Clinical Assessment of Tinnitus Following Concussion

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Abstract

People who experience tinnitus after a concussion represent some of the most challenging clinical cases to see. However, little is known about the underlying mechanisms of this symptom. Concussion may facilitate tinnitus generation at the cortical level or may interfere with a person's ability to continue habituating to existing tinnitus related to damage in the auditory periphery. The sample described here included participants with concussions and a new onset of tinnitus, participants with concussion and no history of tinnitus, and control participants. Explanatory variables were measured for each group, and across the conditions of concussion and tinnitus. Subjective and objective central auditory tests were administered and included the Dichotic Digits Test (DDT) and a comparison of visual versus auditory-evoked event-related potentials (ERPs). Reaction time, accuracy, and ERP component amplitudes and latencies were compared.

Results show that participants with tinnitus after a concussion perform similarly to controls on the DDT, whereas the concussion-only group scored significantly worse. There were no differences for reaction time or accuracy of ERP tasks in auditory or visual conditions. However, the concussion-only group presented with significantly larger P200 amplitudes for frequent auditory stimuli and smaller P300 amplitude for rare stimuli during ERP tasks. These findings do not maintain for visual ERP tasks suggesting the cortical activity related to tinnitus perception may have limited ability to identify concussion specific processing during central auditory testing.

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Chapter 1: Introduction

Concussion has become a buzzword in both healthcare and the media in recent years. Sensationalized cases like the murder allegations and later suicide of Aaron Hernandez highlighted the term CTE, or chronic traumatic encephalopathy, which is thought to occur with repeated concussions (Baugh et al., 2012). In most major contact sports, there are reports of isolated cases where repeated concussions were suspected of causing permanent neurodegeneration (CTE) in a player. These rare, but high-profile cases have helped raise awareness of the potential risks to athletes in contact sports and created almost a media frenzy surrounding concussion prevention and treatment. Although high-profile cases emphasize the risk of severe cortical impairment, there are millions of people living with milder chronic concussion symptoms like those manifesting in the auditory system.

Little to no clinical emphasis is placed on auditory symptoms of concussion outside of dizziness and imbalance. However, concussions are shown to alter the inner ear as well as the auditory pathways in the brainstem and the brain. These alterations result in a host of auditory symptoms beyond dizziness. Temporary sound sensitivity and tinnitus are reported, as well as deficits in more complicated perceptual tasks such as listening in noisy backgrounds, localizing sound, and discriminating signals in complex acoustic environments (Alves, Macciocchi, & Barth, 1993; Brusis, 2011; Chorney, Suryadevara, & Nicholas, 2017). Changes in the auditory pathway have strong implications in the development of learning new tasks and problem solving, especially in young adults. Moreover, there is evidence that head injury can cause auditory deficits that persist over a decade after initial injury (Bergemalm & Lyxell 2005). Importantly, however, patients may fail to associate mild changes in hearing threshold, sound sensitivity or tinnitus with their concussion.

Patients experiencing more debilitating symptoms like severe headache and dizziness may not notice or correlate tinnitus or mild hearing loss until the more severe symptoms like headache improve. The ability to associate and report symptoms declines over time from the injury, and reporting is significantly influenced by stress and emotional impact of the injury. This makes it challenging to ascertain when specific auditory symptoms manifest and at what rate (Belanger et al., 2011; Gouvier, Cubic, Jones, Brantley, & Cutlip, 1992). If we can improve early identification of debilitating auditory symptoms like tinnitus after a concussion, patients will not only understand the source of their symptoms but will be able to earlier begin proper management.

Tinnitus as a symptom itself, is not uncommon. Over 40 million people report experiencing some degree of ringing or buzzing in the ears (Bhatt, Lin, & Bhattacharyya, 2016a). Tinnitus is an expected outcome following noise-induced hearing loss and most patients who hear ringing or buzzing in their ears are not bothered by its presence. However, tinnitus following a head injury represents one of the most debilitating forms as the injured brain cannot appropriately attenuate attention and limbic reaction to the presence of tinnitus (Kreuzer et al., 2012; Rauschecker, Leaver, & Mühlau, 2010). Normalizing the connection to concussion is an important step in improving the outlook for some of the most severe manifestations of tinnitus.

Evaluating new onsets of tinnitus as it follows concussion could help establish a pathway for central tinnitus generation in contrast to the commonly accepted model of tinnitus as a central change following peripheral auditory impairment (Lanting, de Kleine, & van Dijk, 2009; M. C. Liberman, 2017).

Concussion Definition and Pathophysiology

To understand the barriers of recognizing tinnitus as a symptom of concussion, the basic definitions of concussion will be examined. Concussions are a form of mild traumatic brain injury (mTBI), defined as Glasgow Coma Scale (GCS) 13 to 15 in most cases (Ratcliff et al., 2014). MTBI represents 75% or more of all TBI cases and is one of the most common neurologic diseases treated in US emergency departments (CDC, 2015). Although loss of consciousness can occur, it is uncommon in mild forms of TBI like concussion. Loss of consciousness is not as predictive in concussion trajectory as the number and duration of clinical symptoms. This is important given the high variability in concussion definitions and symptom checklists (Leininger, Gramling, Farrell, Kreutzer, & Peck, 1990; McCrory et al., 2013a).

The first concussion is usually mild, with full recovery within 7–14 days. However, symptoms can manifest in almost any system of the body and severity within specific symptom groups is highly varied (Eisenberg, Meehan, & Mannix, 2014). Given the variety of possible concussion presentations it is difficult to determine at what point a mild head injury becomes a moderate or severe head injury without the use of standardized symptom ratings.

Concussion is often used interchangeably with mTBI in clinical care and research. The Brain Injury Association of America offers a helpful distinction of *acquired TBI* (e.g. stroke, oxygen deprivation from heart attack or near drowning, tumor) caused by internal factors versus *traumatic TBI* (e.g. whiplash, fall, blunt trauma) which are caused by external forces (biausa.org). Although researchers, providers and insurers often agree that concussion is a form of traumatic mTBI, there is not a clear consensus as to when a concussion is no longer mild TBI and is more severe (O'Neil et al., 2013). There are several severity guidelines for providers to choose from, which helps with internal classification, but limits comparisons of symptom

trajectory or treatments across facilities. The Department of Defense guidelines (2009) include a commonly used classification of severity (Figure 1).

Criteria	Mild	Moderate	Severe
Structural imaging	Normal	Normal or abnormal	Normal or abnormal
Loss of Consciousness (LOC)	0–30 min	> 30 min and < 24 hrs	> 24 hrs
Alteration of consciousness/mental state (AOC)	a moment up to 24 hrs	> 24 hours. Severity based on other criteria	
Post-traumatic amnesia (PTA)	0-1 day	> 1 and < 7 days	> 7 days
Glasgow Coma Scale (best available score in first 24 hours)	13-15	9-12	< 9

From: APPENDIX C, DEFINITION OF MTBI FROM THE VA/DOD CLINICAL PRACTICE GUIDELINE FOR MANAGEMENT OF CONCUSSION/MILD TRAUMATIC BRAIN INJURY (2009)

Figure 1: DOD Concussion Severity Classification

Additionally, insurers and providers disagree on whether the concussion should be considered the traumatic event *itself* or the disease process following the event (Masel & DeWitt, 2010; Sharp & Jenkins, 2015). To help reduce the many interpretations of concussion, the American Academy of Neurology agreed upon a definition of concussion as "a clinical syndrome of biomechanically induced alteration of brain function, typically affecting memory and orientation, which may or may not involve a loss of consciousness" (C. C. Giza et al., 2013). This definition is useful in that it highlights the sequelae of changes that follow the injury event. A concussion is not a state of injury, rather, it is an event that injures the brain and sets off a variety of associated symptoms depending on the patient's health and previous cognitive function (Almasi & Wilson, 2012; McCrory et al., 2013b; Ropper & Gorson, 2007).

For the purposes of this research, the term concussion will be used, and will refer to the initial head injury with resulting symptom sequalae.

Concussions can also be described in terms of primary and secondary injury which further elaborates the concept of initial injury and sequalae. There is considerable data demonstrating the primary concussive injury involving inertial loading experienced by the brain during an impact (Dashnaw, Petraglia, & Bailes, 2012; Takhounts, Crandall, & Darvish, 2003). Inertial forces may involve impact with an outside force, and/or impact between the brain and the skull interior which directly affect tissue and axons to varying degrees based on origin and orientation (Bigler, 2013; Cloots, van Dommelen, Kleiven, & Geers, 2013).

During typical concussions, both linear and rotational acceleration forces contribute to the unique manifestation of symptoms. Brain mechanics vary by person, but generally, the brain is more sensitive to rotational acceleration given the bulk of brain tissue attached to the spinal cord, within the skull, is roughly five times larger than the shear modulus (Ganpule, Daphalapurkar, Cetingul, & Ramesh, 2018; Zhao, Choate, & Ji, 2018). Figure 2 depicts two different injury trajectories both from a frontal head impact, demonstrating how most skull fractures occur in response to linear acceleration and diffuse injury like those seen in concussion occur in response to rotational acceleration (Kleiven, 2013). The brain's location as soft tissue surrounded by fluid and bone means many concussions involve impact with multiple points inside the skull which are termed "coup" and "contrecoup" for the initial and subsequent impact respectively (Bayly, Clayton, & Genin, 2012). When an acceleration force shifts the brain inside the skull, axons are stretched and sheared initiating a metabolic cascade that includes abnormal signaling between cells and even axonal death (C. C. Giza & Hovda, 2001; Christopher C. Giza & Hovda, 2014).

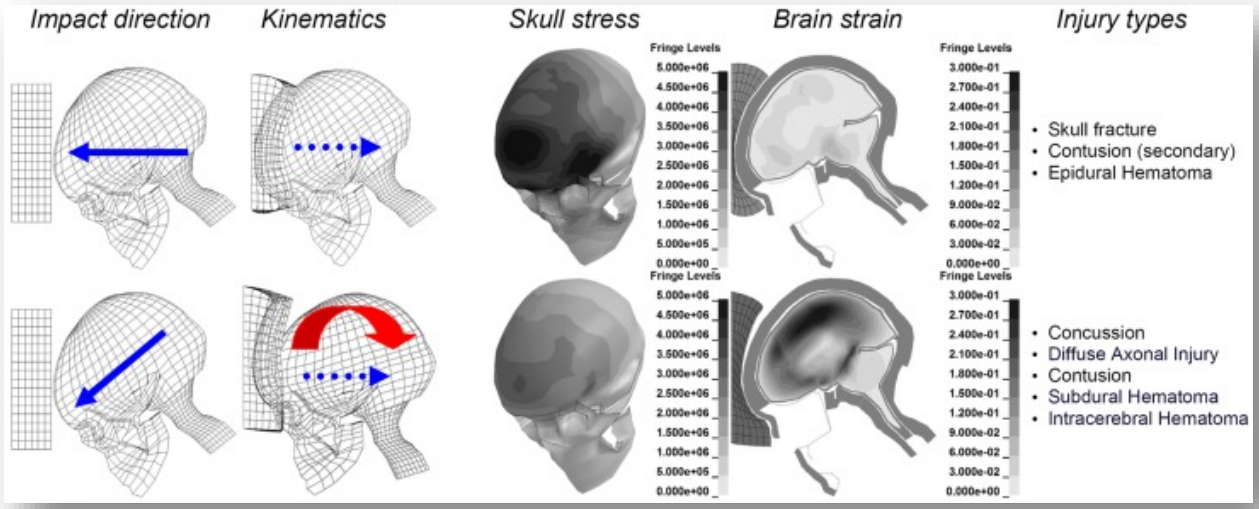

Figure 2: Illustration of the biomechanics of an oblique impact (lower), compared to a corresponding perpendicular one (upper), when impacted against the same padding using an identical initial velocity of 6.7m/s. (From Kleiven, 2013 with permission)

For the auditory system, this means nearly any type or location of concussive injury could result in auditory neuronal and axonal damage given the intricate network of auditory connections connecting ipsilateral and contralateral cortical tissue to the periphery. The basic anatomy of the auditory system alone makes it susceptible to linear and rotational acceleration forces.

Axons contralaterally and ipsilaterally connect the auditory periphery to the cortex through relay centers in the brainstem and midbrain along the way. Despite its proximity to the brain, the auditory system contains disproportionately long axonal tracts like the lateral lemniscus circuit in the brainstem (Henkel, 2018). Focal lesions to the lateral lemniscus are shown to manifest both as auditory processing deficits, particularly with dichotic processing, and tinnitus (Cho et al., 2005). The susceptibility of axons to mechanical force, together with the complex interconnectivity of the auditory system and length of auditory axons, make the

auditory system a likely site of dysfunction following a head impact. Axons in the auditory midbrain degenerate following a TBI, even when the force is mild (Jane et al, 1985).

Similarly, central auditory deficits are documented in the acute concussion phase, which requires contralateral projections at the lateral lemniscus and corpus callosum with projections to the thalamus and primary auditory cortex in the left temporal lobe (Broglio, Pontifex, O'Connor, & Hillman, 2009; Cubon, Putukian, Boyer, & Dettwiler, 2011; K. R. Vander Werff & B. Rieger, 2019; Kathy R. Vander Werff & Brian Rieger, 2019) . Specifically, the frequency-following response (FFR) shows delayed and reduced amplitudes when processing of speech sound details for weeks following a sports-related concussion in adolescents and months to years in collegiate athletes (Nina Kraus et al., 2017; Nina Kraus et al., 2016). Importantly, these skills can be remediated if identified following concussion so it is important to determine what symptoms or specific diagnostic tests may indicate the auditory system has been impacted (Lindsey, 2014; Tremblay, Kraus, McGee, Ponton, & Otis, 2001).

Symptoms of Concussion

The sequalae of central and peripheral damage following concussion is highly influenced by patient health and comorbidity, which has prevented the development of an expected trajectory or even expected symptomology. Further compounding these issues, are the countless studies with disparate methodologies and definitions of symptom and recovery (Broglio & Puetz, 2008). Primary axonal damage and/or metabolic and physiological changes in other systems may manifest as deficits in general cognitive function, affective function, somatic symptoms like imbalance and visual disturbance, and fatigue due to changes in sleep (Ferry & DeCastro, 2021; Laskowski, Creed, & Raghupathi, 2015)

The most common symptoms of concussion include headache and dizziness, but almost any disturbance of function can occur, given the diffuse neural injuries involved (McCrory et al., 2013a). In most people, concussions resolve in two weeks or less and symptoms beyond that period are described as post-concussive syndrome or persistent post-concussive symptoms (Ryan & Warden, 2003). The term post-concussive syndrome as a clinical term is debated given the symptoms are shared by all TBIs and are not exclusive to concussion (Riggio & Wong, 2009). Additionally, this classification puts the emphasis on the concussion as the initial injury not including the metabolic cascade which is not in alignment with the current consensus definition described previously (C. C. Giza et al., 2013). A more common description is to consider concussion recovery as typical (under two weeks) or protracted where symptoms may take months to resolve (Kostyun & Hafeez, 2015; McClincy, Lovell, Pardini, Collins, & Spore, 2006).

Symptoms may also be split into the general categories of somatic (physical changes) or neuropsychiatric (Howell, O'Brien, Beasley, Mannix, & Meehan, 2016). Somatic symptoms include dizziness, headache, and fatigue for example, and generally resolve in less than two months. Neuropsychiatric symptoms may manifest as personality change (irritability, impulsivity, aggression), depression, or anxiety among others and should resolve in under three months (Riggio & Wong, 2009). Less common is the loss of consciousness (LOC) related to a transient disruption of the reticular activating system. LOC is reported in less than ten percent of concussions and is attributed to rotational acceleration and the junction of the midbrain and thalamus (Mullally, 2017; Ropper & Gorson, 2007).

Auditory System Injuries of Concussion

With its location in the temporal lobe leaving the auditory system susceptible to contusions following concussion (Fausti, Wilmington, Gallun, Myers, & Henry, 2009), deficits like dizziness, sound sensitivity, tinnitus, or reduced hearing in noise ability are all expected following even a mild concussion.

Secondary damage is implicated in peripheral symptoms like tinnitus, which explains why this symptom may be delayed in patient reporting(Ceranic, Prasher, Raglan, & Luxon, 1998). Vestibular symptoms garner a great deal of attention in healthcare and research since they occur immediately following concussion and at a high rate; second only to headache (M. S. Choi et al., 2013; Chorney et al., 2017; Ingebrigtsen, Waterloo, Marup-Jensen, Attner, & Romner, 1998; Kraeutler, Currie, Schrock, McCarty, & Comstock, 2017; MacGregor, Dougherty, Tang, & Galarneau, 2013). There is evidence that anywhere from 15% to 65% of patients experience tinnitus with or without sound sensitivity following a concussion. Tinnitus may be immediate or develop weeks to months post-injury, indicating the auditory system has been affected to some degree by the injury (Bhatt, Lin, & Bhattacharyya, 2016b; Ceranic et al., 1998).

Although the incidence of tinnitus following concussion is widely speculative, tinnitus is commonly associated with military blast injuries where noise and head trauma are combined. As many as 38% of active duty TBI cases report tinnitus as a symptom. Tinnitus represents the largest compensation category paid by the Veteran's Affairs (VA) system with over a billion dollars in compensation annually (Lew, Jerger, Guillory, & Henry, 2007; Yankaskas, 2013). Much of the current tinnitus research involving concussion includes military populations; complicating the ability to ascertain whether auditory symptoms resulted from the concussion, noise exposure, or likely the combination of both. If concussions represent a separate process of

central auditory injury from noise trauma, targeted preventative, diagnostic, and treatment processes could be developed which would greatly impact service delivery in the VA system in particular.

Although commonly associated, noise exposure is not a required precursor for the development of tinnitus. In animal models, behavioral manifestation of tinnitus can be reliably induced using noise or high doses of salicylate (Eggermont & Roberts, 2015). Both injuries share common neural correlates as outlined in Figure 3, with hyperactivity shown in the inferior colliculus and dorsal cochlear nucleus across human and animal models (Eggermont & Roberts, 2015; Guernsey, Leder, & Yao, 2016).

Comparison of changes after chronic salicylate and noise exposure

Structure	SFR salicylate	SFR NIHL	2-DG salicylate	2-DG NIHL	Glutamate salicylate	Glutamate NIHL	Gly/GABA salicylate	Gly/GABA NIHL
ANF	≈[d] ⇑[e]	⇓[x]						
VCN		⇑[v]						
DCN	⇓ (FF)[a] ≈ (CW)[a]	⇓[r] ⇑[s]	⇓[n]	⇑[t]	⇑[p]	⇑[z]		⇓[a1]
ICC	⇓[j] ⇑[k]	⇑[a3]	⇓(2-DG)[m] ⇑(FDG)[j]			⇑[y]	⇑[p]	⇓ → ⇑[a1]
ICX	⇑[l]		⇑[j]			⇑[y]		
AI	≈[b] ⇓[c,f,h]	⇑[w]	⇑[j,m]					⇓[a2]
AII	⇑[g]		⇑[j,m]					
Startle	+[h]	+[u]						
Hyperacusis	+	+[u]						

[a]Superfusion in slice (Wei et al. 2010); [b]cat (Ochi and Eggermont 1996); [c]Yang et al. (2007); [d](≤200 mg/kg, acute; Stypulkowski 1990); [e](≥400 mg/kg, chronic; Evans et al. 1981); [f]cat (Zhang et al. 2011); [g]Eggermont and Kenmochi (1998); [h]Yang et al. (2007), Sun et al. (2009); [i]Paul et al. (2009), [j] Ma et al. (2006); [k]Bauer et al. (2008); [l]Manabe et al. (1997), Chen and Jastreboff (1995); [m]Wallhausser-Franke et al. (2003); [n]Wallhäusser-Franke (1997); [p]Peng et al. (2003); [q]Bauer et al. (2000); [r]fusiform cells (in vivo; Ma and Young 2006); [s]fusiform cells FF (slice; Finlayson and Kaltenbach 2009), cartwheel cells CW (slice; Chang et al. 2002); [t]Middleton et al. (2011) using flavoprotein imaging; [u]Chen et al. (2013); [v] Vogler et al. (2011); [w]Noreña and Eggermont (2003; 2006); [x]Liberman and Kiang (1978); [y]Suneja et al. (2000); [z]Potashner et al. (1997), Whiting et al. (2009); [a1]Suneja et al. (1998a, b), Wang et al. (2009); [a2]Llano et al. (2012), Yang et al. (2011). [a3]Mulders and Robertson (2009, 2013)

Figure 3: Comparison of Changes After Chronic Salicylate and Noise Exposure (From Eggermont & Roberts 2015 with permission)

Interestingly, the effects of high-dose salicylate are variable in the cortex and can include increased or decreased neural activity in the primary auditory cortex despite reduced activity in the auditory periphery (Sun et al., 2009; Zhang, Yang, Cao, Qin, & Sato, 2011).

Secondary processes of concussion affecting neurotransmitter function at the peripheral level of the inner hair cells (IHCs) in the cochlea might lead to both increased and decreased cortical activity depending on their respective excitatory or inhibitory control (Ralli et al., 2014; Sahley, Hammonds, & Musiek, 2013). Cochlear IHCs synapse with afferent type I auditory neurons which receive efferent input from the lateral olivocochlear system. They utilize several neurotransmitters for transmission of information including N-methyl-D-aspartate (NMDA), L-glutamate, and gamma-aminobutyric acid (GABA) among others (Oestreicher, Wolfgang, & Felix, 2002).

There are several models describing how neurotransmitter disruption can lead to tinnitus, but enhancement of IHC glutamate release with upregulation of (NMDA) receptors aligns well with both salicylate and noise induced models of tinnitus (Bing et al., 2015; Guernsey et al., 2016). Aberrant NMDA receptor activation and subsequent auditory nerve excitation in the absence of sound are suggested as one origin of tinnitus when the source is peripheral, as in the case of noise exposure or salicylate damage to IHCs.

Concussive secondary processes are also shown to disrupt NMDA receptor activation, giving us a clear process for tinnitus development in the cortex. Upregulation of excitatory NMDA receptors in the basolateral amygdala (BLA) is demonstrated after concussion and importantly, this manifests behaviorally as an increased fear response (Alvarez-Dieppa, Griffin, Cavalier, & McIntyre, 2016; Reger et al., 2012). Often referred to as NMDA-mediated toxicity, much of this data stems from rat models where lateral fluid percussion injuries (LFPI) are used.

Reger et al., 2012 specifically paired a Pavlovian fear conditioning process (foot shock) with an auditory cue. Following LFPI, rats would exhibit fear behavior in response to the auditory cue in absence of the physical pain. This process mirrors the fear response shown in humans with tinnitus, where the hippocampus and amygdala are activated in response to internal phantom sounds regardless of peripheral auditory health (Chen et al., 2017; Qu et al., 2019).

Audiological Assessment of Tinnitus from Concussion

Given the established relationship between concussion and generation of tinnitus, audiologists play an important role in the rehabilitation process. Although there are many options for objective and subjective assessment of tinnitus in audiology, there are no current tests in isolation that are sensitive to tinnitus from any source, much less a concussion. There are expected clinical patterns of psychoacoustic tinnitus properties when compared to the audiogram in cases of hearing loss, but even those patterns have failed to replicate across studies or correlate with patient reported distress (C.-H. Choi, 2012; Flores, Teixeira, Rosito, Seimetz, & Dall'Igna, 2016; Hoare, Edmondson-Jones, Gander, & Hall, 2014).

Noise exposure is the most common source of tinnitus which may complicate the ability to identify tinnitus generators with current audiological tools, given the direct effects noise exposure has on the auditory system and subsequent test results (Joseph Attias, Horovitz, El-Hatib, & Nageris, 2001; Bhatt et al., 2016a; Guest, Munro, Prendergast, Howe, & Plack, 2017). The effects of noise exposure are seen at all points in the auditory system, from the peripheral outer hair cells (OHCS) as evidenced by otoacoustic emissions, all the way to the auditory cortex as evidenced by speech in noise testing (Gallun et al., 2012; M. Charles Liberman, 2016).

