures:

Participants were outfitted with mobile electroencephalography system (EEG; BrainVision LiveAmp ®) and triaxial inertial sensors (APDM OPALs ®) and completed a series of tests for reaction time, mobility, balance, and walking with a perturbation. The

full battery of assessments is described below, but for my thesis I will be focusing on EEG and behavioral data from a balance assessment (i.e., Push and Release Task) and a reaction time task (i.e., Hockey Puck Task) specifically.

Reaction Time Testing:

The Hockey Puck Task: The Hockey Puck Task is a simple reaction time test that is administered with a hockey puck mounted on a stick. The experimenter held the stick while the participant sat with their forearm resting on a table with fingers loosely circling the hockey puck. The puck/stick was then unexpectedly dropped by the experimenter and then caught by the participant. The distance the stick traveled was recorded and provides insight into the participant's reaction time. An inertial sensor was attached to the puck to determine the times of the drop and catch. Each participant performed 8 trials of the Hockey Puck Task.

Instrumented Mobility Testing:

30-Second Sway: The 30-Second Sway assesses postural sway in participants during a 30 second time period. Postural sway occurs during static stance as a result of unstable body properties and can increase with balance dysfunction (Saunders et al., 2015). Triaxial inertial sensors, as used in this study, can approximate linear center of mass acceleration along mediolateral and anteroposterior axes and have been effective in properly assessing postural sway (Saunders et al., 2015). The test was conducted with feet together on a firm surface with eyes open & eyes closed for 30 seconds each trial, for a total of 2 trials.

2-Minute Walk: The 2-Minute Walk was recorded with straight gait and 180° turns under single-task condition. This task was performed twice, once at the beginning

of the testing session and once at the end. The 2-minute walk task is used to assess and quantify spatiotemporal parameters of gaits in order to describe the movement of the body and its variability through space (Swanson et al., 2019). Various gait metrics can be derived from this task, including stride length, gait speed, cadence and more (Swanson et al., 2019).

Balance Testing:

Push and Release: The Push and Release Task assesses postural instability and balance impairments in 4 directions (forward, backward, right and left) and in eyes open and eyes closed conditions, for a total of 8 trials. During the Push and Release Task, the participant leans into the hands of the experimenter. The experimenter supports the weight of the participant with their hands and causes them to lean outside of their base of support. Then, the experimenter unexpectedly releases the participant, who takes a recovery step.

Walking Perturbation Testing:

Shoe Perturbations: The shoe perturbations assess balance recovery during gait. A special shoe was used to administer perturbations to one foot, unexpectedly or expectedly via the sound of a warning beep. There were 4 introductory walking trials with two perturbations, followed by a block of 40 trials with randomized perturbations, followed by 4 final walking trials with 4 perturbations.

EEG Processing and Collection:

Scalp electroencephalography (EEG) was synchronized with the inertial sensors and collected during all tasks from 32-channels of an EEG cap housing a 32-channel BrainVision actiCAP system (Brain Products GmbH). The electrodes were labelled in

accordance with the standard 10-10 geodesic montage (Oostenveld & Praamstra, 2001). The specific electrode sites included, Fp1, Fz, F3, F7, FT9, FC5, FC1, C3, T7, TP9, CP5, CP1, Pz, P3, P7, O1, Oz, O2, P4, P8, TP10, CP6, CP2, Cz, C4, T8, FT10, FC6, FC2, F4, F8, and Fp2, which are also standard (Oostenveld & Praamstra, 2001). The data were online referenced to FCz with a common ground placed at FPz. The electrode impedances were maintained below $25\text{k}\Omega$, with a sampling frequency of 250Hz.

EEG data processing was conducted with the BrainVision Analyzer 2.1.2 software (BrainProducts GmbH). No online filters were applied, but offline the data were band-pass filtered between 0.1 and 40 Hz with 24-dB rolloffs and with a 60 Hz notch filter. The data were manually inspected, and eyeblinks marked for ICA-based ocular correction within BrainVision Analyzer software (BrainProducts 2013). This function was run with the FP2 electrode serving as the VEOG and the HEOG electrode.

Following ocular artifact correction, the data were segmented based on relevant timestamps collected from the triaxial inertial sensors. For the Push and Release Task, we calculated ERPs for the moment of release (i.e., when the experimenter's hands were removed from the participants shoulders) and the heel strike of the recovery step (i.e., the first identifiable ground contact as the participant takes a recovery step). For the Hockey Puck Task, we calculated ERPs for the moment of the drop (i.e., when the sensor records the puck in free fall) and the moment of the catch (i.e., when the puck's downward momentum is halted). For all ERPs, we took a 1 s window from -100 ms before the event to 900 ms after the event. ERPs were then baseline corrected to the average voltage between -100 to 0 ms, to remove any offset in individual trials. Within an event (Release, Step, Drop, and Catch) individual trials were then averaged together to get an average

event related potential for each event type. It is important to note motion artifacts and equipment issues were a major barrier to ERPs in the present study. For each task, we averaged 72% useable trials for the Release, Step, Drop, and Catch events.

Statistical Analyses:

For statistical analysis of the ERPs, we first calculated a grand average ERP across all people and conditions. In this grand average ERP, we found the maximum negativity prior to 250 ms and calculated the average voltage in a 40 ms window centered on that point (Luck, 2014). This time window was then used to define the ERP for each participant in each condition. Average voltages in these time windows were analyzed using a one-sample t-test (for the grand-average ERP) or using different ANOVAs (for comparisons between groups). For the Push and Release Task, ERPs were analyzed with 2 x 2 mixed factorial ANOVA with a repeated measure of Condition (eyes-open versus eyes-closed) and a between-participants factor of Group (healthy controls versus cases with concussion). For the Hockey Puck Task, ERPs were analyzed with a one-way ANOVA with a single between-participants factor of Group (healthy controls versus cases with concussion).

RESULTS

Push and Release Task:

Release ERP. As shown in Figure 1, there was evidence of an N100 related to moment of release. On average across participants, this N100 was maximal between 135 and 175 ms. One-sample t-test for the average voltage in this window showed that the grand average N100 was not statistically significant, $t(8)=-1.48$, $p=0.178$, $\text{mean}=-3.46$, $95\% \text{ CI}=[-8.85, 1.94]$. For the mixed-factorial Group x Condition ANOVA, there was not

a main-effect of Group, $F(1,7)=0.46$, $p=0.52$, a main-effect of Condition, $F(1,7)=0.01$, $p=0.91$, nor a Group x Condition interaction, $F(1,7)=2.21$, $p=0.18$.