In a population with little to no noise exposure where tinnitus develops from a concussion sequala, there is an opportunity to see potential alterations in audiological tests that might

otherwise be masked by the effects of noise. If tinnitus after a concussion can manifest in the auditory cortex and not the periphery like traditional tinnitus from noise exposure, it will lead to more targeted investigation of objective tinnitus assessment. If not, this distinction will not be necessary for future research and comparisons between noise-induced tinnitus and cochleotoxic medication-induced tinnitus may provide better indications of the tinnitus source and potential diagnostic tools. With the current data available, it is not possible to identify an audiological procedure for diagnosing or monitoring tinnitus recovery following concussion. However, there are many tools available that might be beneficial in some combination yet to be determined.

Audiological Protocols for the Assessment of Concussion

There are no standardized protocols for audiological assessment after concussion, which is not surprising given the varying levels at which audiology is included in current published concussion guidelines. The 2017 consensus statement on sports-related concussion fails to mention audiological involvement at all (McCrory et al., 2017). However, the 2016 VA/DoD clinical practice guidelines for concussion report audiological symptoms in nearly 75% of concussions sustained during service and the authors point out the paucity of research separating the effects of noise from head injury on the auditory system. VA/DoD guidelines do not outline recommendations for assessment, but suggest referral to audiology when audiological symptoms like dizziness, tinnitus, or sound sensitivity are reported ("VA/DoD Clinical Practice Guideline for Management of Concussion/Mild Traumatic Brain Injury," 2016). There are over a dozen symptom checklists used in conjunction with neurological assessment and standardized concussion diagnostic tools, but tinnitus is not included as a symptom for the majority of checklists including the more popular Post Concussion Symptom Checklist (PCCS) and the CDC's Concussion Symptom Checklist (Dessy et al., 2017; Randolph et al., 2009).

Assessment of Tinnitus Impact

The VA/DoD practice guidelines for concussion point to recommendations for management of tinnitus, which includes the use of a standardized tinnitus questionnaire. Standardized tinnitus questionnaires are recommended by most generalized tinnitus guidelines including the 2014 American Academy of Otolaryngology (AAOHNS) guidelines, and the 2020 National Institute for health and Care Institute (NICE) guidelines (Tunkel et al., 2014; UK, 2020). These practice guidelines reference several appropriate questionnaires but generally recommend use of the Tinnitus Functional Index (TFI) or Tinnitus Handicap Inventory (THI) due to the broad categories of tinnitus impact assessed, ease of use, and availability.

THI

The THI is likely the most widespread questionnaire in both clinical practice and research due to its broad assessment categories and brief time commitment. Although many predecessors were available for clinical use, the THI was developed to address the lack of a psychometrically strong measure of tinnitus impact in everyday life. The authors designed it to be brief for use in busy clinical practice, easy to administer and interpret, and reflective of tinnitus impact across several categories of daily life function (Newman, Jacobson, & Spitzer, 1996). The final clinical version of the THI demonstrated adequate reliability and validity and has been a popular tool both in clinical practice and research for assessing baseline tinnitus impact and monitoring progress of treatment.

A clinically significant change in tinnitus impact is considered a deviation of +/- 7 points in a range possible points spanning 0-100. Scores are divided into categories of impact for comparison and counseling purposes. A score of 0 to 16 is classified as "no or slight handicap", 18 to 36 indicates "mild", 38 to 56 "moderate", 58 to 76 "severe", and 78-100 is classified as

"catastrophic handicap". These categories are useful for building treatment plans and making appropriate referrals in clinical practice, and for comparison of treatments across groups in research (Newman, Sandridge, & Jacobson, 1998). A sample THI is included in Appendix A.

Although it is important to understand how the perception of tinnitus affects a person psychologically, there is a high emphasis in research on development of objective assessment tools. A diagnosis of tinnitus based on patient report alone is problematic in Veterans' Affairs (VA) claims and workman's compensation cases among other scenarios. The VA Office of Research reported 1.3 million Veterans receiving compensation for service-related tinnitus in 2014, which represents a significant financial burden for the VA system (Affairs, 2016). It is also important in litigious circumstances like head injuries from motor vehicle accidents (MVAs), that the injured party has objective documentation of their tinnitus to receive appropriate compensation and medical coverage. As an expert witness in these cases, it is difficult for audiologists to confirm or deny the possibility of tinnitus following an MVA without objective diagnostic tests to reference.

Beyond compensation concerns, objective measures of tinnitus are needed after a head injury to aid in the determination of recovery projection and ongoing care needs. Presence of dizziness and high initial symptom count are correlated with protracted recovery, as well as female gender in younger populations (Kostyun & Hafeez, 2015; McCrory et al., 2017). We can't even begin to consider whether tinnitus is correlated with protracted recovery without objective means of assessment.

Although there is no gold-standard objective test for tinnitus, and currently available audiological tools fail to objectively identify tinnitus, there may be the potential for a sensitive test battery. By combining current objective assessment options, it might be possible to outline

expected test patterns. Separation of tinnitus following concussion from the more common source of noise exposure, may help to additionally pinpoint regions in the auditory system that are affected when a narrower patient population is targeted.

Peripheral Assessment of Auditory Function Following Concussion

When examining potential objective measures of tinnitus, it is helpful to consider both peripheral and central assessment. Given the countless patterns of structural and metabolic changes that can occur following a concussion, it is important to consider structures at every point along the auditory pathway as potential sites of tinnitus generation.

Otoacoustic Emissions

Otoacoustic emissions (OAEs) are a useful first tool in the assessment of the peripheral auditory system given their generation occurs at the level of the outer hair cells (OHCs) in the cochlea. Kemp described OAEs as sound energy produced within the OHCs of the cochlea as a result of nonlinear mechanical feedback processes which propagates through the middle and external ear (Kemp, 2008). OAEs activity can be recorded as spontaneous activity or evoked through use of transient (TEOAE), distortion-product (DPOAE), or stimulus frequency (SFOAE) stimulation methods. In general, OHCs are like frogs in a contaminated pond in that damage can be recorded via OAEs long before shifts in hearing threshold are recorded on the audiogram.

OHC function is particularly sensitive to high sound pressure moving through the cochlea and it is well documented that OHC function is compromised in excessive noise conditions (Joseph Attias et al., 2001; Shupak et al., 2007). It would make sense to include one measure of OAE assessment in the investigation of tinnitus generation given noise exposure accounts for a large majority of tinnitus reports. However, hundreds of papers have examined the relationship between self-reported tinnitus and OAEs, and the data fail to find a significant, repeatable pattern

(Joseph Attias et al., 2001; Gentil et al., 2015; Keppler, Degeest, & Dhooge, 2017; Sindhusake et al., 2004).

Meta-analysis of OAE research is difficult given there are two common clinical methods, transient-evoked and distortion-product OAEs (TEOAE/DPOAE), and populations include participants with and without noise exposure as well as with and without hearing loss. Some data support increased motility of OHC function and normal OAE amplitudes in tinnitus cases (Sztuka, Pospiech, Gawron, & Dudek, 2010), while other data supports decreased OHC function and OAE amplitude reduction (Ami, Abdullah, Awang, Liyab, & Saim, 2008; Mokrian et al., 2014; Ozimek, Wicher, Szyfter, & Szymiec, 2006; Wang, Tian, & Jiang, 2016). Although OAE assessment may provide limited information on the source of tinnitus, it is beneficial to include as an objective measure of peripheral hearing status.

Given the potential reporting issues with history of noise exposure, OAEs provide an objective assessment of cochlear OHC function and can aid in identifying comorbid peripheral damage from noise or other cochleotoxic agents (K. R. Vander Werff & B. Rieger, 2019). In clinical application, DPOAEs are less sensitive to ambient test room noise and provide better threshold estimation at higher cochlear frequencies than TEOAEs, which is important given the maximal region for noise exposure is between 2-6 kHz for most adult ears (Gorga et al., 1993; M. C. Liberman, 2017). To strengthen the assessment of potential noise effects, the Noise Exposure Questionnaire (NEQ) or the 1-Minute Noise Screen (Appendix B) can be included to estimate an individual's annual noise exposure or identify those at high risk of noise-induced hearing loss (Johnson, Cooper, Stamper, & Chertoff, 2017).

Middle Ear Muscle Reflex (MEMR)

Another potential objective tool for peripheral assessment of the auditory system is the middle ear muscle reflex (MEMR) or "acoustic reflex threshold" (ART) as commonly reported in clinical application. The MEMR represents a descending reflex pathway in the auditory system thought to mitigate external and internal acoustic stimuli by contracting the stapedius muscle during excessive low-frequency acoustic inputs, and the tensor tympani in response to self-generated auditory stimuli (Mukerji, Windsor, & Lee, 2010).

The MEMR is useful in that it requires intact synaptic connection between the IHCs and auditory nerve fibers for a reflex to be elicited by auditory stimuli (Bharadwaj et al., 2019). There is data to support the MEMR may be compromised in ears with tinnitus, as evidenced by shallow growth of reflex strength as the elicitor signal increases (Magdalena Wojtczak, Jordan A. Beim, & Andrew J. Oxenham, 2017).

Although cochlear synaptopathy is most associated with cases of noise exposure, this might provide a viable pathway for tinnitus generation in concussion as well. The MEMR is not commonly performed on patients with tinnitus and/or concussion given the high comorbidity of hyperacusis, or decreased sound tolerance, in both populations. Traditional clinical administration includes puretone elicitor stimuli at increasing levels and often a high stimulus level is needed to elicit the reflex. Wojtczak's team used a contralateral broadband elicitor which elicits the reflex at lower stimulus levels than the traditional puretone stimuli, and this method has been shown to be more sensitive to cochlear synaptopathy than other measures like auditory brainstem response (ABR) (Valero, Hancock, Maison, & Liberman, 2018; Magdalena Wojtczak et al., 2017).

The reduced MEMR growth rate shown in the tinnitus group with normal hearing means this assessment may provide an additional objective measure of tinnitus in the absence of hearing loss beyond OAEs which are limited to describing outer hair cell function in the cochlea and not IHC or auditory nerve fiber health.

Auditory Brainstem Response (ABR)

ABR is another potential tool in evaluating the auditory system following concussion, as responses can be elicited from known neural generators along the pathway with objective time and amplitude normative values. The five main components, waves I-V, are generated at specific locations distally from the cochlea and thus carry specific timing post stimulus (J. Jerger & Johnson, 1988). Wave I and II originate at the distal and proximal sections of cranial nerve VIII respectively. Wave I represents the synchronous activity of auditory nerve fibers in the spiral ganglion cells as the nerve emerges from the cochlea, representing the most peripheral response. Wave III is generated at the anteroventral cochlear nucleus as it projects to the superior olivary complex (SOC), and Wave IV by lateral SOC primary cells as they project to the ventral nucleus of the lateral lemniscus. Wave V originates via medial SOC primary cells that project onto the lateral lemniscus and inferior colliculus, making it the most central response in the brainstem (Bourien et al., 2014; Fobel & Dau, 2004; Melcher & Kiang, 1996; F. E. Musiek & Kibbe, 1986).

Kujawa & Liberman famously identified the notion that auditory damage following noise exposure could remain undetected on traditional hearing tests but be detected via ABR. After two hours of noise exposure (100 dB SPL), mice in their study experienced a temporary shift in hearing that resolved within days but the mice were left with a permanent reduction of the amplitude of wave I on the ABR (Kujawa & Liberman, 2009).

There is similar, but limited data that patients with tinnitus and normal hearing show similar amplitude reductions of wave I, supporting the concept that noise exposure may cause lasting auditory damage that is not necessarily apparent at the time of the event (Schaette & McAlpine, 2011). This is one of the foundations for our investigation into whether concussions cause similar damage in the auditory system outside of the influence of noise.

ABR was not included in the current study at this point, but it warrants mention as a useful contrast between groups experiencing tinnitus from noise exposure versus concussion in future comparisons should central auditory damage and objective signs of tinnitus be identified in the current data at the cortical level.

Central Assessment of Auditory Function Following Concussion

There are several objective and subjective assessment tools that have the potential to identify damage to the auditory cortex following concussion. Given that the intent of this project was to evaluate audiological test utility following concussion, auditory-evoked potentials (AEPs) were explored and imaging techniques such as MRI, MEG, and PET were not compared. Although there is evidence that specific brain activity related to tinnitus perception can be pin-pointed through magnetoencephalography (MEG), this equipment is costly to operate and scarce in the clinical setting in addition to being outside the scope of audiology (Bowyer et al., 2007). Similarly, both functional magnetic resonance imaging (fMRI) and positron emission tomography (PET) have demonstrated utility in tinnitus research by identifying functional changes outside of the expected auditory cortex in non-auditory areas like the frontal and parietal regions of the cortex (Carpenter-Thompson, Schmidt, & Husain, 2015; Lobarinas, Sun, Stolzberg, Lu, & Salvi, 2008; Song, De Ridder, Van de Heyning, & Vanneste, 2012). Again,

these techniques exceed the training of a typical clinical audiologist and a goal of the current study was to evaluate accessible tools for audiologists to use, particularly in cortical assessment.

Objective Tests of Central Auditory Function

Beyond the evaluation of low brainstem auditory function using AEPs through the ABR, AEPs can also be used to assess higher cortical responses. There are two commonly used components when recording AEPs; stimulus-related components sensitive to the physical characteristics of the stimulus, and event-related components dependent on the content of the stimulus (Sutton, Braren, Zubin and John, 1965). Both components can be recorded using electroencephalography (EEG), which is a non-invasive and relatively inexpensive technique compared to cortical imaging techniques. EEG is a measurement of the time-varying voltage within the neurons of the brain, measured through electrodes on the scalp (İnce, Adanır, & Sevmez, 2020). Diagnostic use of EEG can include recording spontaneous activity over a period of time, or activity in response to an event (Puce & Hämäläinen, 2017). For auditory applications, EEG activity can be evaluated in terms of time-locked responses to auditory stimuli or during the more complex processing of requiring a behavioral response at the onset or absence of sound (Winkler, Denham, & Escera, 2015). The latter category of event-related responses offers an opportunity to objectively compare individuals with and without tinnitus, regardless of the source given there are typical patterns of responses in the presence and absence of expected acoustic targets.

Auditory ERPs

Auditory event-related potentials (ERPs) are small voltages generated in the brain that appear when a subject 'attends' to stimuli, and then only when a stimulus has meaning for the subject. They may also appear in the absence of stimulus-related potentials when the eliciting

event is the omission of an expected stimulus (Picton, 1992; Vaughan & Ritter, 1970; Weinberg, Walter, & Crow, 1970). ERP recording is one of the most common procedures in the study of human cognition given the relatively low cost, short procedure duration, and dense cortical resolution available through electrode montages of 128 and even 256 channels (Gevins, Cutillo, & Smith, 1995).

ERPs reflect the summed activity of pyramidal neurons in the cortex when firing synchronously in response to cognitive, sensory, or motor events (Peterson, Schroeder, & Arezzo, 1995). Although they reflect processes as part of a larger group, ERP components are often discussed individually and defined by their polarity, timing, location on the scalp, and sensitivity to different task manipulations (Woodman, 2010).

In human studies, ERP components are classified as 'early' when their waveform peaks (positive or negative going voltage) occur in < 100 msec after a stimulus, and 'late' when peaks occur > 100 msec. The early components are dependent on the physical characteristics of the stimuli, whereas the late components reflect cognitive processes as the individual evaluates the stimuli (Blackwood & Muir, 1990; Sur & Sinha, 2009).

Components are described by their latency following stimulus onset (msec) and amplitude (μV) and include N1/N100 (negative first peak ~ 100msec), P2/P200 (positive second peak ~ 200 msec), P3/P300 (positive third peak ~ 300 msec), and Mismatch Negativity (MMN) which describes a difference wave of common and deviant stimuli occurring around 150-200 msec post stimuli (Fishman, 2014; Helfrich & Knight, 2019). There are many additional components, but these four will be highlighted as they relate to auditory processing and tinnitus. Figure 4 portrays an idealized auditory ERP waveform at a central scalp location like Cz.

N1 is a component of interest in this research due to the large pool of auditory-ERP studies incorporating this potential as the auditory cortex has tonotopic organization to N1 and the component is linked to arousal/attention to sound (Delb et al., 2008; Kadner et al., 2002; Pantev et al., 1988).

P2 represents perceptual processing and is elicited as part of a normal response to visual stimuli, thought to represent part of the cognitive matching cortical system that compares new sensory information with stored memory (Freunberger, Klimesch, Doppelmayr, & Holler, 2007). Reductions in P2 amplitude have been demonstrated in both concussion and tinnitus studies, with attention to increased N1/P2 slope (Cartocci et al., 2012; Gosselin et al., 2012).

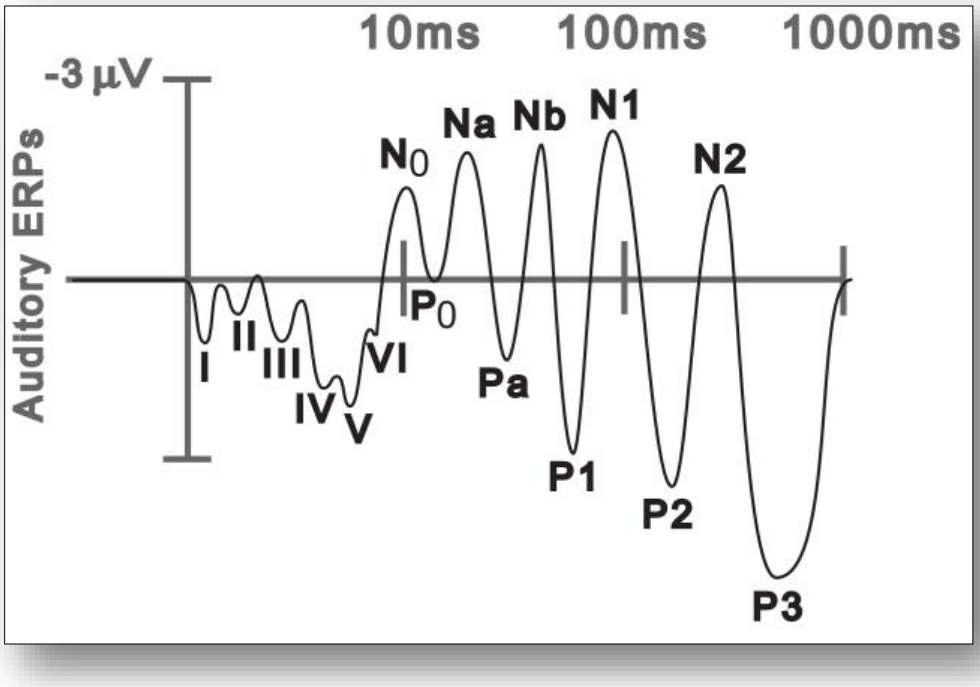

Figure 4: Auditory ERP Peak Components (From Woodman 2010 with permission)

The MMN component is considered an auditory ERP that is pre-attentive and elicited when stimuli deviate from the expected pattern. Most commonly it is evaluated using "Oddball"

paradigms where repetitive acoustic patterns deviate unexpectedly in either frequency, duration or intensity (Fishman, 2014). Neural generators in the frontal and temporal lobe are thought to be responsible for general of the MMN and these regions are important for sensory memory, auditory discrimination and attention, all of which are implicated in patients who fail to habituate to their tinnitus in chronic cases (Holdefer, Oliveira, & Venosa, 2013; Näätänen, 2003).

P3 is the primary peak of interest in this study and was included as it is thought to reflect cognitive categorization, particularly during oddball paradigms. The component can be divided into the earlier P3a related to novelty, and P3b, related more to general information processing (Polich, 2007). P3a is thought to represent bottom-up attention to the novelty of a stimulus change when no response to the change is required. P3a peaks medially near Cz with a latency 25-50 msec earlier than P3b. P3b, which hits a maximum peak more parietally near Pz, is thought to reflect top-down processing that is required when someone is instructed to respond to a change in stimuli (Polich, 2007; Squires, Squires, & Hillyard, 1975). P3 amplitude in general, is often largest in the parietal region with values reported in reference to Pz or more medially in reference to Cz or FCz depending on whether the task is active or passive. Although P3 describes the third peak at roughly 300 msec following a novel stimuli, its latency varies with the complexity of the novel stimuli; more complex stimuli resulting in longer processing time. Additionally, amplitude is expected to vary with how meaningful the novel stimuli are to the subject and how novel the stimuli are in reference to baseline or frequent stimuli presented (Didoné et al., 2016; Falkenstein, Koshlykova, Kiroj, Hoormann, & Hohnsbein, 1995; Schröder, Kajosch, Verbanck, Kornreich, & Campanella, 2016).

Auditory ERP studies in subjects with noise-induced tinnitus have shown alterations in amplitude and reaction time for N1 (negative first peak), P2 (positive second peak), and P3 (positive third peak) components at Cz / Fz (Attias et al 1993, Delb et al 2008, Yang et al 2013).

The foundation for this study includes work from both Rodrigo Araneda and Haidi Yang, both of whom compared auditory ERPs in patients with tinnitus versus controls (Araneda, Volder, Deggouj, & Renier, 2015; Yang et al., 2013). These data among others represent an emerging pool describing abnormal auditory ERPs in subjects with tinnitus as its perception is thought to be a disordered process of auditory 'habituation', a cognitive process in response to acoustic stimulation.

Habituation describes a reduction in behavioral response to a repeated stimuli that is separate from typical sensory or motor fatigue and more related to that stimuli no longer holding importance (Rankin et al., 2009). Habituation to stimuli is distinct in that it can be stimulus-specific, and even frequency-dependent where recovery is more rapid following high frequency stimuli. Although millions of people worldwide experience tinnitus as symptom, only a small percentage are unable to habituate to its presence and experience the debilitating effects of paying constant attention to a phantom auditory stimuli. Since tinnitus involves representation of sound without true stimuli, auditory ERPs are useful given they allow for assessment of the cognitive processes involved in both the presence and absence of acoustic stimuli. In the case of tinnitus, where phantom auditory perception is maintained in the cortex and habituation has not occurred, ERP amplitude for the auditory P3 is of particular interest.

A 2020 systematic review included eight papers that compared auditory-evoked ERPs in tinnitus versus control participants and the results collectively suggest changes in latency and or amplitude for long-latency ERPs including the auditory P3. Results were irrespective of tinnitus

severity and proposed site of lesion (Azevedo, Figueiredo, & Penido, 2020). Early work by Joseph Attias and his team specifically identified reduced wave amplitudes in the N1, P2, and P3 for subjects reporting tinnitus yet normal wave latencies (J. Attias, Urbach, Gold, & Shemesh, 1993). This change in amplitude was attributed to a reduction or timing mismatch in central auditory neuron firing in response to reduced and/or mismatched peripheral neuronal activity. Although tinnitus has long been described as a peripheral injury, mainly in response to noise exposure, these ERP findings suggested a central change as well.

Expanding on this concept, Walpurger and team evaluated whether the severity of tinnitus distress could be explained by central auditory differences given the wide range of impact tinnitus impact shown in clinical populations. They found that subjects with severe tinnitus failed to habituate to acoustic stimuli when compared to participants with mild tinnitus and normal controls. They reported an expected reduction in N1 and P2 amplitudes across repeated trials for the normal controls and mild tinnitus groups demonstrating appropriate habituation to the repeated auditory signal. In contrast, the severe tinnitus group showed significantly less reduction in amplitude, suggesting they failed to habituate to the auditory signal (Walpurger, Hebing-Lennartz, Denecke, & Pietrowsky, 2003). These early papers led to the development of this dissertation topic; tinnitus from a concussion might be quantified using ERP methods which would give both an objective and non-invasive clinical tool for audiologists.

ERP measures are not widely used in clinical tinnitus assessment but may provide a non-invasive option for objective diagnostic and recovery monitoring applications. EEG applications are currently used in monitoring recovery of concussion (Brain Network Activation), but supporting data is limited (Reches et al., 2017). It is important to investigate the influence of tinnitus on such EEG applications, as BNA specifically uses auditory-evoked potentials which

may or may not influence test results. This has not been previously explored, and the current proposal is one step toward understanding the patterns of ERP data in patient with concussion who are experiencing tinnitus compared to those are not.

To better understand the effects of auditory injuries on ERPs, both auditory and visual stimuli were included in this research. A concussion may affect multiple sensory neural networks irrespective of tinnitus, so evaluating a person's ability to complete visual and auditory oddball ERP tasks may help shed light on what differences are related to tinnitus presence and what differences are related to concussion in general. For the visual control tasks, ERPs are recorded in the same manner, but there are a few differences in the resulting components of interest.

Depending on the stimulus elevation in the visual field, the first component, C1, inverts polarity and occurs around 50-90 ms post-stimuli. There is no auditory-equivalent component, so C1 was not included as a component in this research. The first positive peak (P1 80-130 ms) reflects early sensory processing and can be modulated by attention. It is important in P1 recordings to differentiate if the task includes asking participants to attend to a specific space where targets will appear, or whether targets appear in regions of the visual field where participants were not attending, as it influences the P1 component. Directing attention to the location of a stimuli typically results in enhancement of the P1 and N1 amplitude (Hillyard & Anllo-Vento, 1998). The first negative peak is expected around 140-200 ms post-stimuli, the second positive peak 160-275ms post-stimuli, and the third positive peak 250-500ms post-stimuli (Luck & Hillyard, 1994). Similar to auditory stimuli, N1 reflects arousal to changes in the visual field and reflects normal conduction of stimuli from the retina to the cortex. P2 reflects top-down feature classification needed to identify a stimuli and amplitude changes depending on the number of memory associations needed to recall a stimuli or how difficult (how many

distractors) a visual task is (Phillips & Takeda, 2009). The P3 component is considered a general measure of cognitive efficiency across auditory, visual, or somatosensory stimuli and reflects neural activity related to attention and memory processes (Polich, 1999).

In theory, any ERP component could be affected by concussion and the location and degree of injury may result in different alterations to amplitude or latency of components. However, the P3 component is the most widely studies ERP component and is often used to assay cognitive diseases, brain injury, and changes related to aging of the brain (Lavoie, Dupuis, Johnston, Leclerc, & Lassonde, 2004; Pavarini et al., 2018; Praamstra, Meyer, Cools, Horstink, & Stegeman, 1996). Concussions have been shown to slow reaction times during ERP tasks and affect P3 amplitude and or latency. P3 amplitude reduction is reported in most research and there are limited reports of repeatable reductions in P2 or P1 (Brush, Ehmann, Olson, Bixby, & Alderman, 2018; Lavoie et al., 2004).

Subjective Tests of Central Auditory Function

There are different categories of subjective (behavioral) tests of central auditory function, each evaluating a different auditory processing skill including both speech and non-speech stimuli. Common assessment categories include sound localization, lateralization, auditory discrimination, temporal processing, pattern processing, dichotic listening, competing signal listening, and degraded signal listening (Heine & O'Halloran, 2015). Our primary central objective test, the P3, is a cognitive measure, so a comparable behavioral test needed to be affected by impaired cognition and specifically evaluate central auditory structures thought to be impacted by tinnitus and/or concussion. Recent work comparing the effects of overall cognitive processing (i.e. sustained attention, auditory working memory) on auditory processing indicated tests of dichotic listening, frequency patterns, and listening in spatialized noise-sentences showed

significance for both inter-task correlations and functional outcomes (Tomlin, Dillon, Sharma, & Rance, 2015).

Patients with concussion experience a variety of focus and diffuse effects depending on the level of direct impact to tissue and damage to cortical microstructures (Pasternak et al 2014). Loss of white and grey matter volume and cortical thinning, especially in the left frontal area have been shown using MRI (Sussman et al 2017). Tests of central auditory function, including auditory integration tests like dichotic listening tasks, consistently show deficits following concussion (Atcherson & Steele, 2016; Bialunska & Salvatore, 2017; Colucci, 2015; Turgeon, Champoux, Lepore, Leclerc, & Ellemberg, 2011). The Dichotic Digits Test specifically evaluates binaural integration of auditory information in the brain, and gives an idea if patients present the expected "right-ear advantage" demonstrated by healthy brains on these tasks (Fischer et al., 2017).

The right-ear advantage is consistently lost in lesions of the cortex or brainstem and is particularly influenced by lesions of the corpus callosum, which is responsible for interhemispheric transmission of auditory signals (Bellis et al 2008, Sparks et al 1970). Binaural integration of auditory signals occurs almost simultaneously at three auditory centers, the superior olivary complex (SOC), the nuclei of the lateral lemniscus (NLL) and the inferior colliculus (IC) (Moore, 1991). These structures have all been implicated in the perception or maintenance of tinnitus (Cho et al., 2005; Lee & Godfrey, 2015; Stimmer, Borrmann, Löer, Arnold, & Rummeny, 2008). Including the Dichotic Digits Test allows for a subjective companion assessment to the ERP task to provide information on the functional impact of concussion versus concussions with tinnitus.

Digits Testing (DDT)

Dichotic listening tasks present competing auditory signals simultaneously to both ears. This technique has been shown to repeatedly distinguish subjects with normal or abnormal central auditory function, and the Dichotic Digits Test is one such measure (Frank E. Musiek, 1983). In the double-pairs version of the DDT, participants are asked to repeat four digits back; two presented to each ear simultaneously. In normal listeners, there is a clear "right-ear advantage" (Geffen 1978, Kimura 1967), where words or digits presented to the right ear are recalled 2-6% more accurately (left primary auditory cortex).

The right-ear advantage means the left temporal lobe, which is specialized in speech processing, is more responsible for the integration of auditory input from the two ears. This is due to stronger contralateral connections from the right ear to the left temporal lobe, which causes an expected asymmetry in ability on tasks like binaural integration testing (F. E. Musiek, Gollegly, Kibbe, & Verkest-Lenz, 1991). The integration of contralateral auditory input is affected by disorders of the corpus callosum in addition to the temporal lobe and frontal lobe, as evidenced by work with multiple sclerosis and specific brain lesions (Hugdahl, Bodner, Weiss, & Benke, 2003; Rubens, Froehling, Slater, & Anderson, 1985; Springer & Gazzaniga, 1975). Binaural integration systems are often altered following a concussion, but it remains to be seen if changes are correlated with the presence of tinnitus and whether they persist over time with recovery.

There is emerging evidence that patients with tinnitus experience alterations in the prefrontal cortex which increases sensitivity to cross-modal interference and reduces inhibitory control during auditory/visual tasks (Araneda et al 2015). Tinnitus is thought to affect one or more points along the auditory network, with imaging studies documenting changes in the

inferior colliculus and auditory cortex specifically (Finlayson & Kaltenbach 2009, Kaltenbach et al 2005). Given that tinnitus may interfere at several points along the central auditory system; especially in the auditory cortex, located in the superior temporal gyrus, this study targeted Dichotic Digits as a test of function that would include both the auditory cortex and the contralateral connection network that includes the corpus callosum (F. E. Musiek, 1983; Frank E. Musiek & Weihing, 2011). A sample double-pairs test is included in Appendix D.

Statement of the Problem

Patients experiencing a new onset of tinnitus after a head injury represent some of the most severe tinnitus cases in the clinic. It is unknown whether tinnitus develops after a concussion as a byproduct of some pre-existing hidden peripheral hearing damage that the brain can no longer manage, or if it represents a distinct pattern of central injury to the auditory system. Identifying a diagnostic tool that provides objective assessment of tinnitus will help identify the structures involved, which importantly may lead to more targeted tinnitus therapies.

Chapter 2: Method

Participants

Participants were recruited from the University of Kansas Health System Center for Concussion Management (KU-CCM). Research oversight and approval was provided by the University of Kansas Medical Center Internal Review Board (STUDY00142025). Data was collected from 8 participants with mild hearing loss or better (puretone thresholds < 40 dBHL) and no history of concussion, tinnitus, or significant noise exposure for the control group (2 male; 6 female; M_{age} = 36.13 years, range: 24-66 years). There were 9 participants with a history of recent concussion (< 60 days) who reported a new onset of tinnitus following their injury (3 male; 6 female; M_{age} = 47.78 years, range: 25-65 years) with hearing thresholds < 40 dBHL. Finally, 7 participants with a history of recent concussion (< 60 days) who denied tinnitus before or after their injury (2 male; 5 female; M_{age} = 40.71 years, range: 19-62 years) with hearing thresholds < 40 dBHL were included.

There were 14 interested participants who did not pass the initial telephone screening that included the Noise Equivalent Questionnaire (NEQ) 1-minute screening as they scored > 3 which is indicative of significant noise exposure history. Additionally, 9 interested participants did not pass the initial telephone screening due to a history of tinnitus pre-concussion or reported disturbances in vision following concussion. One subject was excluded during onsite audiological testing due to hearing loss exceeding the 40 dBHL cutoff at one or more frequencies 250 – 8kHz.

Measures

Inclusion Measures

For study inclusion purposes, participants completed the Noise Equivalent Questionnaire (NEQ) 1-Minute Screen (Johnson et al., 2017), tympanometry, and puretone air and bone conduction audiometry. All test data was completed for the left and right ear individually.

Puretone air conduction testing was performed using Sennheiser HDA200 circumaural headphones in a sound-treated booth according to clinical standard, the modified Hughson-Westlake technique (American National Standards Institute, 1997; (Hughson & Westlake, 1944)). Participants were excluded if any octave air test frequency threshold 250-8kHz or interoctaves 3kHz & 6kHz exceeded 40 dBHL.

Bone conduction was tested if any air threshold exceeded 15 dBHL. Participants were excluded if indication of middle ear pathology was noted through air-bone gaps exceeding 10 dB at test frequencies of 500, 1k, 2k and 4kHz using the HighSense Bone Conduction headband in the sound booth. The modified Hughson-Westlake test procedure was also used for bone-conduction thresholds.

Tympanometry was conducted at 226 Hz to additionally control for middle ear pathology using the Madsen Otoflex 100 Diagnostic Immitance device (GN, Denmark). Inclusion required a Jerger Type A, normal tympanogram for each ear (James Jerger, Anthony, Jerger, & Mauldin, 1974).

Study Measures

Study data included the Post-Concussion Symptom Scale (PCSS(M. R. Lovell et al., 2006)) total score at initial KU-CCM evaluation, the PCSS total score at the study session, with the addition of tinnitus as an unscored symptom. The KU-CCM includes one extra measure of

neck mobility to the standard 22 items on the PCSS and patients rate their symptom from absent (0) to worst level of symptom possible (6). A sample checklist is included in Appendix C.

Since the PCCS does not include tinnitus as a measure, participants self-identified tinnitus following the concussion and completed a THI (Newman et al., 1996). The THI was administered to the group experiencing tinnitus only and total score between 0 and 100 was reported (Appendix A).

Additionally, the participants with tinnitus completed a subjective pitch-assessment of tinnitus (Henry et al 2013) where pairs of puretones were presented under circumaural headphones in the sound treated booth via the Madsen Astera Audiometer (GN, Denmark) until a repeatable pitch (Hz) was selected as the reference. This information was included to establish presence of tinnitus and set the rare tone for subsequent ERP tasks. Subjects without tinnitus did not complete this procedure and a standard reference pitch of 4kHz was used for ERP rare tones. This tone was selected by the reference study to most approximate the cochlear regions influenced by noise and to represent a commonly reported tinnitus frequency (Araneda et al., 2015). Tinnitus often follows sensorineural hearing loss, and even in the cases of normal puretone thresholds, is above 2kHz in most cases (Han, Lee, Kim, Lim, & Shin, 2009; Henry & Meikle, 2000; Keppler et al., 2017).

DPOAE testing was conducted using the Biologic Navigator PRO Scout OAE (Natus Medical) in a sound-treated booth. Testing was conducted at 13 independent f_2 frequencies with L_1/L_2 amplitudes set at 65/55 dBSPL with a ratio of 1.22 for the F_1/F_2 primaries, which is the clinical standard and thought to evoke the largest DPOAEs in humans (Abdala, 1996). DPOAEs were evaluated with respect to the $2F_1$-F_2 amplitudes (dB SPL) at various F_2 frequencies 750 – 8016 Hz for each ear with corresponding signal to noise ratios (SNR) for each F_2 per Audiology

Systems standard (MacDougall, 2013; *Halmagyi & Curthoys,* 1988). Clinically, individual DPOAEs are determined interpretable if the signal-to-noise ratio (SNR) exceeds 6 dB. Results are compared to (Gorga et al 1997) normative values as threshold in dB SPL per frequency (Hz). For the purposes of this application, DPOAE data was compared across groups in respects to both the overall amplitude in dB SPL and the SNR in dB to include data where SNR values were below 6 dB. The purpose of this data was to evaluate cochlear health as a possible influence on event-related potential (ERP) differences at the central level, so inclusion of all SNR data was important for this comparison given the small sample size. SNRs below 6 dB clinically means that an emission may be absent or too small in amplitude to exceed the noise floor and be measured. For the purposes of this research, SNR was included as a supplement to DPOAE amplitude data for the overall group and not to determine presence or absence of individual emissions.

MEMR testing was conducted using broadband noise (BBN) elicitor and 226 probe tone stimuli with contralateral stimulation levels in 5 dB increments from 65-90 dB SPL for each ear to better simulate the research protocol used by Wojtczak et al. (2017) instead of the traditional threshold seeking protocols used clinically. The Madsen Otoflex 100 Diagnostic Immitance device was used for data collection (GN, Denmark) which limited the amplitude resolution to two decimal places and did not allow for the use of click stimuli with contralateral noise.

Dichotic Digits testing (Frank E. Musiek, 1983) was presented via Sennheiser HDA200 circumaural headphones and the Madsen Astera Audiometer (GN, Denmark) to the left and right ear in a sound-treated booth. Fifty sets of monosyllabic digits (1-9, 7 is excluded) were presented simultaneously to each ear in double pairs at 50 dBSL re: puretone average at 500, 1k, 2k & 4kHz (PTA). Normative data is available from the authors, and the DDT score was recorded as

percent correct out of one hundred. Normative data suggests a right-ear advantage, where digits presented to the right ear are repeated more easily than digits to the left, with all normal performance expected above 90% for adults (F. E. Musiek et al., 1991).

High Density EEG (HD-EEG) was used to evaluate auditory and non-auditory cortical function by use of acoustic and visual stimuli. An Electrical Geodesics, Inc. (EGI) 256-channel electrode system was used to record EEGs sampled at 1000 Hz, referenced to Cz, while subjects were seated 60 cm 0° azimuth from a monitor and dual speaker system (Bose 401) at 45°. Signals of interest were near Fz, FCz, and CZ windowed -.2 to .5 s around the audio signal onset. The signal onset was marked by the audio threshold after amplification by a Presonus Audiobox USB interface or visual threshold in the screen-mounted photodiode using a Cedrus StimTracker for the auditory and visual ERP tasks respectively.

The ERP components of interest for both auditory and visual tasks were the N100 (N1) which is the first negative peak ~50-120 ms after stimulus, P200 (P2) which is the first positive peak ~150-220 ms after stimulus, and P300 (P3) a positive peak occurring roughly 250-600ms after stimulus onset. Component latency (ms) was determined at the location of the average peak ERP response for each subject and amplitudes were marked as the highest or lowest wave deflection. Amplitudes are generally expected < 10 μV but given the population and potential for hyper or hypoactivity related to concussion and/or tinnitus, amplitudes < 15 μV were analyzed (Picton, 1992).

An auditory and visual go/no-go (Oddball) paradigm was used to evaluate ERP amplitude and latency as well as participant reaction time. The oddball paradigm consisted of 400 stimuli per block with a 75/25 no-go/go ratio, which, in the auditory condition included 100 high-frequency tones (4kHz or tinnitus pitch-matched) as the rare, “go” stimulus and 300 low-

frequency tones as the “no-go” stimuli (440 Hz for all participants). The specific high-frequency, rare stimuli used in this study were kept at 4kHz for normal listeners and subjects without tinnitus, and the pitch-matched frequency for participants with tinnitus. All tones had a duration of 250 msec with a rise and fall time of 10 msec per the (Araneda et al., 2015) protocol on which this research design was derived. For the auditory conditions, participants were instructed to keep their eyes open and gaze at a grey fixation cross displayed on the black computer screen.

The rationale for using a pitch-matched rare stimulus is that tinnitus perception is thought to be related to altered inhibition of activity in the auditory cortex (Araneda et al., 2015). Araneda et al (2015) demonstrated that subjects with tinnitus have slower reaction times and higher false-alarm rates when asked to identify a target stimulus matched to their tinnitus versus a distinct target tone where those abnormalities are diminished.

The visual version of this task included a black computer screen with 100 small grey circles (7mm diameter) as the rare stimulus and 300 large grey circles (14mm diameter) as the frequent stimulus for all participants. In between visual stimuli presentation, a grey fixation cross was shown on screen, as was used in the auditory task to keep the participants’ attention on the screen. Once again participants were seated 60 cm 0° azimuth from a computer screen. In both tasks, participants were asked to click a mouse button following the rare stimuli only. Reaction time, false positive rate and ERP data were collected. Figure 5 illustrates the EEG participant setup and Figure 6 shows the ERP oddball paradigm used. This paradigm included unimodal presentation of stimuli; either auditory or visual. For all participants, the mouse was kept on a table to the right of the participant as all participants were right-handed.

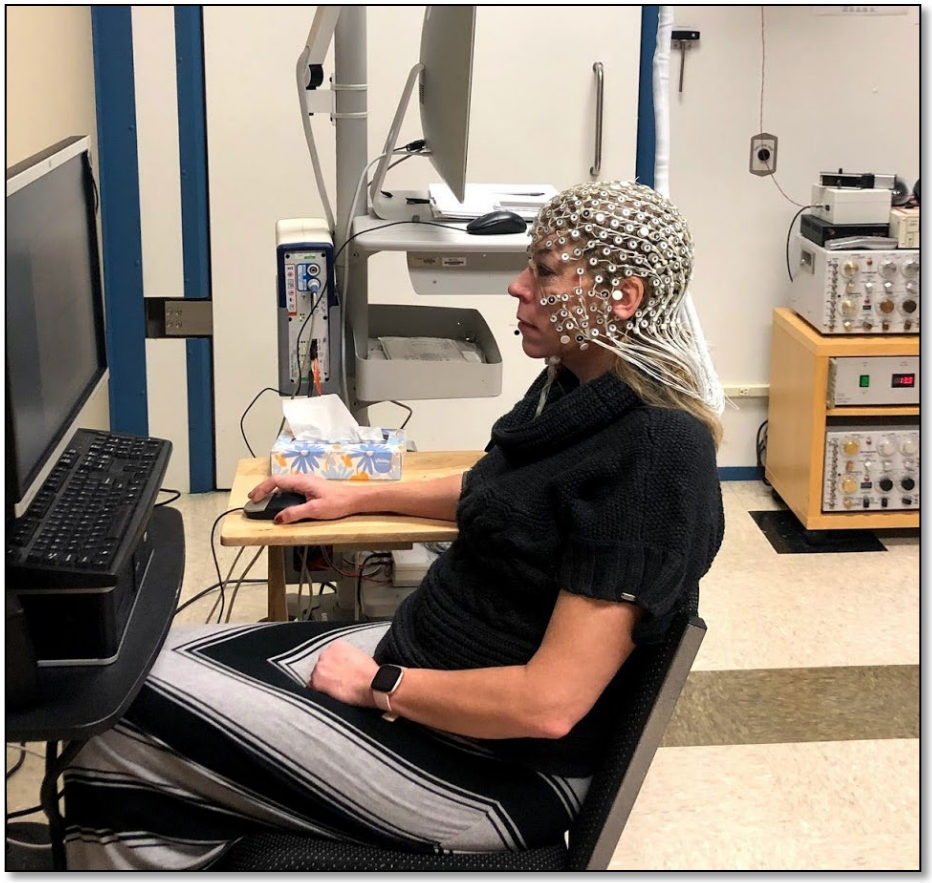

Figure 5: EEG Setup for ERP Tasks

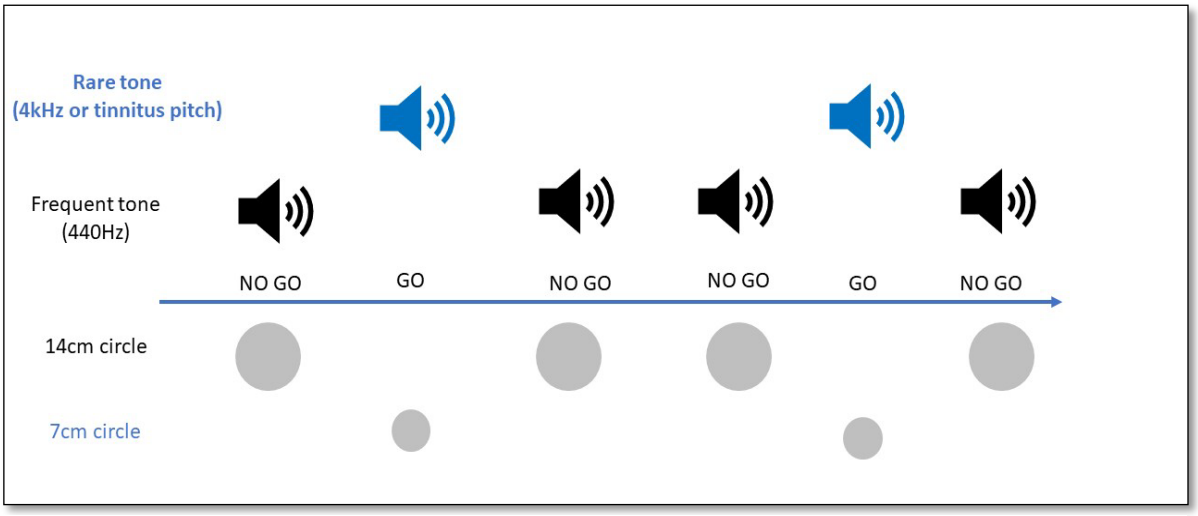

Figure 6: Auditory and Visual Go-No-Go Task Design

ERP Data Acquisition and Processing

Participant reaction time (ms) and false positive/negative rate (out of 100 rare stimuli/300 frequent) during the go-no-go trials were recorded in the EGI system and processed using e-Prime (Psychology Software Tools). To examine N1, P2, and P3 components, raw EEG signals from the EGI system were reprocessed in Matlab (Mathworks, Inc.). The EGI reference sensor (257) is in a cortical location of interest for this data and was thus re-referenced (See Appendix D) to a left mastoid location (94). Initial processing included a high-pass filter 1 – 30 Hz with responses windowed from −.2 to .5 ms relative to the audio or visual trigger onset . Independent component analysis (ICA) was conducted to remove eye and facial muscle artifact, and heartbeat. Following artifact removal, any trials with EEG amplitudes over ± 150 μV were rejected from the analysis (10%).

Component peaks were identified visually and confirmed using one-sample, left-tailed t tests for per-participant ERP averages. Condition and group were verified to ensure putative N1, P2, P3 negativities and positivities were statistically less than zero. A Tukey-Kramer correction was used given the multiple time points evaluated in the ERP window for each participant.