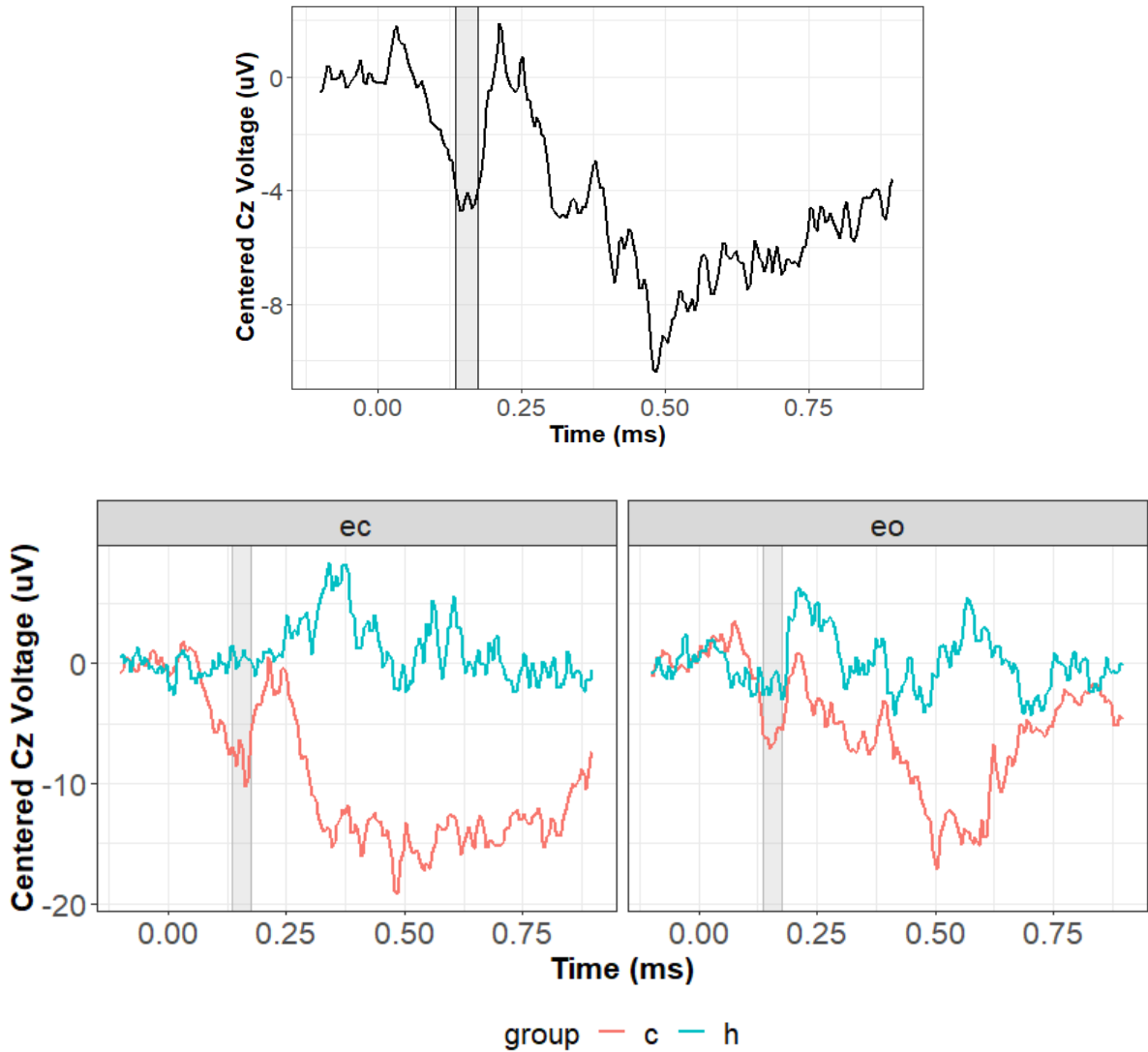


Figure 1. Event-related potentials time locked to the point of release. The grand-average ERP is shown above, and the ERPs for each group are shown below. “h” = healthy and “c” = concussed, “eo”= eyes open; “ec” = eyes closed.

Recovery Step ERP. As shown in Figure 2, there was not evidence for a reliable N100 related to the recovery step. As there was no reliable evidence of an ERP across participants, we did not conduct further analyses of the data related to the recovery step.