Statistical Analysis

G*Power analysis was used for a-priori power analysis (Faul, Erdfelder, Lang, & Buchner, 2007). To detect a small effect (0.25) with (α =.05), based on Araneda (2015) critical F (1.64), 159 total subjects were needed for a repeated measures and one-way ANOVA. Only 24 participants were included in this data which represents a significant limitation that is discussed in the study limitations section later. To determine if ERP differences could be linked to differences in group makeup, comparisons were made for age, gender, puretone hearing

thresholds and for both DPOAE amplitude and SNR at 750 Hz and 3982 Hz to represent cochlear health near the rare and frequent ERP stimuli sites.

One-Way Analysis of Variance (ANOVA) was used to compare group means for Dichotic Digits score (left and right ear), grand-average ERP amplitude and latency for P1, P2, and P3 at Fz/Cz/FCZ, participant reaction time, and false-positive/false-negative rate. Participants were additionally regrouped by presence of tinnitus then concussion and compared using independent samples t-tests and a Tukey correction. Prior to analysis of reaction time data, incorrect trials, and trials with response rates outside 2 standard deviations of the participants' own average response time were removed (2.15%). In addition to visual peak latency and amplitude marking, ERP pre-analysis included independent samples t-tests with Bonferroni corrections to confirm average peak amplitude for N1, P2, and P3 for all time points in the ERP window. Electrodes that did not have a negative/positive peak at the average timepoint or peaks that were not statistically significantly less than zero were not included in subsequent statistical analysis comparing group mean (< 10%). Grand-average ERPs were evaluated at the FZ, CZ and FCZ scalp location for rare and frequent conditions during both the auditory and visual go-no-go tasks. Table 1 outlines the group comparisons for participant characteristic, peripheral, and central differences included in the statistical analysis. Additional comparisons were evaluated when appropriate for statistically significant main effects and planned comparisons included tinnitus and concussion as factors.

Table 1

Dependent Variables Included in the Statistical Analysis

Participant Characteristics	Peripheral Dependent Variables	Central Dependent Variables
Age	DPOAE Amplitude (dB SPL)	Dichotic Digits Total Score
Gender	DPOAE SNR (dB)	ERP Response Time (ms)
Puretone Air Thresholds (dB HL)	MEMR Amplitude (mmho)	ERP False Positive / False Negative Rate
		ERP N1, P2, P3 Amplitude (μV)
		ERP N1, P2, P3 Latency (ms)

Chapter 3: Results

Participant Characteristics

It was important to compare group characteristics and peripheral auditory function in an effort to demonstrate that any central changes related to tinnitus were distinct from the typical peripheral patterns of tinnitus that might be influenced by age, gender, or hearing acuity. A one-way between subjects Analysis of Variance (ANOVA) was conducted to compare the effect of age and gender across groups (see Table 2).

Table 2

Means and Standard Deviations on the Measure of Group Membership as a Function of Age & Gender

		Age	
Group	*n*	*M*	*SD*
Control	8 (2 male)	36.13	14.78
Concussion	7 (2 male)	41.00	17.94
Concussion + Tinnitus	9 (4 male)	47.56	12.01

Although the concussion group with tinnitus appeared older than the control group, there was not a significant effect of age (See Table 3) at the $p<.05$ level [$F(2, 21) = 1.274$, $p = .300$].

Table 3

One-Way Analysis of Variance of Age Across Groups

Source	*df*	*SS*	*MS*	*F*	*p*
Between Groups	2	560.23	280.12	1.274	.300
Within Groups	21	4617.09	219.86		
Total	23	5177.33			

The concussion with tinnitus group also contained the most male participants, but there was not a significant effect of gender (See Table 4) at the $p<.05$ level for the three groups [$F(2, 21) = .063$, $p = .939$].

Table 4

One-Way Analysis of Variance of Gender Across Groups

Source	*df*	*SS*	*MS*	*F*	*p*
Between Groups	2	.030	.015	.063	.300
Within Groups	21	4.929	.235		
Total	23	4.958			

Hearing acuity was compared across groups with concussion, concussion with tinnitus, and controls for octave puretones 250 to 8kHz. Interoctaves of 3kHz and 6kHz were also included to represent cochlear health at the region most associated with early effects of noise exposure. There were no significant differences between groups at any test frequency for the right or left test ears at the $p<.05$ level (see Table 5).

Table 5

One-Way Analysis of Variance of Puretone Threshold Across Groups

	Source	*df*	*SS*	*MS*	*F*	*p*
250 Hz R	Between Groups	2	39.683	19.841	0.702	0.507
	Within Groups	21	593.651	28.269		
	Total	23	633.333			
250 Hz L	Between Groups	2	150.099	75.050	3.326	0.506
	Within Groups	21	473.859	22.565		
	Total	23	623.958			
500 Hz R	Between Groups	2	65.030	32.515	1.458	0.255
	Within Groups	21	468.304	22.300		
	Total	23	533.333			
500 Hz L	Between Groups	2	39.683	19.841	0.702	0.507
	Within Groups	21	593.651	28.269		
	Total	23	633.333			
1kHz R	Between Groups	2	130.754	65.377	2.064	0.152
	Within Groups	21	665.079	31.670		
	Total	23	795.833			
1kHz L	Between Groups	2	101.141	50.570	1.639	0.218
	Within Groups	21	647.817	30.848		
	Total	23	748.958			
2kHz R	Between Groups	2	288.641	144.320	2.867	0.079
	Within Groups	21	1057.192	50.342		
	Total	23	1345.833			
2kHz L	Between Groups	2	252.976	126.488	1.924	0.171
	Within Groups	21	1380.357	65.731		
	Total	23	1633.333			
3kHz R	Between Groups	2	103.522	51.761	0.727	0.495
	Within Groups	21	1495.437	71.211		
	Total	23	1598.958			
3kHz L	Between Groups	2	230.308	115.154	1.578	0.230
	Within Groups	21	1532.192	72.962		
	Total	23	1762.500			
4kHz R	Between Groups	2	117.212	58.606	1.027	0.375
	Within Groups	21	1198.413	57.067		
	Total	23	1315.625			
4kHz L	Between Groups	2	543.254	271.627	2.998	0.072
	Within Groups	21	1902.579	90.599		
	Total	23	2445.833			
6kHz R	Between Groups	2	556.101	278.051	3.010	0.071
	Within Groups	21	1939.732	92.368		
	Total	23	2495.833			

6kHz L	Between Groups	2	225.744	112.872	1.099	0.352
	Within Groups	21	2157.589	102.742		
	Total	23	2383.333			
8kHz R	Between Groups	2	563.244	281.622	2.017	0.158
	Within Groups	21	2932.589	139.647		
	Total	23	3495.833			
8kHz L	Between Groups	2	535.268	267.634	1.855	0.181
	Within Groups	21	3030.357	144.303		
	Total	23	3565.625			

Group mean hearing threshold across frequency is plotted by group (see Figure 7 for control, Figure 8 for Concussion and Figure 9 for Concussion with Tinnitus) to show the mean audiogram for participants.

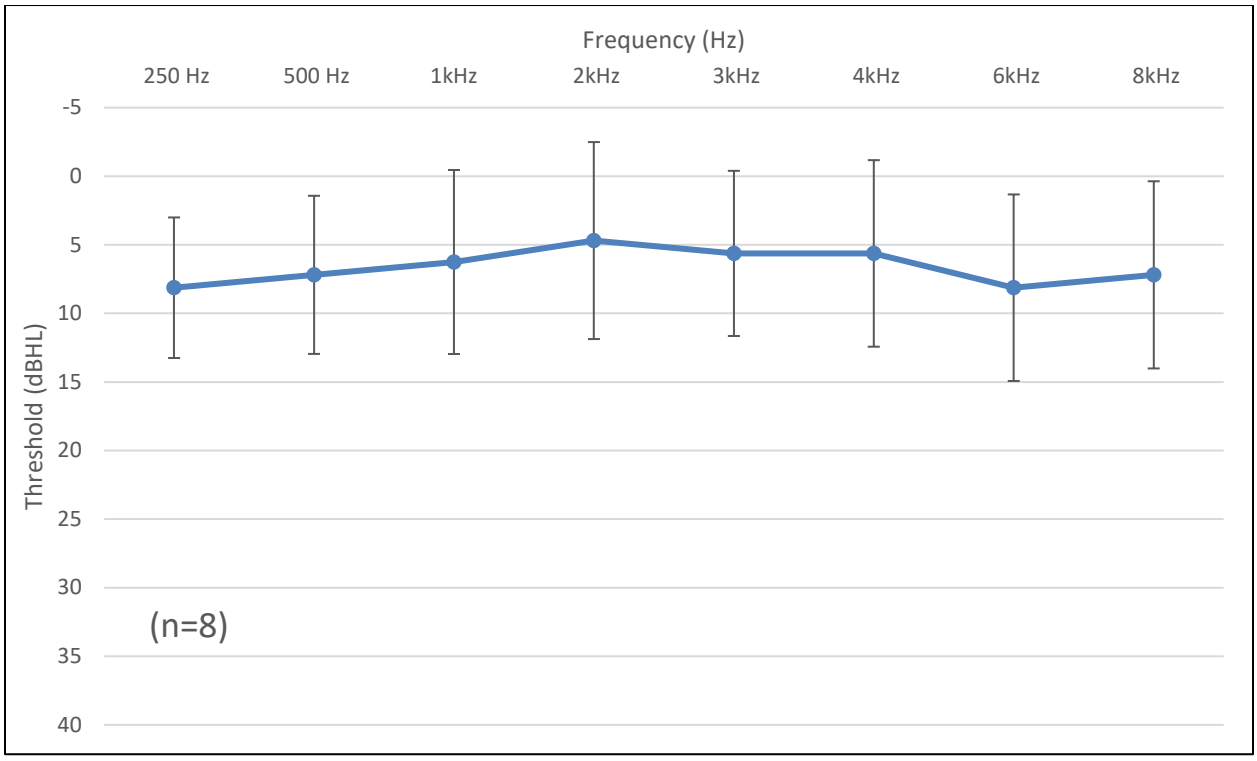

Figure 7: Control Group Mean Audiogram

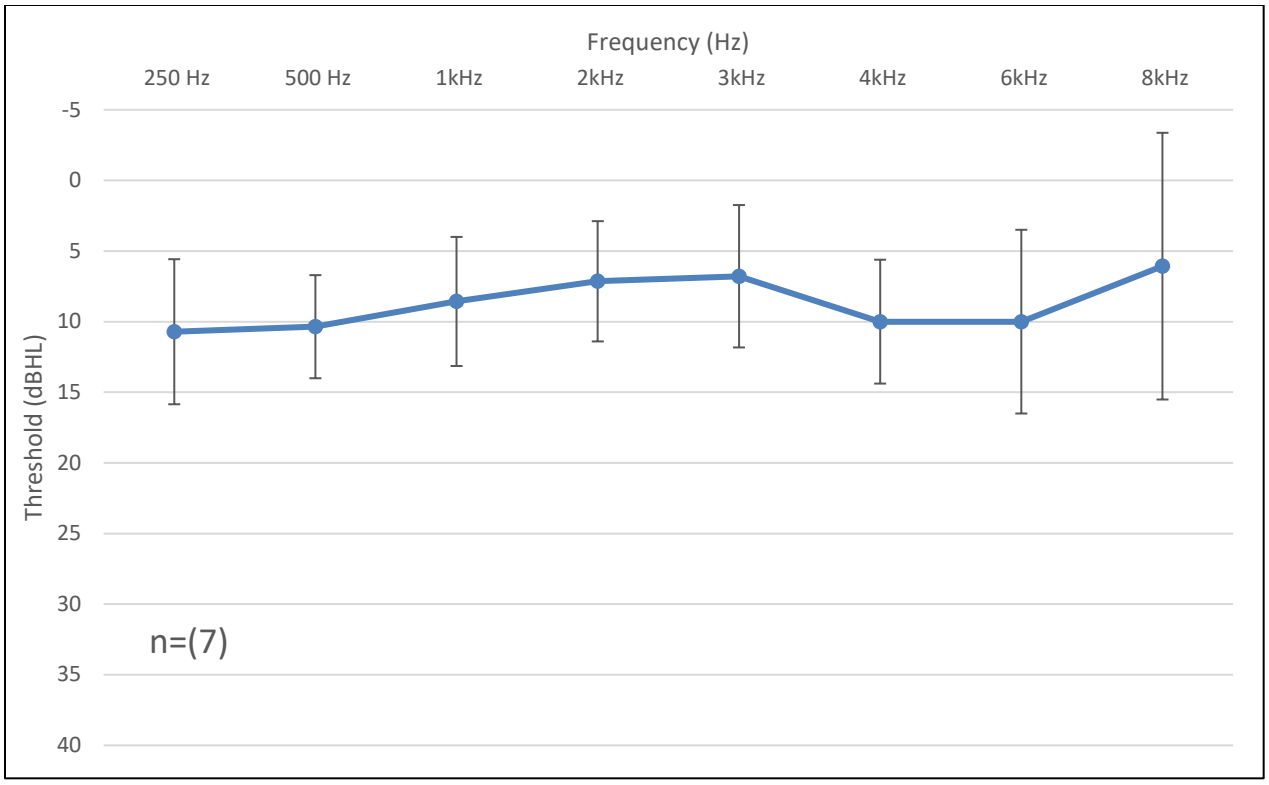

Figure 8: Concussion Group Mean Audiogram

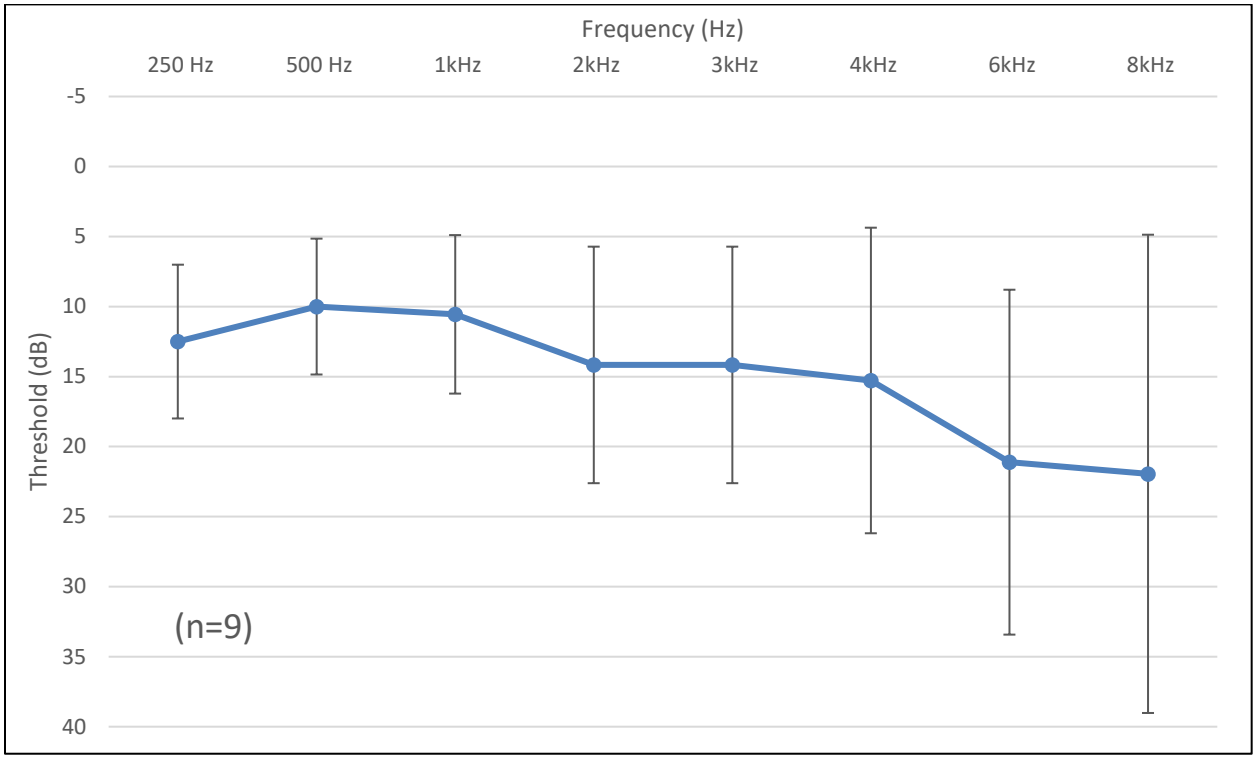

Figure 9: Concussion with Tinnitus Group Mean Audiogram

During later ERP tasks, participants without tinnitus were presented with 4kHz rare stimuli and tinnitus participants were presented with rare stimuli matched to their reported tinnitus pitch measured during audiometric testing. To set up ERP stimuli, participants with tinnitus underwent a pitch-match procedure during audiometry along with puretone threshold testing. Results ranged from 3kHz to 8kHz for tinnitus-matches which is consistent with tinnitus seen in noise exposure and not in the low frequency range where Meniere's Disease or other otologic sources of tinnitus might be suspected.

Participants would be excluded for low-frequency pitch-matches for this reason, but none of the tested individuals met this criteria. The average tinnitus pitch for the group was 5812 Hz but each auditory ERP task was set with the individual participant's self-matched tone (See Figure 10).

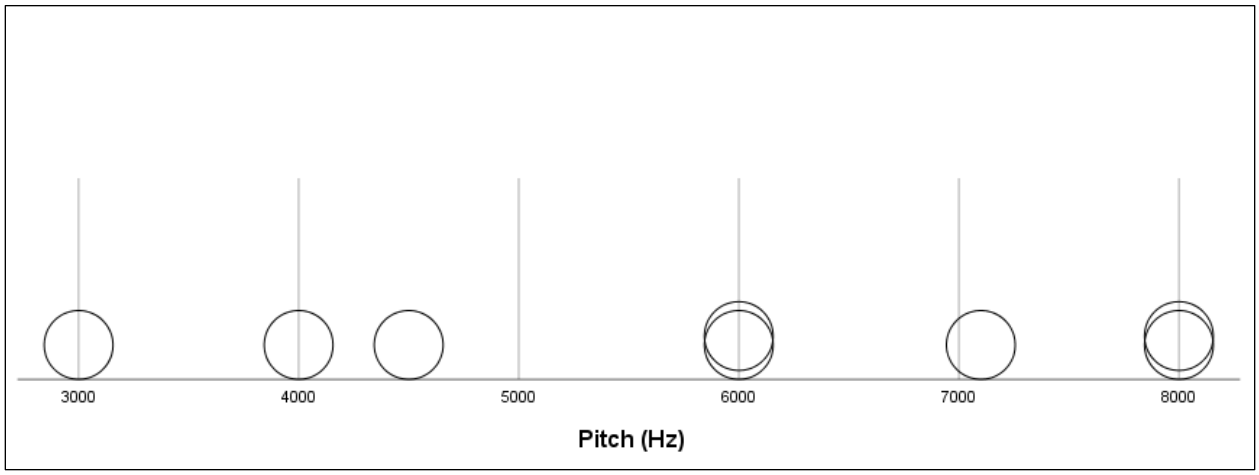

Figure 10: Tinnitus Pitch Matches (n=8)

Peripheral Auditory System

DPOAES

To further compare peripheral hearing and potential effects of noise damage on the cochlea, DPOAE data were included to represent distinct regions of the cochlea and to provide a comparison of cochlear health specifically near the reported tinnitus pitch.

Near the frequent ERP tone, a low frequency of 440 Hz, DPOAEs were assessed at an F_2 frequency of 750 Hz, given this was the most apical frequency that could be recorded using the available clinical OAE device. A one-way ANOVA was conducted to compare the effect of DPOAE amplitude across groups. There were no significant differences between groups for right [$F(2, 21) = .258$, $p = .775$] and left [$F(2, 21) = 3.149$, $p = .064$] ears respectively at the $p<.05$ level. However, the left ear approached significance and this data is revisited later in the discussion. Signal-to-noise-ratios (SNRS) for 750 Hz were not significantly different across groups for right ears [$F(2, 21) = 1.399$, $p = .269$], or for left ears [$F(2, 21) = .844$, $p = .444$] at the $p<.05$ level (See Table 6 and Table 7). Figure 11 and Figure 12 show a graphical representation of DPOAE amplitude and SNR by group respectively.

Table 6

One-Way Analysis of Variance of Right Ear DPOAE Amplitude at F_2 750 Hz Between Groups

Source	*df*	*SS*	*MS*	*F*	*p*
Between Groups	2	13.268	6.634	.258	.775
Within Groups	21	539.652	25.698		
Total	23	552.920			

One-Way Analysis of Variance of Right Ear DPOAE SNR at F_2 750 Hz Between Groups

Source	*df*	*SS*	*MS*	*F*	*p*
Between Groups	2	93.304	46.652	1.399	.269
Within Groups	21	700.333	33.349		
Total	23	793.636			

Table 7

One-Way Analysis of Variance of Left Ear DPOAE Amplitude at F_2 750 Hz Between Groups

Source	*df*	*SS*	*MS*	*F*	*p*
Between Groups	2	313.839	156.930	.258	.314
Within Groups	21	1046.326	49.825		
Total	23	1360.165			

One-Way Analysis of Variance of Left Ear DPOAE SNR at F_2 750 Hz Between Groups

Source	*df*	*SS*	*MS*	*F*	*p*
Between Groups	2	53.408	6.634	26.704	.844
Within Groups	21	664.386	25.698		
Total	23	717.793			

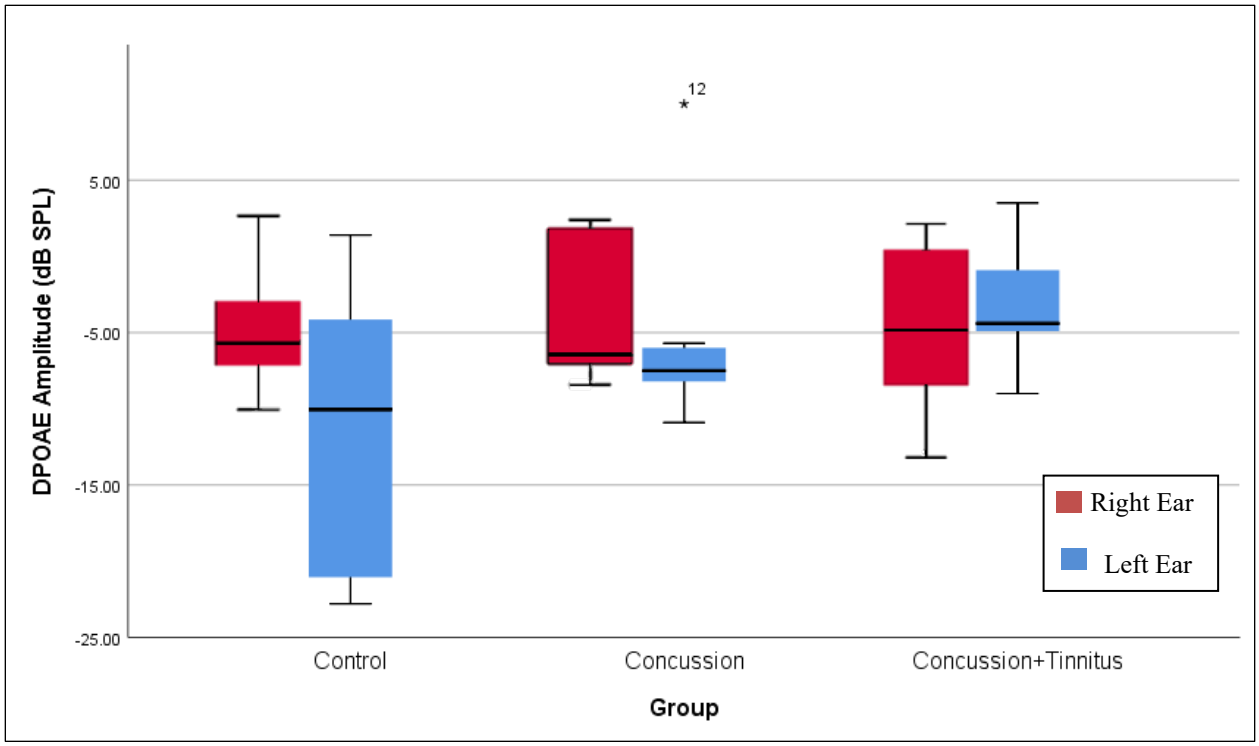

Figure 11: DPOAE Amplitude at 750 Hz

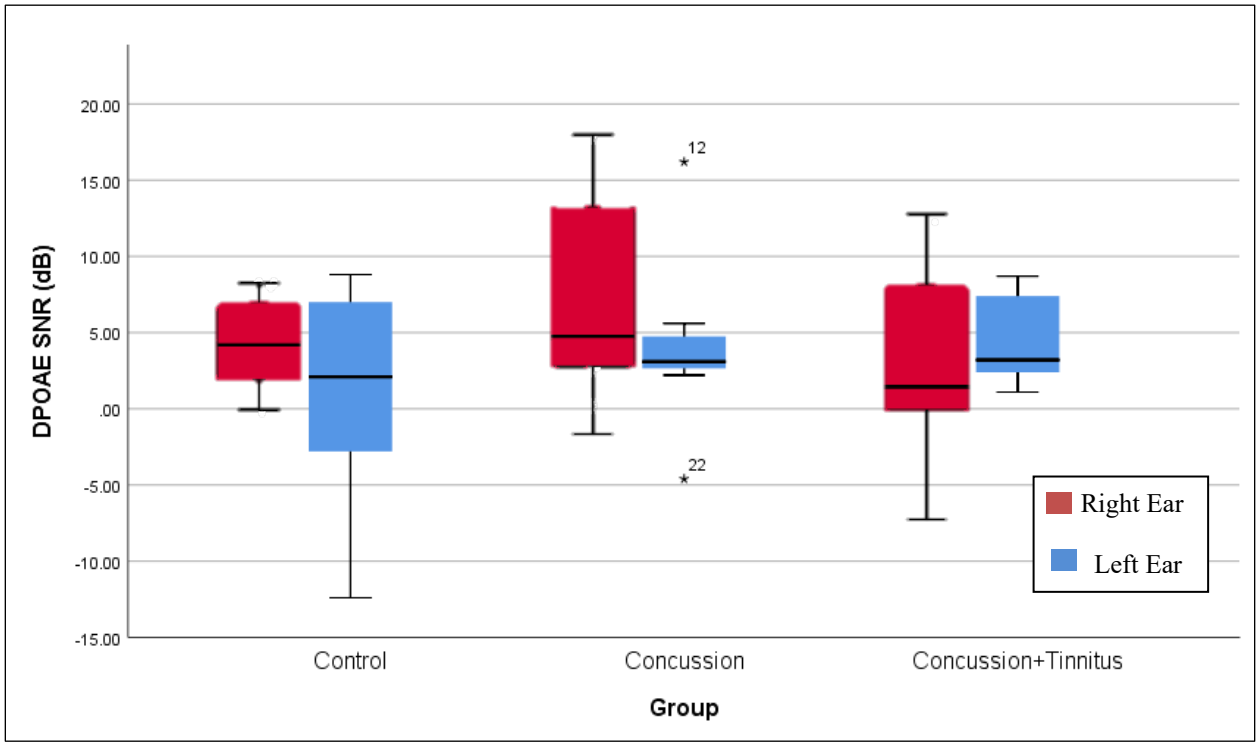

Figure 12: DPOAE SNR at 750 Hz

Similarly, DPOAE amplitudes and SNRs were compared at an F_2 frequency of 3984 Hz near the rare ERP tone of 4kHz and more basal end of the cochlea. A one-way ANOVA was conducted to compare the effect of DPOAE amplitude between groups at 3948 Hz. There were no significant differences between DPOAE amplitudes for right [$F(2, 21) = .644$, $p = .535$] and left [$F(2, 21) = .770$, $p = .475$] ears respectively at the $p<.05$ level. Similarly, DPOAE SNRs for 3948 Hz were not significantly different between groups for right ears [$F(2, 21) = .377$, $p = .691$], or for left ears [$F(1, 23) = .628$, $p = .543$] at the $p<.05$ level (See Table 8). Figure 13 and Figure 14 show a graphical representation of DPOAE amplitude and SNR between groups respectively.

Table 8

One-Way Analysis of Variance of Right Ear DPOAE Amplitude at F_2 3948Hz Between Groups

Source	*df*	*SS*	*MS*	*F*	*p*
Between Groups	2	72.397	36.199	.644	.535
Within Groups	21	1179.99	56.190		
Total	23	1252.39			

One-Way Analysis of Variance of Right Ear DPOAE SNR at F_2 3948 Hz Between Groups

Source	*df*	*SS*	*MS*	*F*	*p*
Between Groups	2	77.283	38.642	.377	.691
Within Groups	21	2153.806	102.562		
Total	23	2231.090			

One-Way Analysis of Variance of Left Ear DPOAE Amplitude at F_2 3948 Hz Between Groups

Source	*df*	*SS*	*MS*	*F*	*p*
Between Groups	2	108.828	54.414	.770	.476
Within Groups	21	1483.912	70.662		
Total	23	1592.740			

One-Way Analysis of Variance of Left Ear DPOAE SNR at F_2 3928 Hz Between Groups

Source	*df*	*SS*	*MS*	*F*	*p*
Between Groups	2	92.934	46.467	.628	.543
Within Groups	21	1553.506	73.976		
Total	23	1646.440			

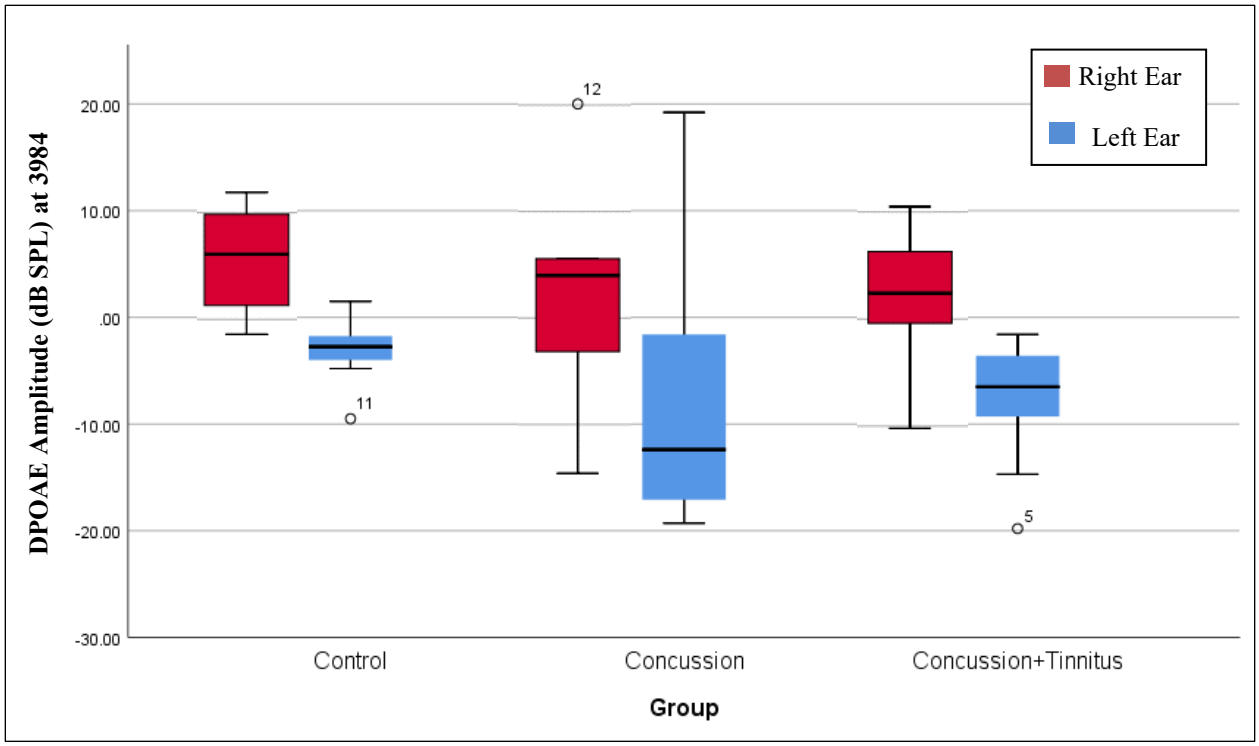

Figure 13: DPOAE Amplitude near Rare ERP tone

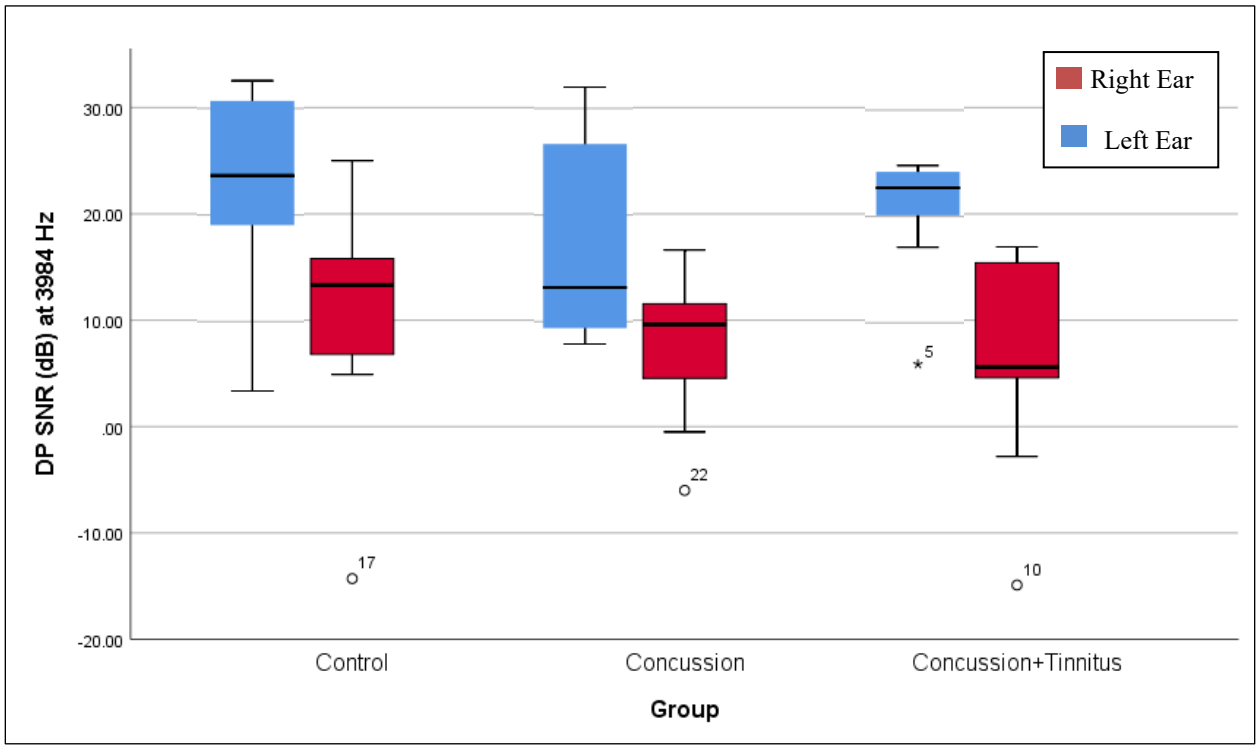

Figure 14: DPOAE SNR at Rare ERP Stimuli

Finally, one-way ANOVA was used to compare DPOAE amplitudes and SNRs at individual tinnitus-matched frequencies for the concussion group with tinnitus to evaluate cochlear health at the rare ERP tones presented to each participant (Table 9). DPOAE amplitudes at individual tinnitus-matched frequencies were not significantly different than the 4kHz data obtained from the control or concussion without tinnitus groups for the right ears [$F(2, 21) = 2.711$, $p = .090$], or for left ears [$F(2, 21) = 1.590$, $p = .228$]. DPOAE SNRs at tinnitus-matched frequencies were not significantly different than the 4kHz data obtained from the control or concussion without tinnitus groups for the right ears [$F(2, 21) = .200$, $p = .820$], or for left ears [$F(2, 21) = 1.231$, $p = .312$].

Table 9

One-Way Analysis of Variance of Right Ear DPOAE Amplitude at F_2 3948Hz & Tinnitus F_2 Between Groups

Source	*df*	*SS*	*MS*	*F*	*p*
Between Groups	2	312.101	156.051	2.711	.090
Within Groups	21	1208.972	57.570		
Total	23	1521.073			

One-Way Analysis of Variance of Right Ear DPOAE SNR at F_2 3948 Hz & Tinnitus F_2 Between Groups

Source	*df*	*SS*	*MS*	*F*	*p*
Between Groups	2	30.361	15.181	.200	.820
Within Groups	21	1590.56	75.741		
Total	23	1620.92			

One-Way Analysis of Variance of Left Ear DPOAE Amplitude at F_2 3948 Hz & Tinnitus F_2 Between Groups

Source	*df*	*SS*	*MS*	*F*	*p*
Between Groups	2	250.227	125.11	1.590	.228
Within Groups	21	1652.538	78.692		
Total	23	1902.765			

One-Way Analysis of Variance of Left Ear DPOAE SNR at F_2 3928 Hz and Tinnitus F_2 Between Groups

Source	*df*	*SS*	*MS*	*F*	*p*
Between Groups	2	188.621	94.310	1.231	.312
Within Groups	21	1609.279	76.632		
Total	23	1797.90			

Amplitude group mean data at the individual rare stimuli pitch (3948 for control and concussion; tinnitus pitch otherwise) were driven by one outlier in the concussion group with much larger emission than any other participant. Once removed, ANOVA was recalculated and showed a significant effect for right [$F(2, 20) = 3.946$, $p = .036$] and left [$F(2, 20) = 3.946$, $p = .036$] ears respectively at the $p<.05$ level (See Table 10). A post-hoc Tukey test indicated the control group mean DPOAE at 3982 Hz for the left ear (M= -3.13 dB, SD=3.156) was higher and approached significance for both the concussion group mean (M=-11.516, SD=8.05) at (p=.066) and the concussion with tinnitus group (M=-10.811, SD=7.499) at (p=.061).

For the right ear, the Tukey test indicated the control group mean DPOAE at 3982 Hz (M= -4.375, SD=4.97) was significantly higher than the concussion with tinnitus group mean

(M=-12.90, SD=6.51) with (p=.033). The control mean was not significantly higher than the concussion group mean (M= -10.966, SD=6.51) with (p=.133).

Table 10

One-Way Analysis of Variance of Left Ear DPOAE Amplitude at F_2 3948 Hz & Tinnitus F_2 Between Groups

	Source	df	SS	MS	F	p
DPOAE_RareL	Between Groups	2	333.067	166.533	3.947	*.036
	Within Groups	20	843.812	42.191		
	Total	22	1176.879			
DPOAE_RareR	Between Groups	2	326.960	163.480	3.946	*.036
	Within Groups	20	828.568	41.428		
	Total	22	1155.529			

MEMR

MEMR amplitudes (mmho) were averaged across broadband noise (BBN) elicitor levels 65-90 dB SPL for control, concussion, and concussion with tinnitus groups. Repeated measures ANOVA was used to compare groups at increasing BBN elicitor levels (dB SPL) and showed a difference in average amplitude that was not significant [$F(2, 21) = .200$, $p = .156$]. A Greenhouse-Geisser adjustment ($p<.05$) correction was used given the data violated sphericity for repeated measures. Linear trend analysis (See Figure 15).

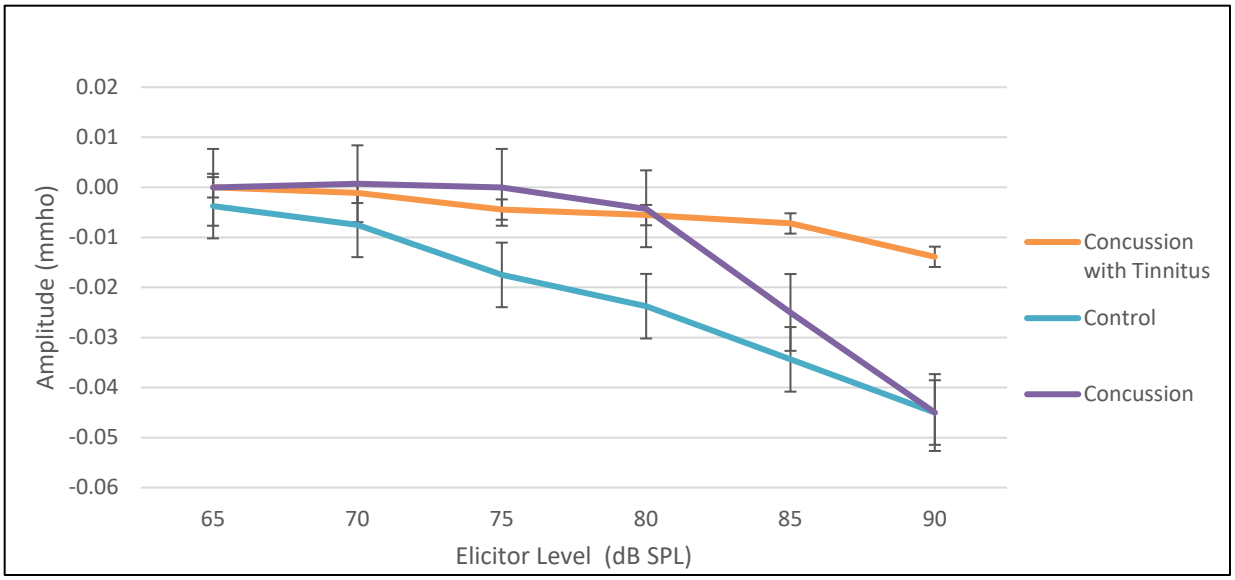

Figure 15: BBN Group MEMR Amplitude by Elicitor Level

Central Auditory System

Dichotic Digits

To provide a measure of subjective central auditory function, Dichotic Digits Double Pairs Test scores were compared across participants using a One-way ANOVA (See Table 11 and Table 12). Total score showed a significant difference between groups for both the left [$F(2, 21) = 8.341$, $p = .002$], and right total scores [$F(2, 21) = 5.422$, $p = .013$]. Post hoc comparisons using the Tukey HSD test indicated that the mean score for the groups with concussion (M = 75.71, SD = 11.842) and concussion with tinnitus (M=78.33, SD=12.728) were significantly lower than the control group (M = 95.13, SD = 2.850) for the left ear. Similarly, the mean scores for the groups with concussion (M = 83.22, SD = 13.674) and concussion with tinnitus (M=87.00, SD=7.211) were significantly lower than the control group (M = 97.75, SD = 1.581) for the right ear. Taken together, these results suggest that acute concussion resulted in significantly lower Dichotic Digits score regardless of tinnitus presence (See Figure 16).

Table 11

Means and Standard Deviations for the Left Ear Dichotic Digits Total Score by Group

Group	*n*	*M*	*SD*
Control	8	95.13	2.850
Concussion	7	75.71	4.476
Concussion + Tinnitus	9	78.33	4.243

Means and Standard Deviations for the Right Ear Dichotic Digits Total Score by Group

Group	*n*	*M*	*SD*
Control	8	97.75	0.559
Concussion	7	87.00	2.726
Concussion + Tinnitus	9	83.22	4.551

Table 12

One-Way Analysis of Variance of Dichotic Digits Total Score Between Groups for Left Ears

Source	*df*	*SS*	*MS*	*F*	*p*
Between Groups	2	1743.030	871.515	8.341	.002*
Within Groups	21	2194.304	91101.4		
Total	23	3937.333			

One-Way Analysis of Variance of Dichotic Digits Total Score Between Groups for Right Ears

Source	*df*	*SS*	*MS*	*F*	*p*
Between Groups	2	940.278	470.139	5.422	.013*
Within Groups	21	1821.056	86.717		
Total	23	2761.33			

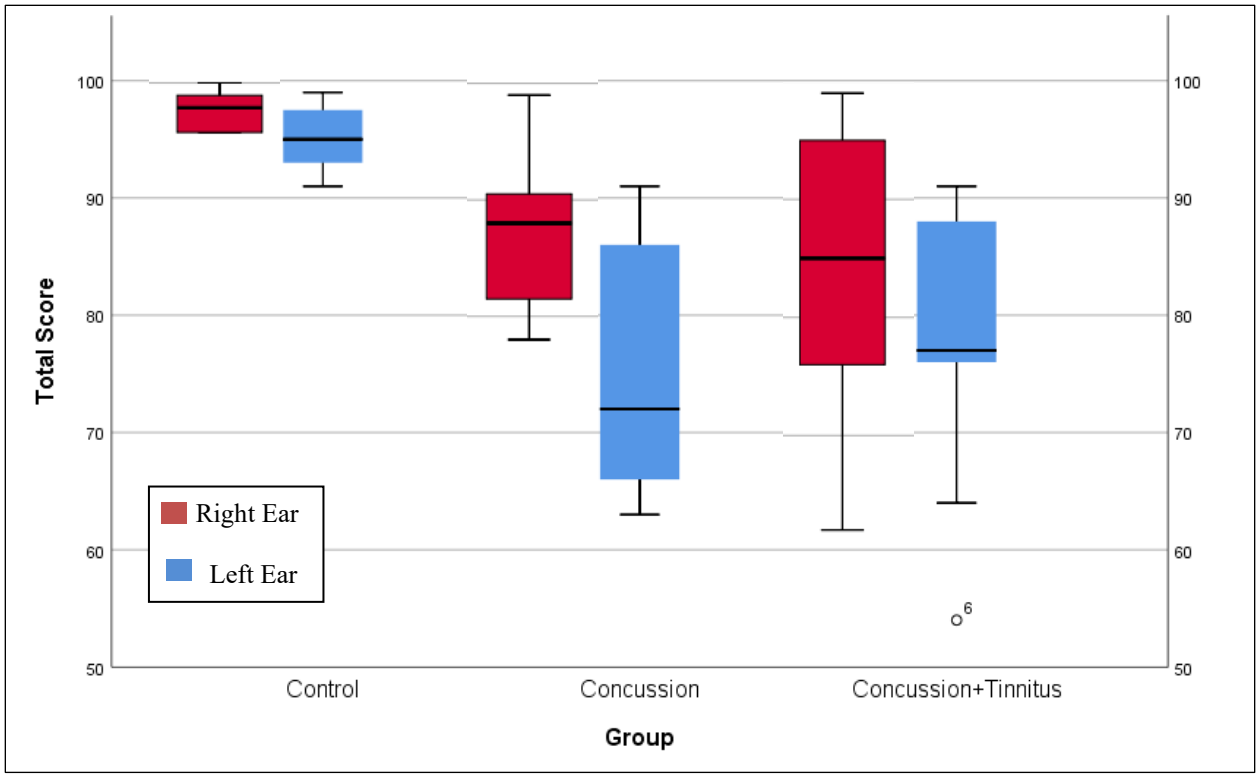

Figure 16: Dichotic Digits Double Pairs Total Score by Group

Individual comparisons were made between participants with and without concussion for Dichotic Digits total score using independent samples t-tests. There was a significant effect for concussion [$t(22) = 4.123$, $p < .05$] with control participants scoring higher than participants with concussion (See Figure 17). The control participants average scores for the right (M=97.75, SD=11.135) and left ears (M=95.13, SD=2.850) were significantly better than participants with concussion for the right (M=84.88, SD=2.784) and left ears (M=77.19, SD=12.012).

Right ear scores were higher than left with and without concussion, upholding the expected "right-ear advantage" expected for this measure.