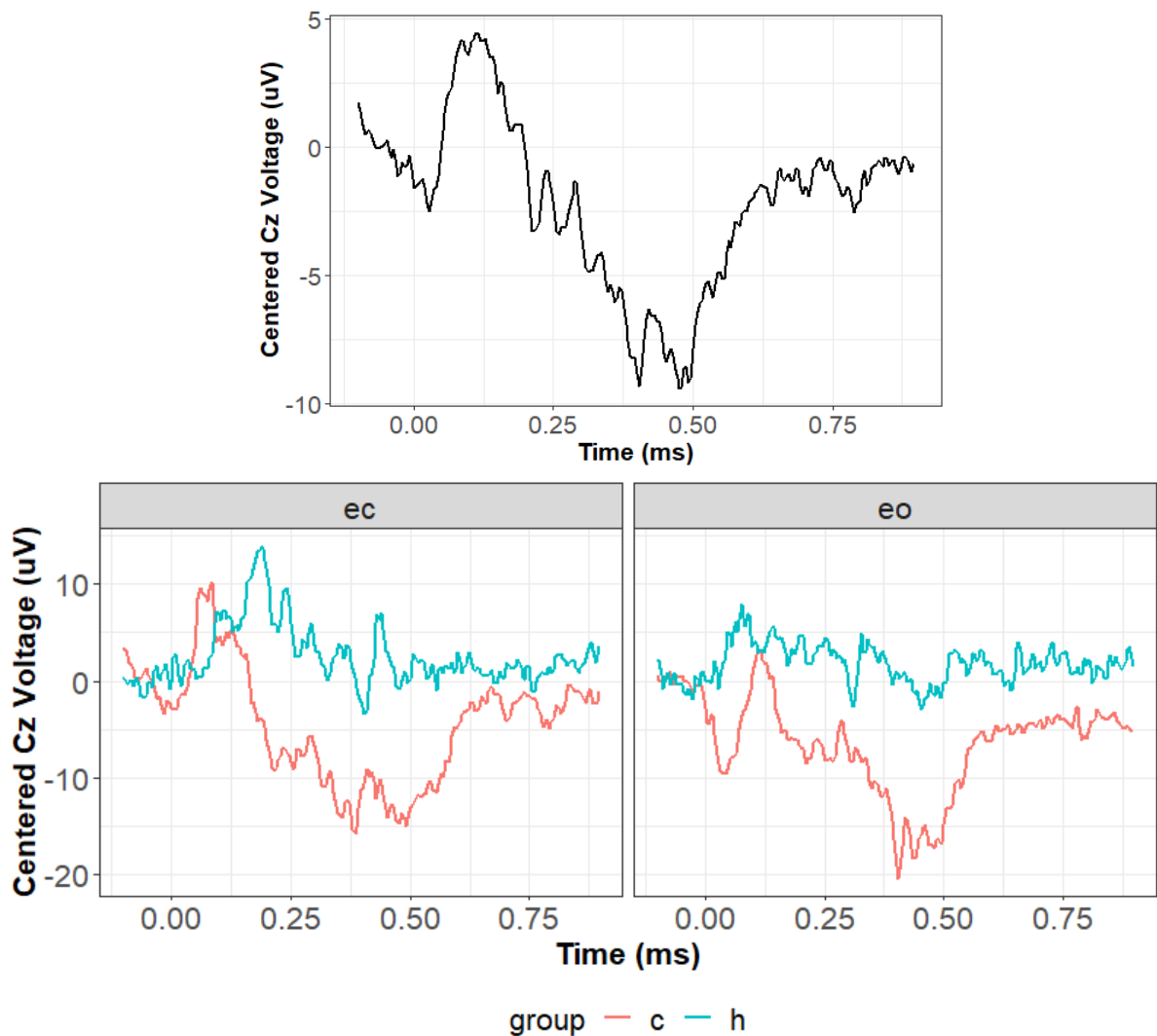


Figure 2. Event-related potentials time locked to the point of the recovery step. The grand-average ERP is shown above, and the ERPs for each group are shown below. “h” = healthy and “c” = concussed, “eo”= eyes open; “ec” = eyes closed.

Hockey Puck Task:

Drop. As shown in Figure 3, there was no evidence of a characteristic N100 in the grand average ERP during the drop of the puck/stick. However, there was a reliable positive trending potential following the drop of the puck/stick by the experimenter. This positivity was maximal between 260 and 300ms, consistent with a P300 (Polich, 2007). The average voltage in this time window was significantly positive, $t(7)=3.79$, $p=0.007$. Although the healthy participants tended to show greater positivity than their concussed counterparts, this difference was not statistically significant, $F(1, 6)=3.57$, $p=0.108$.

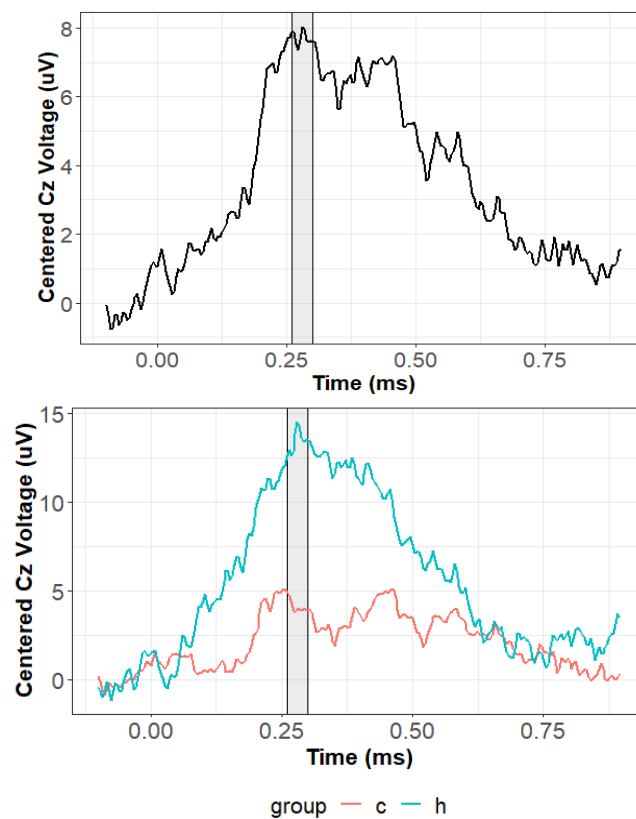


Figure 3. Event-related potentials time locked to the point of the experimenter dropping the puck. The grand-average ERP is shown above, and the ERPs for each group are shown below. “h” = healthy and “c” = concussed.

Catch. As shown in Figure 4, the event related potential for the moment that participants caught the dropped puck/stick was very similar to the ERP observed for moment that the experimenter released the puck/stick; there was a strong positive going component that was maximal between 90 and 130ms following the moment of catch. Given that the average reaction time was 249 ms, this is not necessarily the same component that we observed for the drop ERP (i.e., $300\text{ ms} - 249\text{ ms} = 51\text{ ms}$, which is less than 90 ms), but it is very close in time. As this is potentially the same component merely shifted time, we did not statistically analyze it again.

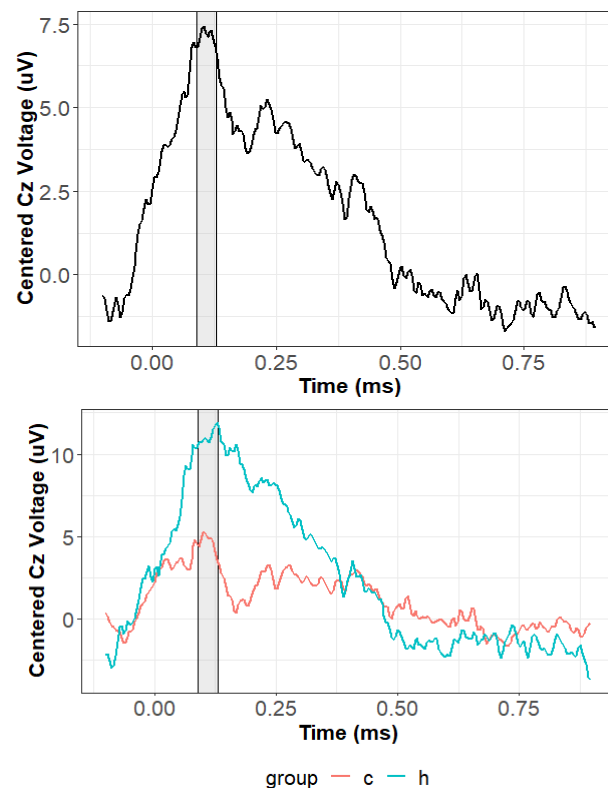


Figure 4. Event-related potentials time locked to the point of catching the dropped puck. The grand-average ERP is shown above, and the ERPs for each group are shown below.

“h” = healthy and “c” = concussed.

Reaction Time. The average reaction time was 249 ms and there was small difference in the mean reaction time in the sample. Healthy control participants had a faster reaction time (241 ms) than mTBI participants (259 ms). Although the difference was in the predicted direction, the difference was not statistically significant, $F(1,7)=0.60$, $p=0.463$. However, there is a large literature on mTBI leading to slow reaction times (Eckner et al., 2014), so a lack of statistical significance in the present study is likely a limitation of the small sample size and a lack of statistical power.