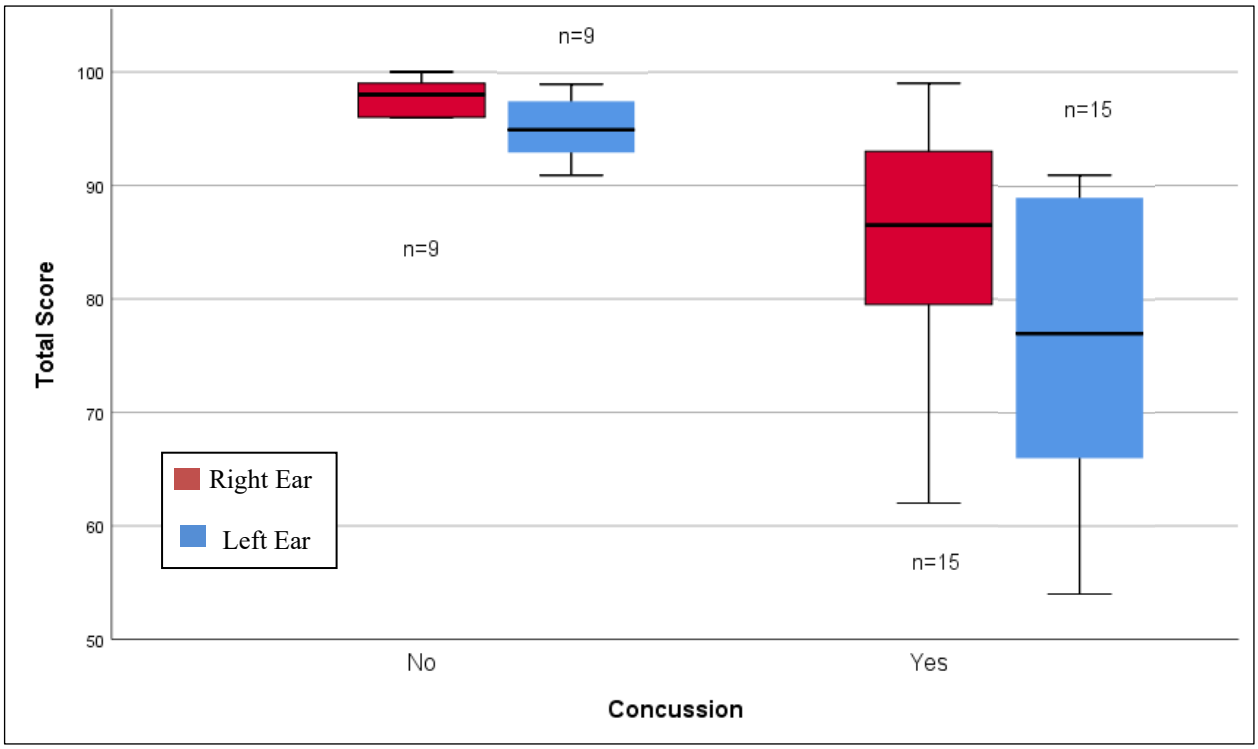

Figure 17: Dichotic Digits Total Score by Concussion Status

There was not a significant effect when collapsing participants by tinnitus [t(22) = 1.362, p > .05], however, right ear scores (M=85.11, SD=11.69) were again higher than left (M=85.93, SD=13.06) for participants with tinnitus, again upholding the expected "right-ear advantage" expected for this measure and seen in the control participants.

Event-Related Potentials

Behavioral response data included reaction time to rare stimuli, and accuracy (hit rate). ERP amplitude and latency data were compared across groups for the N1, P2, and P3 components at Fz, Cz, and FCZ scalp locations. Incorrect trials were removed prior to analysis of reaction time.

Reaction Time and Accuracy for Auditory and Visual ERPs

There was a trend where mean reaction time (ms) in the auditory condition for the control group (M=343.05, SD=60.57) was faster than the groups with concussion (M=381.20, SD=58.27) and concussion with tinnitus (M=382.68, SD=23.01). However, the reaction times were not significantly different when compared with one-way ANOVA [$F(2, 21) = 1.012$, $p = .381$].

Similarly, there was no significant difference in group mean reaction times for the visual conditions [$F(2, 21) = 2.026$, $p = .157$] at the $p<.05$ level. Mean reaction time was faster for the control group (M=384.36, SD=19.44) than for the group with concussion (M=414.57, SD=27.62) and concussion with tinnitus (M=405.33, SD=38.41), but again, these differences were not statistically significant (See Table 13).

Table 13

One-Way Analysis of Variance of Group Mean Auditory Oddball Task Reaction Time

Source	*df*	*SS*	*MS*	*F*	*p*
Between Groups	2	8112.299	4056.150	1.012	.381
Within Groups	21	84193.67	4009.222		
Total	23	92305.97			

One-Way Analysis of Variance of Group Mean Visual Oddball Task Reaction Time

Source	*df*	*SS*	*MS*	*F*	*p*
Between Groups	2	3672.617	1836.31	2.026	.157
Within Groups	21	19030.14	906.19		
Total	23	22702.75			

Hit rate in the auditory condition was evaluated in terms of missed rare tones and false positive hits on frequent tones for the groups with concussion, concussion with tinnitus and controls using one-way ANOVA (See Table 14). There were no significant differences between groups for missed tones [$F(2, 21) = 1.81$, $p = .326$], or for false positive tones [$F(2, 21) = 1.229$, $p = .313$].

Similarly, there were no group differences for missed target (small) circles [$F(2, 21) = 1.288$, $p = .297$], or for false positive hits on large circles [$F(2, 21) = 2.398$, $p = .115$].

Table 14

One-Way Analysis of Variance of Group Mean Auditory Oddball Task Missed Targets

Source	*df*	*SS*	*MS*	*F*	*p*
Between Groups	2	9.355	4.678	1.181	.326
Within Groups	21	83.145	3.959		
Total	23	92.500			

One-Way Analysis of Variance of Group Mean Auditory Oddball Task False Positive Responses

Source	*df*	*SS*	*MS*	*F*	*p*
Between Groups	2	1.397	.698	1.229	.313
Within Groups	21	11.937	.568		
Total	23	13.333			

One-Way Analysis of Variance of Group Mean Visual Oddball Task Missed Targets

Source	*df*	*SS*	*MS*	*F*	*p*
Between Groups	2	40.349	20.17	1.288	.297
Within Groups	21	328.984	15.66		
Total	23	369.333			

One-Way Analysis of Variance of Group Mean Visual Oddball Task False Positive Responses

Source	*df*	*SS*	*MS*	*F*	*p*
Between Groups	2	61.611	30.806	2.398	.115
Within Groups	21	11.937	.568		
Total	23	13.333			

Additional comparisons were made between participants with and without concussion to evaluate the effects of concussion on reaction time and accuracy in the oddball tasks. There were no significant findings for auditory or visual tasks, however, there was a trend approaching significance where reaction time for participants with concussion (n=16) was slower in the visual task (M=409.37 ms, SD=33.36) than control (n=8) reaction time, (M=384.36 ms, SD=19.45) (See Table 15). False positive rate for the visual task also approached significance with the trend that participants who had concussion (M=3.88, SD=4.27) made more errors than controls (M=0.75, SD=.88). Figure 18 and Figure 19 show graphical representations of group mean errors for participants with concussion.

Table 15

One-Way Analysis of Variance of Concussion and Reaction Time in the Visual Oddball Task

Source	*df*	*SS*	*MS*	*F*	*p*
Between Groups	2	3336.501	336.501	3.790	.064
Within Groups	21	19366.25	880.28		
Total	23	22702.75			

One-Way Analysis of Variance of Concussion and False Positive Rate in the Visual Oddball Task

Source	*df*	*SS*	*MS*	*F*	*p*
Between Groups	2	52.083	52.083	4.103	.055
Within Groups	21	279.250	12.693		
Total	23	331.333			

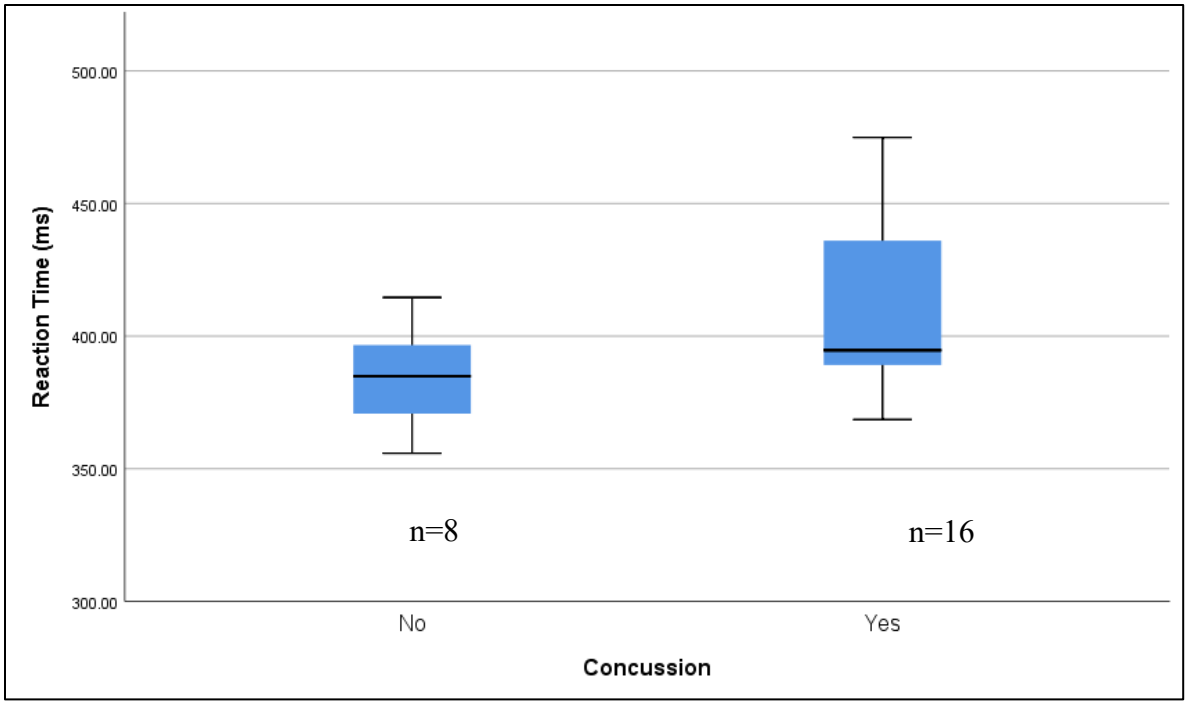

Figure 18: Visual Task Reaction Time for Participants with Concussion

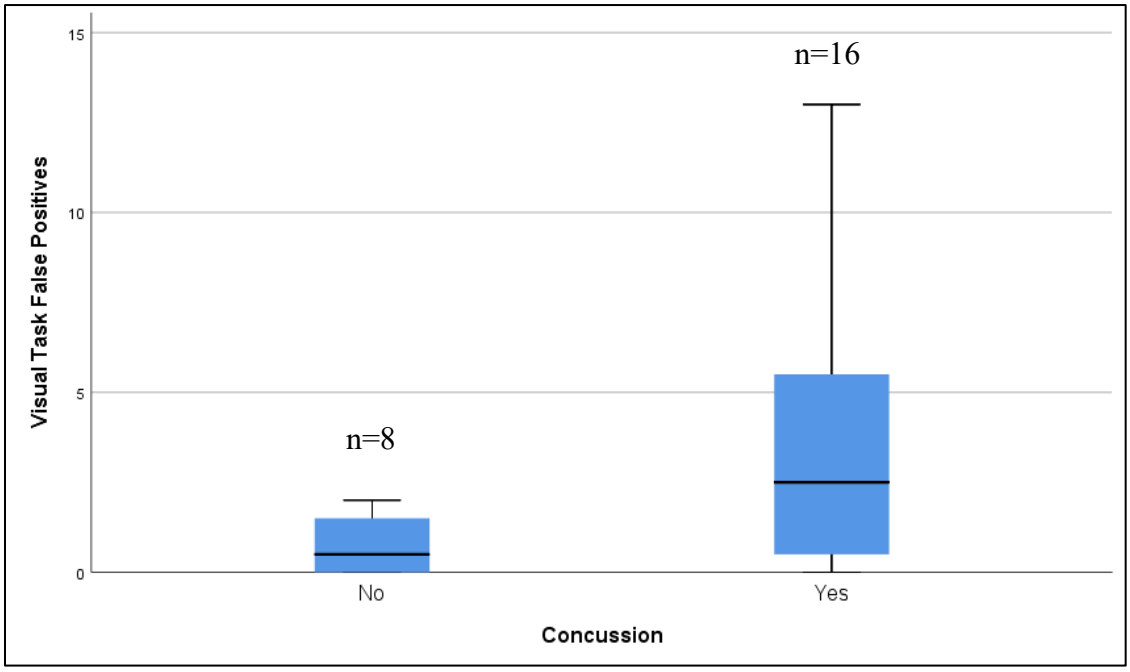

Figure 19: Visual Task False Positive Responses for Participants with Concussion

Within the concussion group, accuracy was compared in terms of date from injury and there was initially a significant effect for missed rare visual targets (small circles) [$F(2, 13) = 24.846$, $p = .039$]. Participants did not perform differently for auditory tasks, but closer to the concussion, there were more missed rare targets. Data were driven by one outlier who missed 19 targets, and once removed, the significant effect was also removed (See Figure 20).

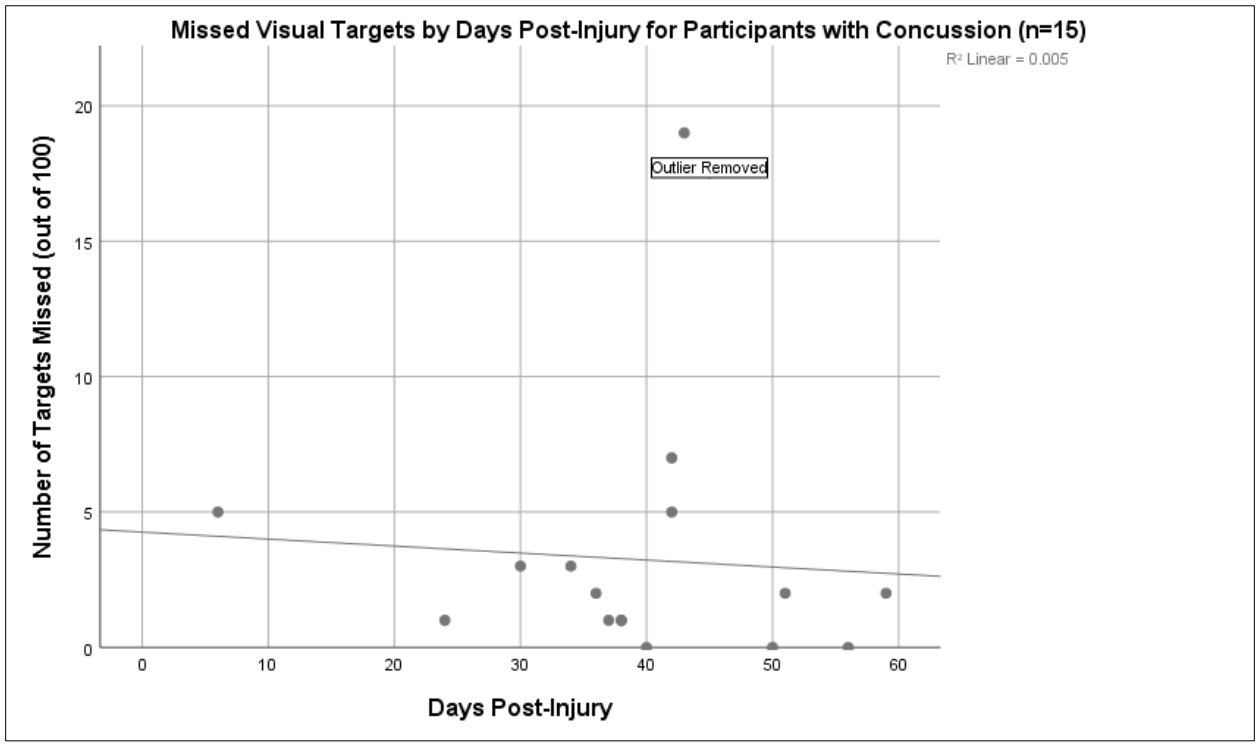

Figure 20: False Negative Targets by Concussion

Finally, reaction time and accuracy were evaluated in reference to the location of the primary concussion injury. Injuries were categorized as absent, anterior, posterior, left temporal, right temporal, or whiplash where no primary impact was reported (See Table 16). There were significant main effects of injury location for false positives in both the auditory [$F(5, 18) = 3.979$, $p = .013$] and visual [$F(2, 13) = 3.158$, $p = .032$] oddball conditions. Post-hoc analysis to

determine which group means were different could not be completed since one or more conditions contained less than two participants. A graphical trend shows how each concussion location group mean compares to participants with no concussion location (none, n=8). All concussion location group means were slower than control participants with whiplash giving the slowest auditory reaction time. The trend did not maintain for visual reaction time (See Figure 21 & Figure 22).

Table 16

One-Way Analysis of Variance of Primary Injury Location as a Factor of ERP Reaction Time and Accuracy

Source		df	SS	MS	F	p
False Positive Tones	Between Groups	5	7.000	1.400	3.979	**.013***
	Within Groups	18	6.333	.352		
	Total	23	13.333			
False Positive Circles	Between Groups	5	154.833	30.967	3.158	**.032***
	Within Groups	18	176.500	9.806		
	Total	23	331.333			
Auditory Reaction Time	Between Groups	5	18368.356	3673.671	.894	.506
	Within Groups	18	73937.614	4107.645		
	Total	23	92305.971			
Visual Reaction Time	Between Groups	5	5923.331	1184.666	1.271	.319
	Within Groups	18	16779.424	932.190		
	Total	23	22702.755			
Missed (Rare) Target	Between Groups	5	35.208	7.042	2.212	.098
Tones	Within Groups	18	57.292	3.183		
	Total	23	92.500			
Missed (Small) Target	Between Groups	5	102.667	20.533	1.386	.276
Circles	Within Groups	18	266.667	14.815		
	Total	23	369.333			

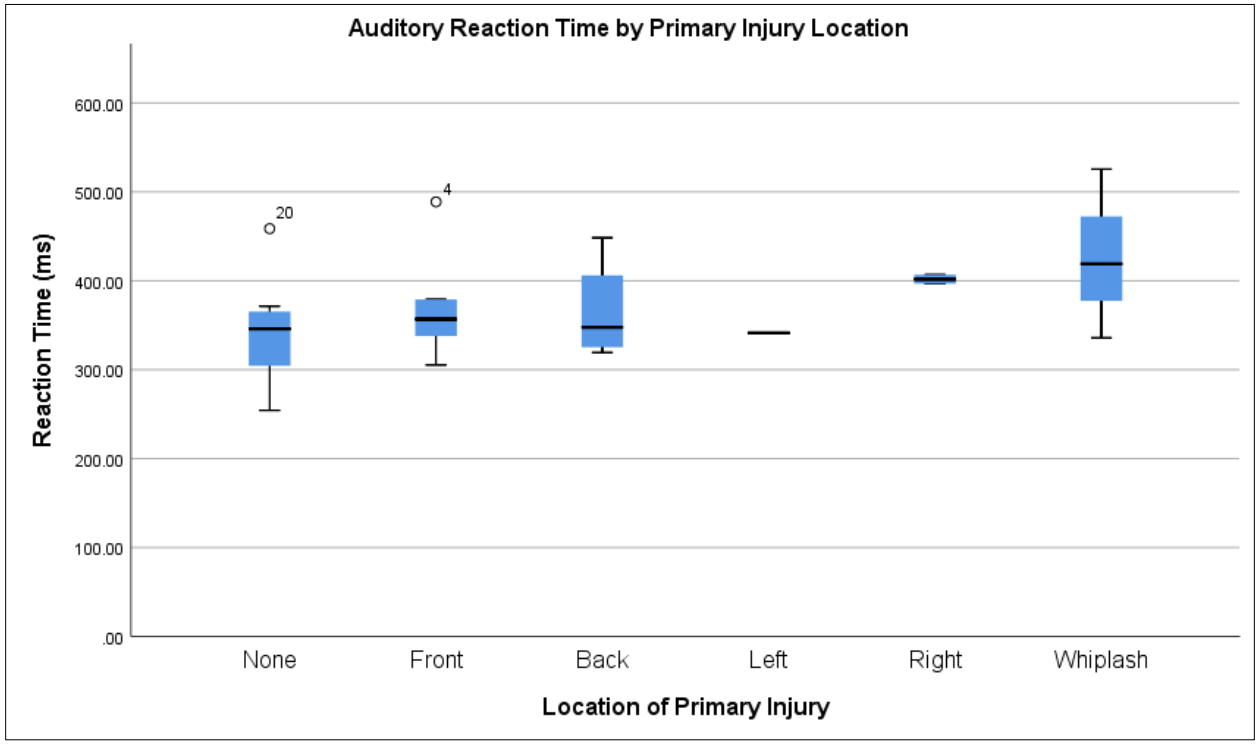

Figure 21: Auditory Reaction Time with Reported Location of Primary Injury as a Factor

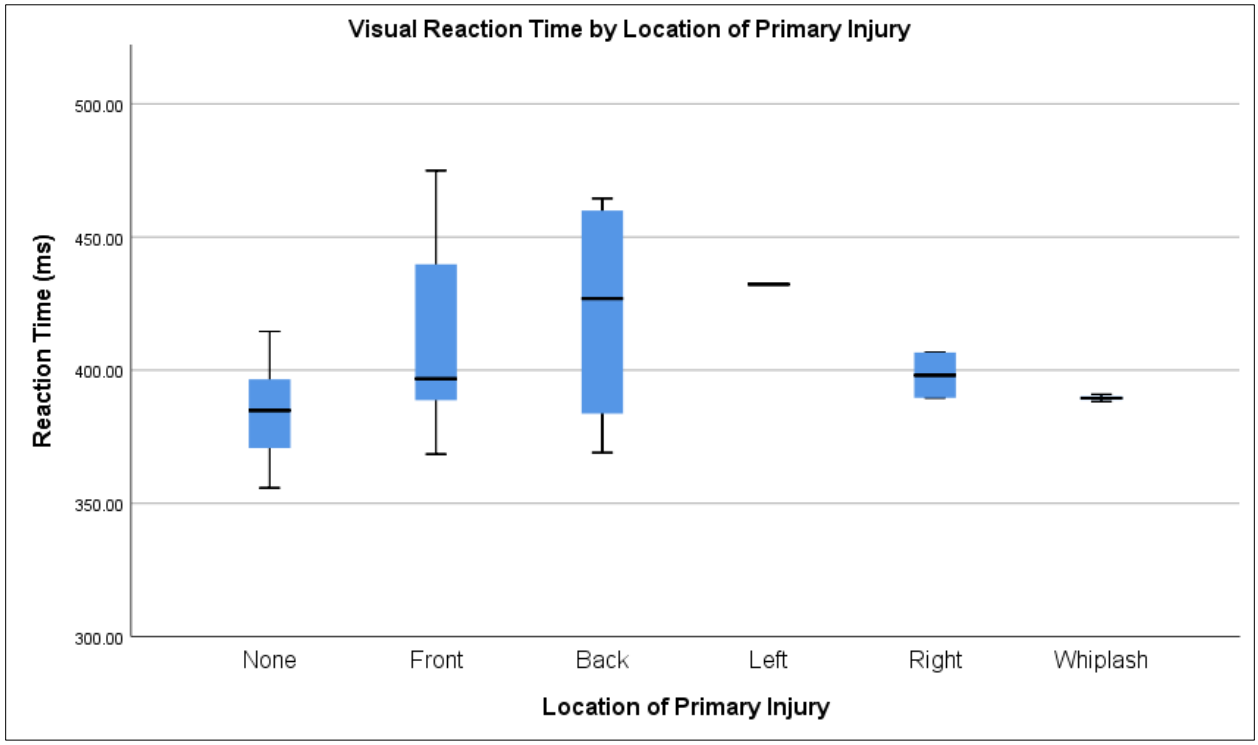

Figure 22: Visual Reaction Time with Reported Location of Primary Injury as a Factor

Auditory ERP Component Analysis

A one-way ANOVA was conducted to compare the effect of group membership on ERP component latency and amplitude for N1, P2, and P3 components near the Fz, FCz and Cz scalp locations. There were no significant main effects between groups for any ERP component at the FCz or Fz locations at the $p<.05$ level. ERP waveforms by group are shown in Figure 23 and results below are in reference to the Cz location only (See Table 17).