DISCUSSION

The main goal of this study was to investigate the existence and magnitude of the N100 ERP in concussed versus healthy participants during perturbation response, balance recovery and a reaction time test (Hockey Puck Task). Specifically, we examined the data for ERPs during the release of the participant and recovery step during the Push and Release Task and the moment of the puck/stick drop and catch of the puck/stick during the Hockey Puck Task. We were not able to collect reliable data during perturbation response while walking.

Within the Push and Release Task there was evidence of an N100 related to moment of release of the participant. On average across participants, this N100 was maximal between 135 and 175 ms. There was no evidence for a reliable N100 related to the recovery step. The N100 appeared to be greater in concussed individuals but this difference was not significant. This was different from what we hypothesized, because we generally expected the N100 to be smaller for people with concussion since their sensory processing is disrupted by the injury. The release of the Push and Release Task is

a moment of unpredicted postural perturbation that elicits a rapid balance-recovery reaction, and previous studies have shown that this condition can trigger the N100 (Maki & McIlroy, 2007). The N100 may have been present during the release of the participant, but not during the recovery step, because there is evidence that the N100 is not specifically associated with motor events, and studies have shown that comparable N100 responses occur whether or not the perturbation evokes a motor response (Maki & McIlroy, 2007). In this case, a motor response had not been initiated at the moment of release and thus it is reasonable that the N100 might be observed at that moment but not during the recovery step. This could also indicate that the N100 is a reflection of the brain recognizing a postural disturbance because previous findings suggest that the N100 potential is not simply related to sensory processing but may be more closely linked to “event detection” (Maki & McIlroy, 2007).

Within the Hockey Puck Task, there was no evidence of an N100, but there was a reliable positive trending potential following the drop of the puck/stick by the experimenter, which was maximal between 260 and 300 ms. This positive trending potential is consistent with a P300 ERP. The P300 is typically observed during a task when an individual must react to a target sound that is played at random (Mertens & Polich, 1997). In our study, participants had to respond to catch the stick attached to the puck when it was unexpectedly dropped. This unexpected stimulus onset is a similar condition to what typically evokes the P300. It has also been hypothesized that the P300 and its underlying subprocesses could reflect neural inhibition of extraneous activity so that stimulus/task information can be transmitted (Polich, 2007). The P300 following the drop of the puck/stick could be present because the brain is trying to focus only on

catching the stick attached to the puck and thus inhibits unnecessary activity. This ERP had a greater magnitude for healthy participants than concussed participants, although this difference was not significant. This could indicate the concussion decreases the magnitude of the P300 ERP.

We cannot make any definitive statements on the neurophysiology of concussion based on these data, but the results are useful to us as researchers and for future studies. The results suggest that we may be able to elicit ERPs with these tasks, but we will likely need many more trials and participants in order to reliably establish (1) the presence of the ERPs and (2) if the ERPs differ based on concussion.

Limitations:

This study's main limitations were the low number of participants and well as the low number of trials performed. There is a lot of noise/error present in the recording of mobile EEG because the sensors pick up various artifacts, including eye blinks and movement. This is addressed during processing, but it cannot be known for sure if all artifacts have been removed. In future EEG studies, more trials and participants are needed in order to potentially gain statistically significant results. Other EEG studies have had closer to 15-30 participants (Mochizuki et al., 2008; Cao et al., 2008) and can range from 45 to almost 2000 trials, depending on the study (Quant et al., 2004; Kasai et al., 2003). In our study, it would not have been feasible to have more trials because of the original study design. Due to technical difficulties, EEG setup, and many walking trials (in which the data had too many movement artifacts to be used), we only averaged half of a trial per minute. Some trials took longer than others, specifically the walking trials. In

addition, only 72% of trials were usable. With a different study design in the future, more time could be spent carrying out Push and Release and Hockey Puck trials.

Conclusions:

Over the course of this experiment, we learned that it is safe and feasible to collect ERPs in the various tasks we carried out. We did not observe any reliable, statistically significant differences between groups, although the P300 ERP during the drop of the puck in the Hockey Puck Task was greater in magnitude for healthy participants, and the N100 during the release of the Push and Release Task was greater in magnitude for concussed participants. To improve future studies, more trials should be carried out and more participants recruited, as well as a more diverse range of participants in regard to age and race.

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