Table 17

ANOVA for Group Grand Average P2 / P3 Amplitude & Latency at Cz Scalp Location

Source		df	SS	MS	F	p
Frequent Tone P2 Amplitude	Between Groups	2	1.714	.857	.461	.637
	Within Groups	20	37.132	1.857		
	Total	22	38.846			
Frequent Tone P2 Latency	Between Groups	2	.001	.001	.917	.416
	Within Groups	20	.013	.001		
	Total	22	.014			
Rare Tone P2 Amplitude	Between Groups	2	40.667	20.333	11.391	.000*
	Within Groups	20	35.701	1.785		
	Total	22	76.367			
Rare Tone P2 Latency	Between Groups	2	.000	.000	.570	.574
	Within Groups	20	.005	.000		
	Total	22	.005			
Frequent Tone P3 Amplitude	Between Groups	2	4.768	2.384	2.755	.090
	Within Groups	18	15.574	.865		
	Total	20	20.342			
Frequent Tone P3 Latency	Between Groups	2	.006	.003	1.170	.333
	Within Groups	18	.044	.002		
	Total	20	.050			
Rare Tone P3 Amplitude	Between Groups	2	6.820	3.410	1.031	.377
	Within Groups	18	59.556	3.309		
	Total	20	66.375			
Rare Tone P3 Latency	Between Groups	2	.007	.004	1.532	.243
	Within Groups	18	.041	.002		
	Total	20	.048			

At the Cz scalp location, there was a significant main effect of P2 component amplitude for the rare tone condition [$F(2, 20) = 11.391$, p = .000]. Data approached significance for the P3 component amplitude at the Cz scalp location for the frequent tone condition [$F(2, 18) = 2.755$, p = .090]. ANOVA was also completed on the P3 Frequent minus Rare difference for each group to further investigate the P3 amplitude effect and did not show any significant differences (See Table 18).

Table 18

ANOVA for Group Grand Average P3 / P2 Frequent Minus Rare Condition Amplitude & Latency

Source		df	SS	MS	F	p
P2 Freq-Rare	Between Groups	2	.382	.191	.018	.982
Difference	Within Groups	18	187.445	10.414		
Amplitude	Total	20	187.827			
P2 Freq-Rare	Between Groups	2	.001	.000	.282	.758
Difference Latency	Within Groups	18	.028	.002		
	Total	20	.029			
P3 Freq-Rare	Between Groups	2	22.519	11.259	2.384	.121
Difference	Within Groups	18	85.002	4.722		
Amplitude	Total	20	107.521			
P3 Freq-Rare	Between Groups	2	.000	.000	.302	.743
Difference Latency	Within Groups	18	.004	.000		
	Total	20	.004			

An additional comparison was investigated with tinnitus as a factor in P2/P3 amplitude to evaluate individual differences within the participants experiencing tinnitus, given this group did not differ from controls. THI score was included as a measure of subjective tinnitus severity. THI score and rare tone grand average P2 amplitude was not correlated, $r(7) = .21$, $p = .351$. THI score and rare tone P3 amplitude were also not correlated, $r(7) = .89$, p=.43.

Figure 23 displays the grand average waveform for the control group, Figure 24 displays the concussion group, and Figure 25 displays the concussion with tinnitus group, visually demonstrating the significant effect of P2 in the rare condition and P3 in the frequent tone condition. Condition 1 (frequent) is shown in blue and condition 2 (rare) is shown in orange.

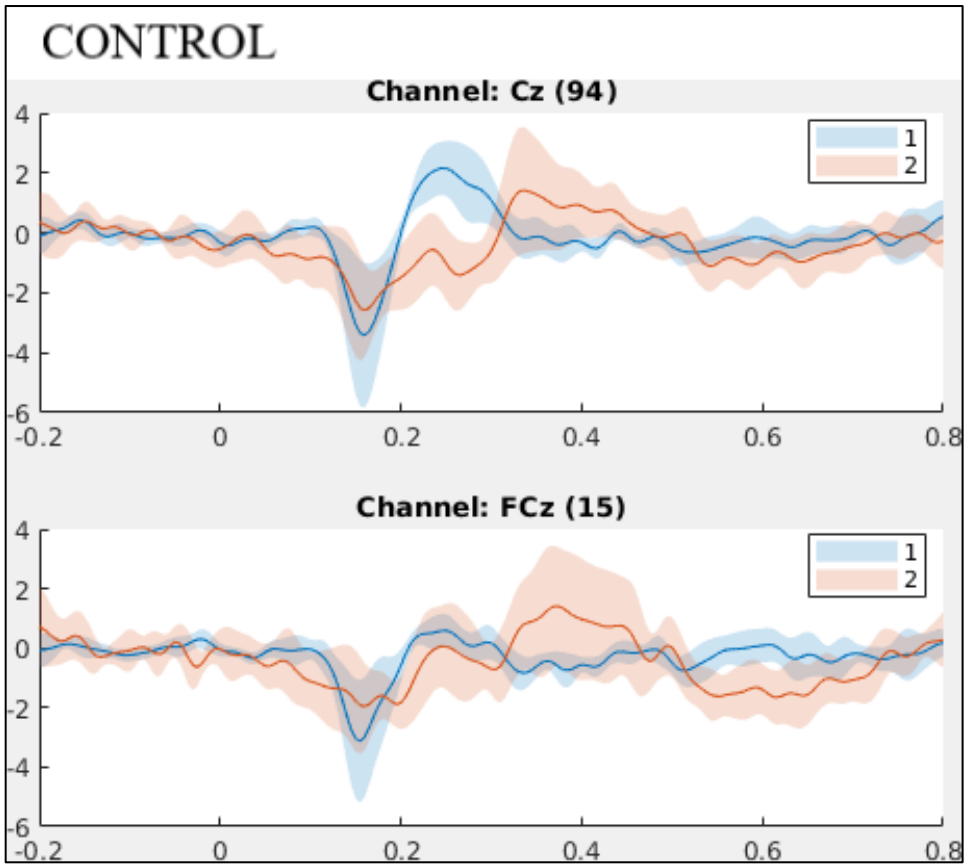

Figure 23: Control Grand Average ERP Waveform

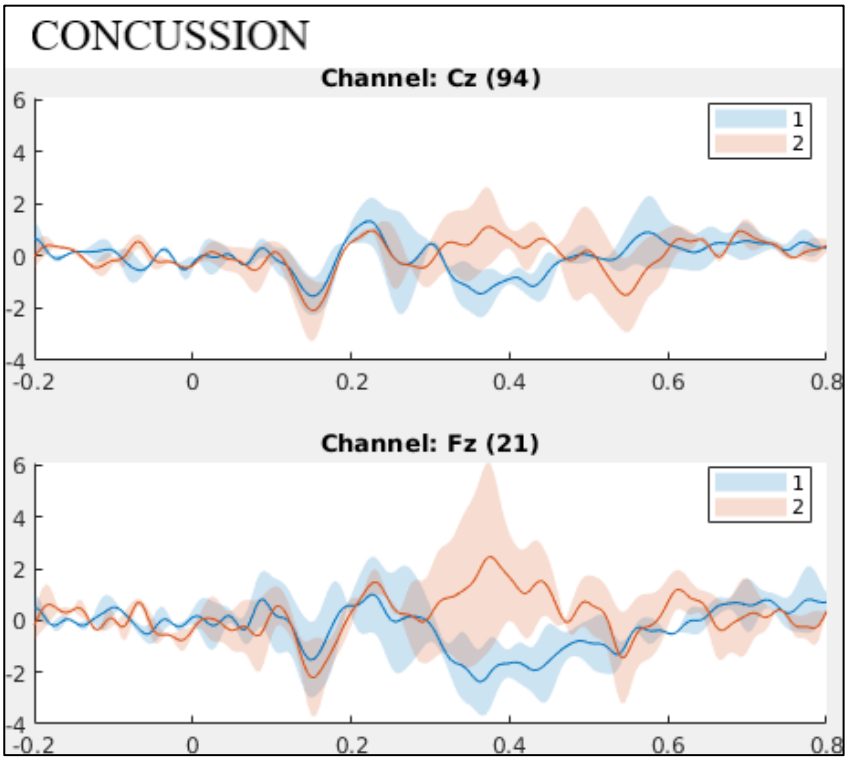

Figure 24: Concussion Grand Average ERP Waveform

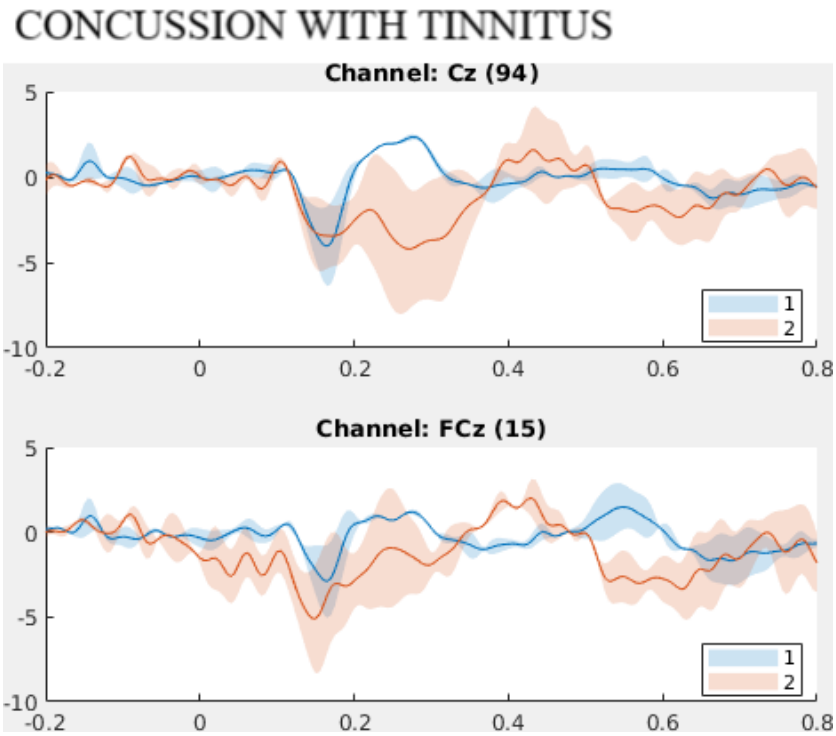

Figure 25: Concussion with Tinnitus Grand Average ERP Waveform

EEG Heatmaps of the entire scalp associated with each grand average for group mean response at N1, P2, and P3 components are illustrated in Figure 26 for the Concussion Group, Figure 27 for the Control Group, and Figure 28 for the Concussion with Tinnitus Group. The top row represents the frequent tone condition and the bottom row represents with the rare tone condition. Negativity is shown as blue and positivity is shown as yellow on the heat maps. The maps are oriented as a 'top down' view with the participants' eyes oriented toward the top of the figure. Cz is marked with a red star near the center of the map.

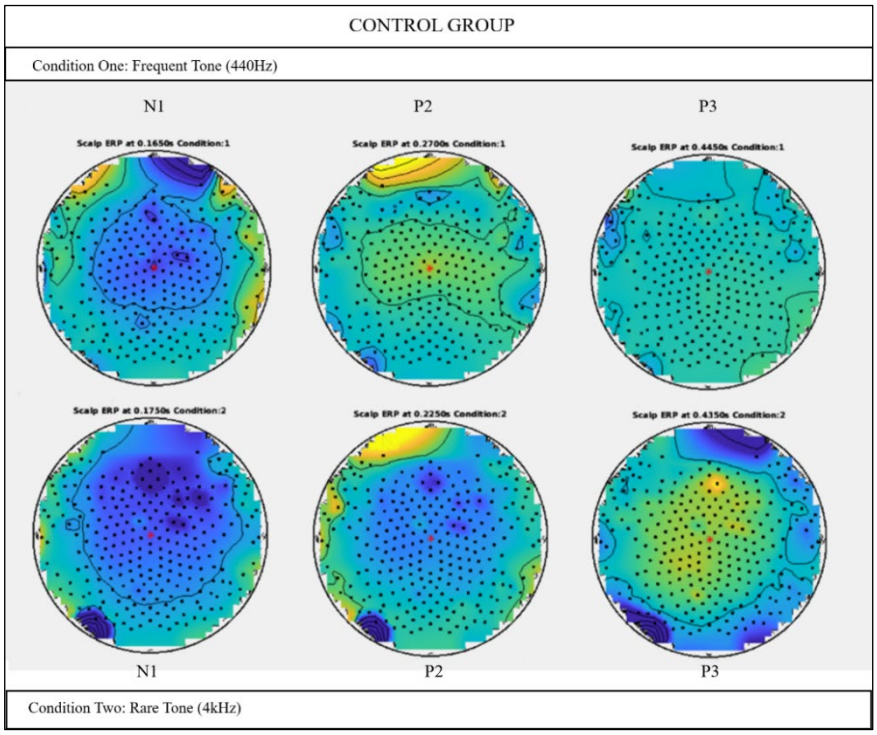

Figure 26: EEG Heatmap for Control Group Grand Average Response for Auditory ERP N1, P2, and P3 for the Cz Scalp Location

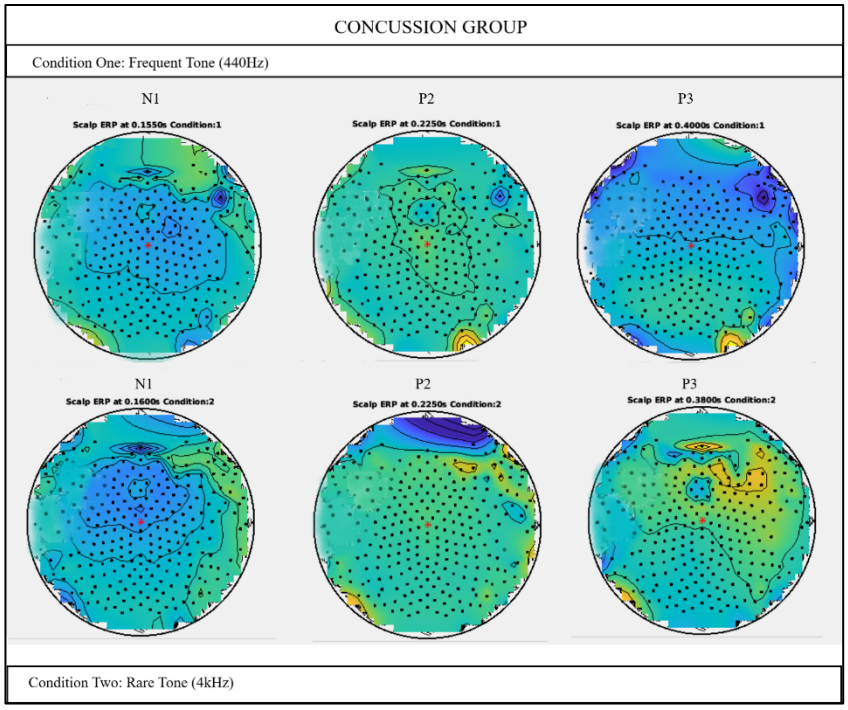

Figure 28: EEG Heatmap for Concussion Grand Average Auditory ERP N1, P2, and P3

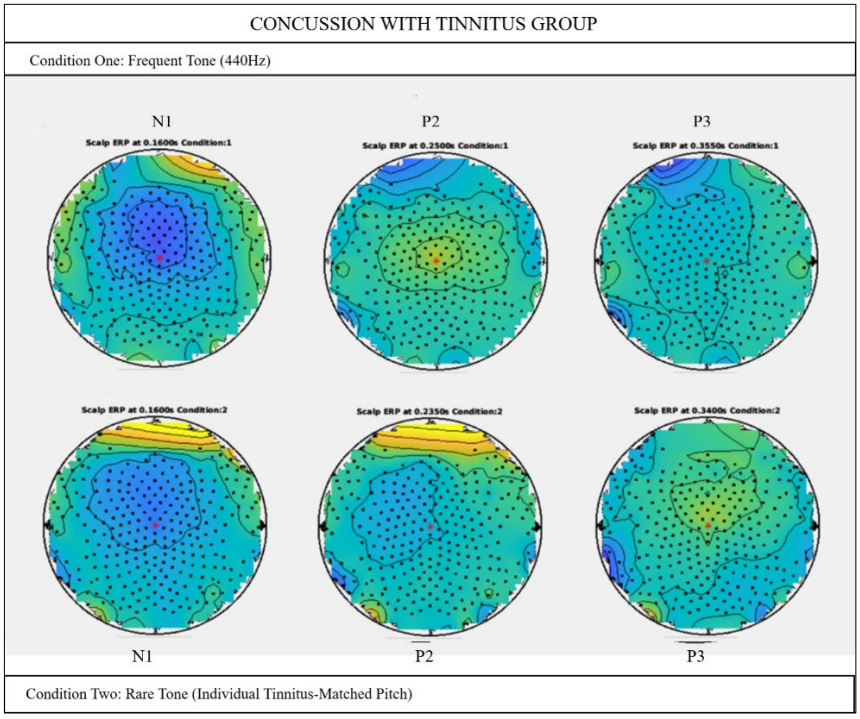

Figure 27: EEG Heatmap for Concussion with Tinnitus Grand Average Auditory ERP N1, P2, and P3

Bonferroni post-hoc analysis indicated grand average P2 amplitude for the rare tone stimuli was higher in the concussion group (M= 1.514 μV, SD=1.126) than controls (M=-1.806 μV, SD=1.593), and the concussion with tinnitus group (M=-.760, SD=1.267). The grand average P2 amplitudes were not significantly different between controls and the concussion with tinnitus group (M=(p=.408). Figure 29 shows a graphical representation of group mean for auditory P2 amplitude during the rare tone ERP condition.

For comparison, Figure 30 shows a graphical representation of group mean for auditory P3 amplitude during the frequent tone ERP condition that approached but did not meet significance.

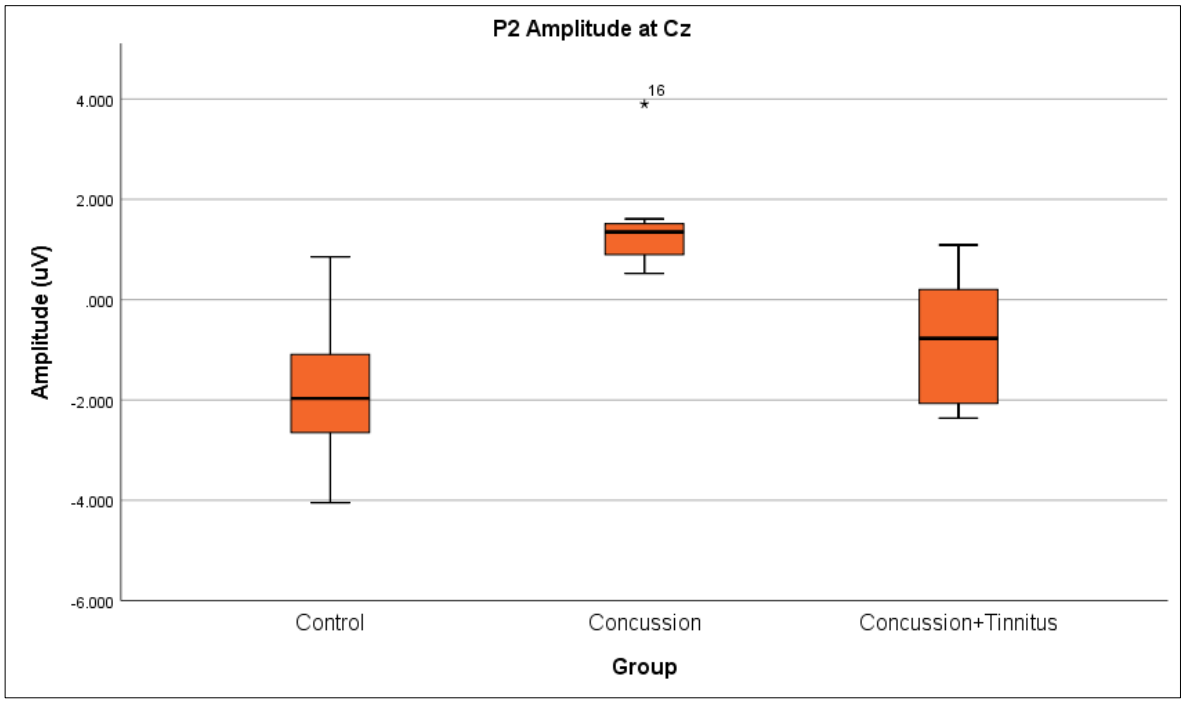

Figure 29: ERP Component P2 Amplitude by Group for Rare Tone at the Cz Scalp Location

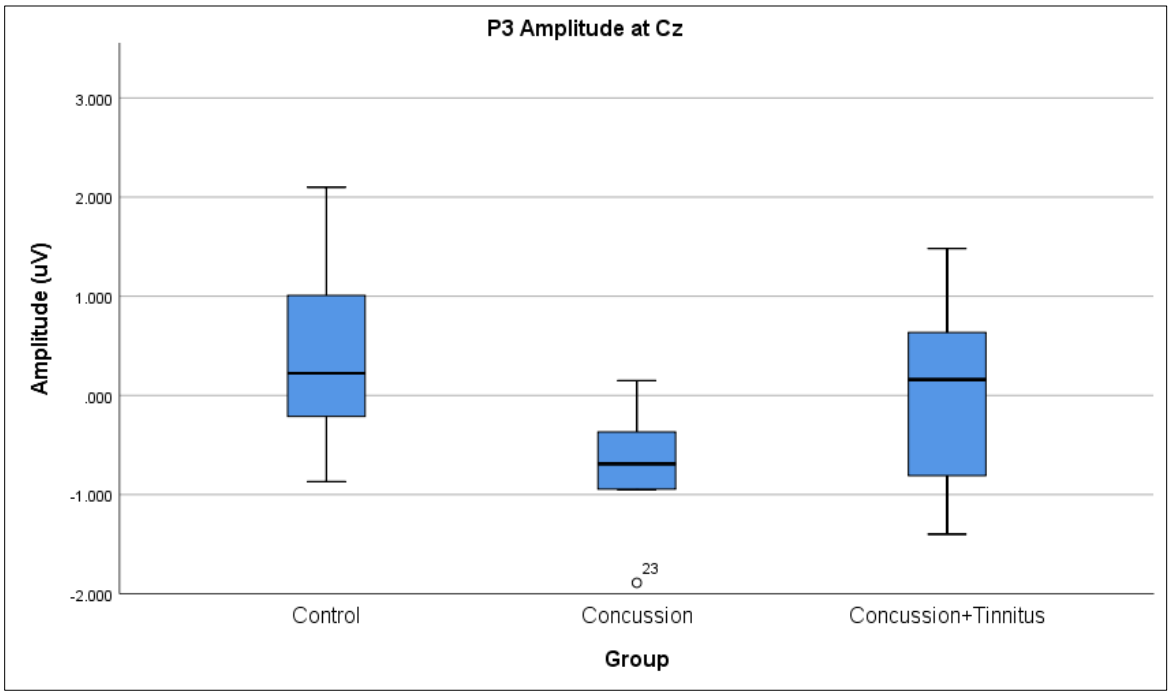

Figure 30: ERP Component P3 Amplitude by Group for Frequent Tone at the Cz Scalp Location

ERP component P2 is shown visually by group grand average as an EEG heat map in Figure 31. The heat maps portray a top-down look at cortical responses with the participants eyes oriented toward the top of the figure. The group with concussion showed higher P2 amplitude than control or concussion with tinnitus participants and positivity is shown as yellow on the heat map. This difference is evident near the red indicator star marking Cz where both the control and concussion with tinnitus groups are bluer (negative) than the concussion group.

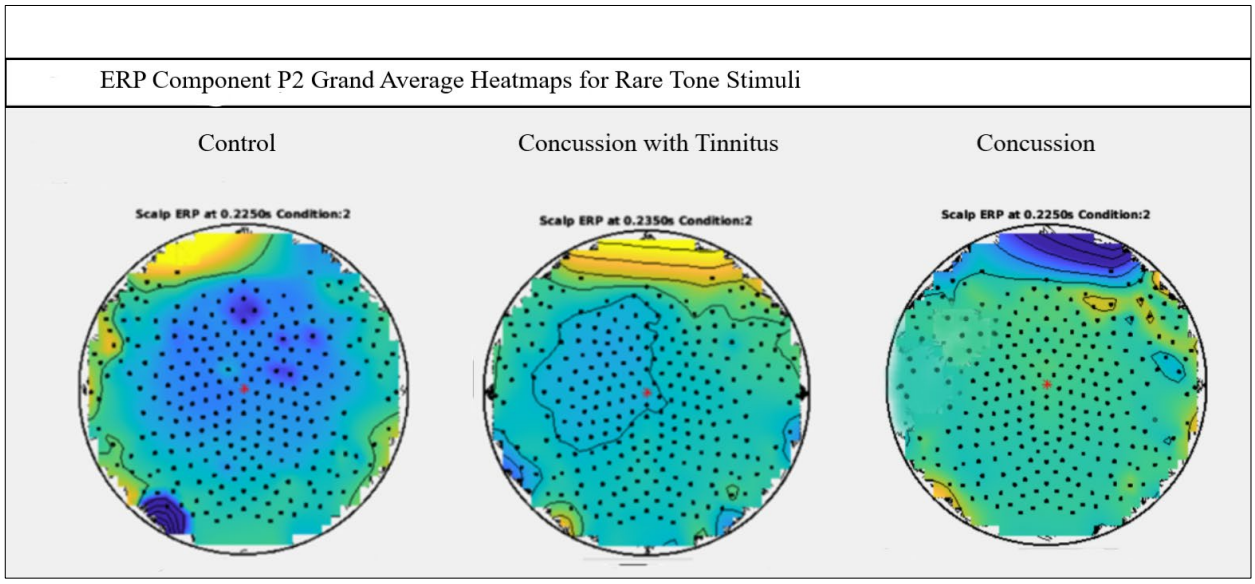

Figure 31: EEG Heatmaps by Group for ERP Component P2 Rare Tone Condition

Conversely, the group with concussion is more negative (bluer) at the central Cz location than the control or concussion with tinnitus group for the P3 component demonstrating the P3 amplitude differences approaching statistical significance where the concussion group showed lower P3 amplitude (Figure 32).

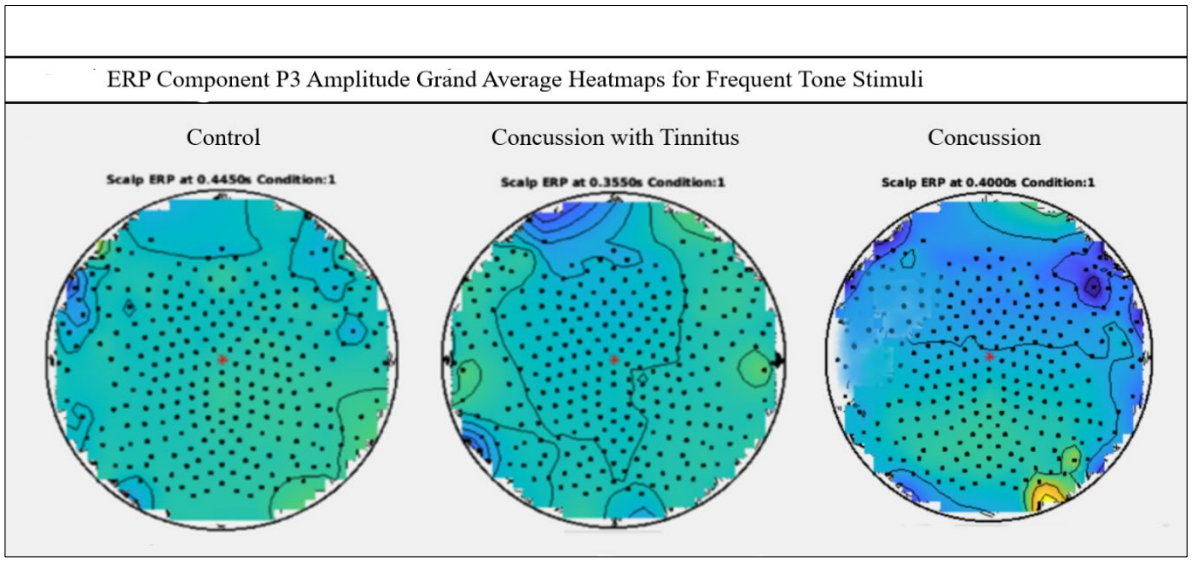

Figure 32: EEG Heatmaps by Group for ERP Component P3 Frequent Tone Condition

Independent samples t-tests were used to evaluate concussion as a factor in the P2 amplitude differences shown in the main effect for rare tones (See Figure 33). There was a significant effect for concussion, $t(21) = .015$, $p=.012$, where participants with concussion ($M=.235$, $SD\ 1.649$) displayed higher average P2 amplitudes than participants without concussion ($M=-1.806$, $SD=1.59$).

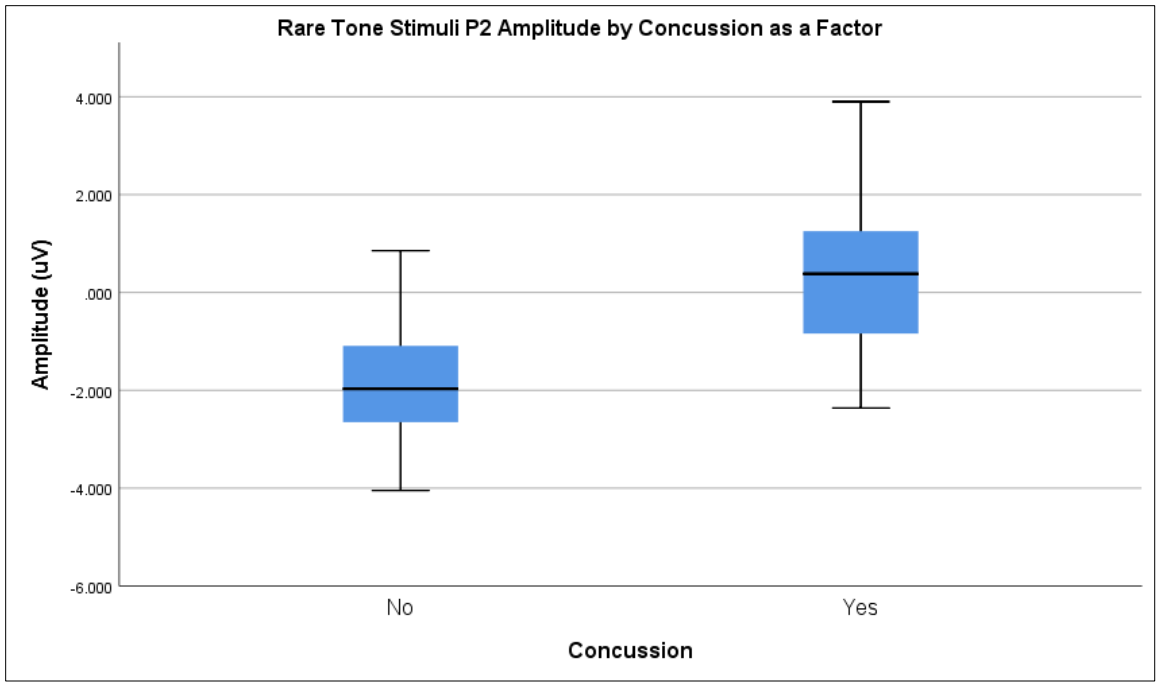

Figure 33: Component P3 Amplitude in the Rare Tone Condition for Participants with and Without Concussion

Similarly, independent samples t-tests were used to evaluate concussion as a factor in the P3 amplitude differences approaching statistical significance for the frequent tone. There was no significant effect for concussion, t(19) = .073, p=.085, despite participants with concussion (M= -.368, SD .915) displaying lower average P3 amplitudes for rare stimuli than participants without concussion (M= .435, SD=1.03).Participant PCCS scores and time from injury were compared to evaluate whether concussion severity and recency influenced resulting P3 amplitude.

A linear regression was used to predict P3 amplitude for rare stimuli from PCCS score and days post injury at the time of data collection. PCCS score and time from injury did not explain a significant amount of the variance in P3 amplitude for participants with concussion, $F(1,12) = .621$, $p=.446$, $R^2 = .049$, $R^2_{adjusted}=-.030$.

Visual ERP Component Analysis

A one-way ANOVA was conducted to compare the effect of group membership on ERP component latency and amplitude for P1, N1, P2, and P3 components near the Cz scalp location. There were no significant main effects of group for any ERP component (P1, N1, P2, P3) amplitude with frequent visual stimuli or rare visual stimuli (See Table 19).

Table 19

One-Way Analysis of Variance of Group Mean ERP Component Amplitude for Visual Frequent and Rare Stimuli

Source		df	SS	MS	F	p
VISUAL FREQ P1	Between Groups	2	.555	.278	.149	.863
	Within Groups	15	27.886	1.859		
	Total	17	28.441			
VISUAL RARE P1	Between Groups	2	.399	.199	.333	.722
	Within Groups	15	8.973	.598		
	Total	17	9.371			
VISUAL FREQ N1	Between Groups	2	.129	.064	.033	.967
	Within Groups	14	27.138	1.938		
	Total	16	27.267			
VISUAL RARE N1	Between Groups	2	3.966	1.983	.758	.486
	Within Groups	15	39.234	2.616		
	Total	17	43.199			
VISUAL FREQ P2	Between Groups	2	21.685	10.843	1.884	.188
	Within Groups	14	80.550	5.754		
	Total	16	102.235			
VISUAL RARE P2	Between Groups	2	.978	.489	.206	.816
	Within Groups	15	35.567	2.371		
	Total	17	36.545			
VISUAL FREQ P3	Between Groups	2	5.066	2.533	.345	.714
	Within Groups	15	110.279	7.352		
	Total	17	115.346			
VISUAL RARE P3	Between Groups	2	2.340	1.170	.390	.683
	Within Groups	15	44.956	2.997		
	Total	17	47.296			

Similarly, there were no significant main effects of group for any ERP component (P1, N1, P2, P3) latency with frequent visual stimuli or rare visual stimuli (See Table 20).

Table 20

One-Way Analysis of Variance of Group Mean ERP Component Latency for Visual Frequent and Rare Stimuli

Source		df	SS	MS	F	p
VISUAL FREQ P1	Between Groups	2	.002	.001	.897	.429
	Within Groups	15	.013	.001		
	Total	17	.014			
VISUAL RARE P1	Between Groups	2	.001	.000	.183	.835
	Within Groups	15	.023	.002		
	Total	17	.024			
VISUAL FREQ N1	Between Groups	2	.001	.001	1.277	.308
	Within Groups	15	.008	.001		
	Total	17	.009			
VISUAL RARE N1	Between Groups	2	.000	.000	.094	.910
	Within Groups	15	.018	.001		
	Total	17	.019			
VISUAL FREQ P2	Between Groups	2	.002	.001	.453	.644
	Within Groups	15	.032	.002		
	Total	17	.034			
VISUAL RARE P2	Between Groups	2	.003	.002	.638	.542
	Within Groups	15	.035	.002		
	Total	17	.038			
VISUAL FREQ P3	Between Groups	2	.011	.006	2.020	.167
	Within Groups	15	.042	.003		
	Total	17	.054			
VISUAL RARE P3	Between Groups	2	.008	.004	1.214	.325
	Within Groups	15	.048	.003		
	Total	17	.055			

Individual comparisons were made between participants with and without concussion for visual ERP component (P1, N1, P2, P3) amplitude and latency. Independent samples t-tests indicated there were no significant effects for concussion for any component amplitude or latency.

Similarly, there were no significant effects of tinnitus for any component amplitude or latency. Although no significant differences between groups or additional factors of concussion and tinnitus were found, EEG heatmaps for the visual ERP tasks are shown for comparison between concussion (Figure 34), concussion with tinnitus (Figure 35), and control group (Figure 36). Negativity is shown as blue and positivity as yellow; bad channels in the control group are indicated as focal dark blue/yellow areas. Cz is indicated by the centrally located red star. The view is top down with participant eyes toward the top of the figures.

Additionally, ERP waveforms by group are shown in Figure 37 to illustrate the wave morphology where no significant differences were shown between groups despite the P2 frequent circle amplitude looking visually distinct as they did for auditory ERPs.

Finally, an independent samples t-test was used to compare participants with and without photophobia as reported on the PCSC as a comparison to the contrast made for auditory ERPs with and without tinnitus. There were 8 participants reporting photophobia, 5 from the concussion with tinnitus group and 3 from the concussion without tinnitus group. This comparison failed to find significant differences in visual-evoked ERP amplitude or latency of P1, N1, P2, or P3.

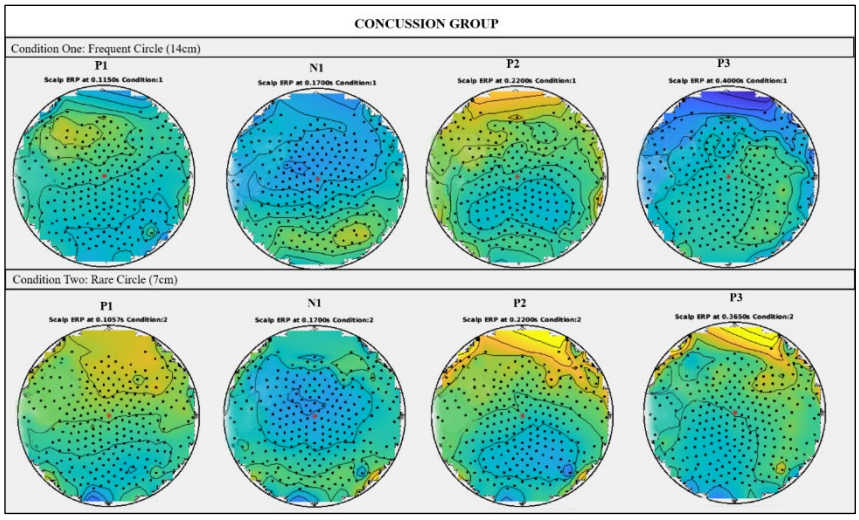

Figure 3434: Concussion EEG Heatmaps for Visual ERP

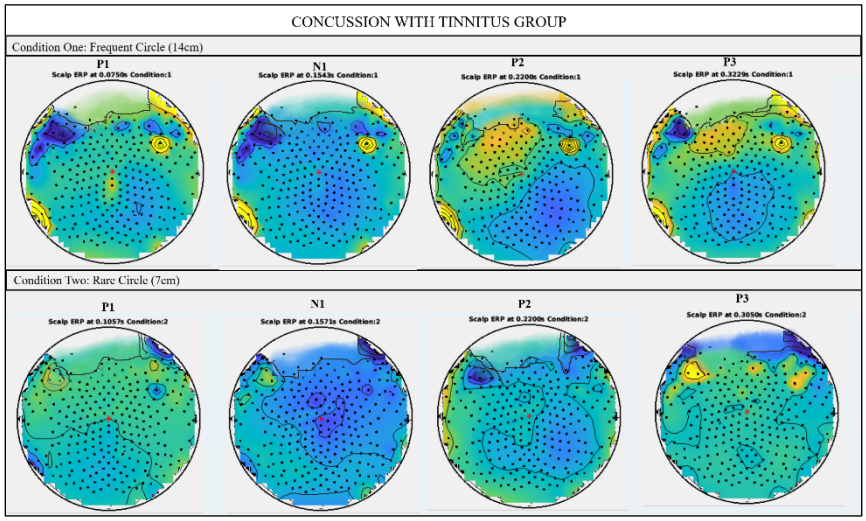

Figure 35: Concussion with Tinnitus EEG Heatmaps for Visual ERP

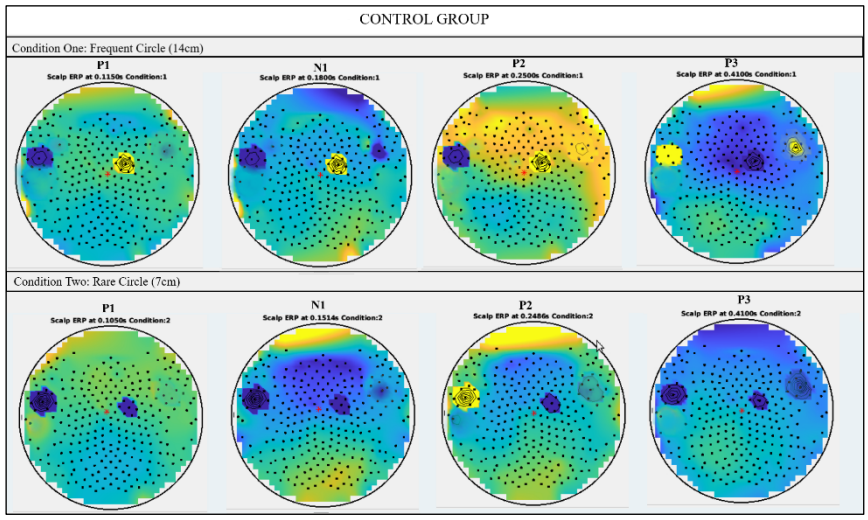

Figure 36: Control EEG Heatmaps for Visual ERP

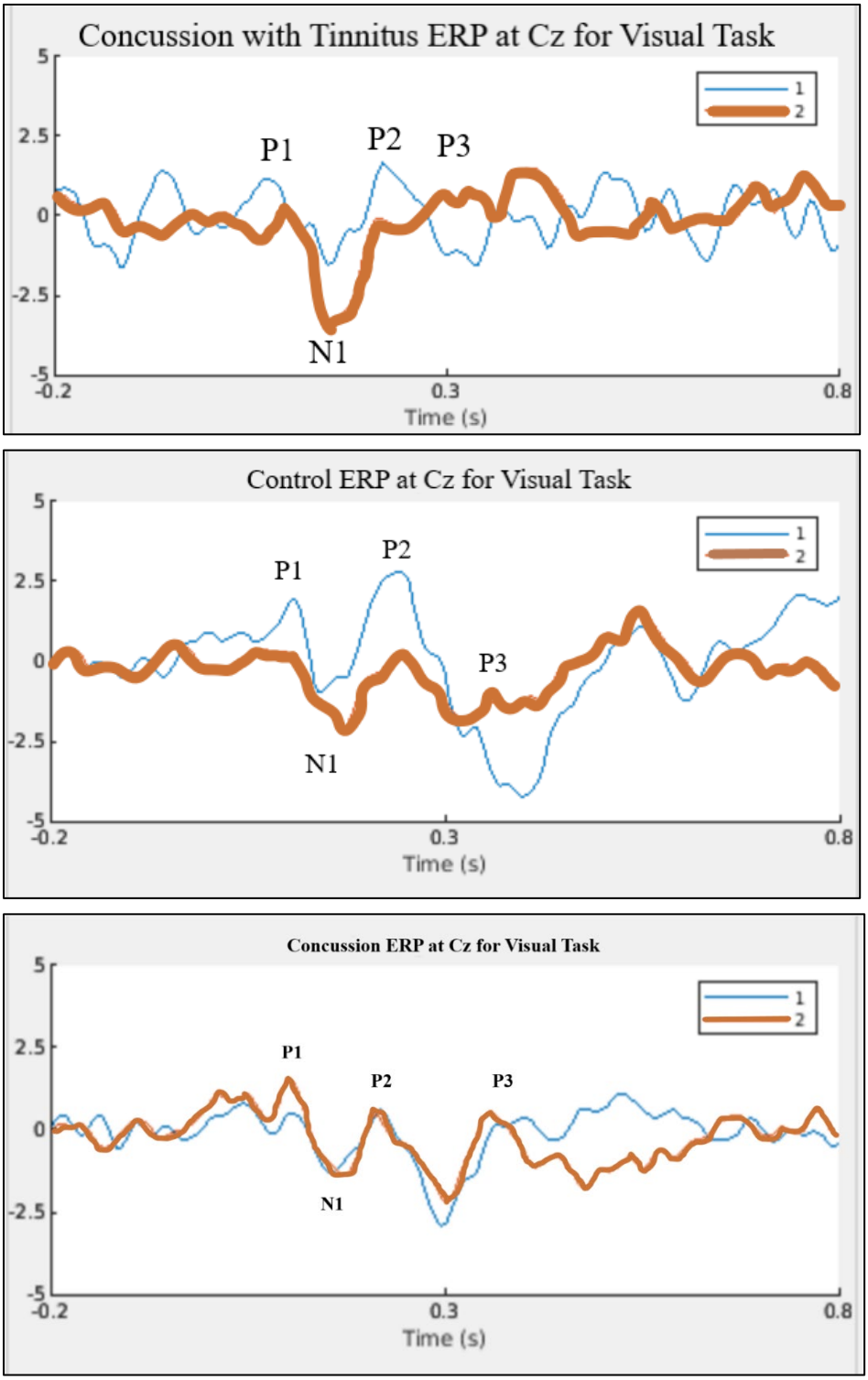

Figure 35: Visual-Evoked ERP Waveform for Frequent (1) and Rare (2) Circle Stimuli

Chapter 4: Discussion

The purpose of this study was to evaluate central auditory changes following concussion and specifically to determine if the presence of an auditory symptom like tinnitus influenced auditory-evoked ERPs. Beyond implications for identifying an objective assessment of tinnitus, ERPs are currently used to track brain injury and recovery. It is important to understand if tinnitus disrupts a person's cortical response to auditory stimuli; if that is the case then new techniques and stimuli should be considered for brain injury purposes.

To establish if tinnitus due to central factors as it appears following concussion, participants were recruited with low noise history and seemingly normal hearing so that peripheral hearing loss or underlying effects of noise exposure might be minimized. A few research groups have suggested that auditory-ERPs are abnormal for participants with traditional peripheral tinnitus (Araneda et al., 2015; Yang et al., 2013). This suggests that a peripheral deficit in hearing influences central representation of sound, which is a commonly held concept.

Particularly for the P3 component, there are reports of reduced amplitude and increased latency compared to normal controls. Additionally, participants with tinnitus show slower reaction times and higher false-positive rates when completing auditory oddball ERP tasks (Araneda et al., 2015; J. Attias et al., 1993; Azevedo et al., 2020). These data represent tinnitus from a myriad of sources, but likely peripheral in generation given the lack of differentiation in current research. This project aimed to evaluate ERPs in tinnitus following a cortical injury instead of noise exposure or peripheral auditory damage in general. Patients with a new onset of tinnitus after a cortical injury like concussion, represent some of the most severe clinical cases of tinnitus despite often having normal hearing thresholds. If the ERP patterns persist in a population where tinnitus is generated without peripheral hearing involvement, it would help

establish that this group may indeed represent a divergent population with tinnitus that warrants investigation into the underlying mechanisms involved.

In a recent chart review of 179 patients with tinnitus from the KU Health Partners clinic, only head injury accounted for a significant proportion of variance in reported tinnitus severity $R^2 = .245$, $F(1, 241) = 42.64$, $p < .05$ when compared with age, gender, degree of hearing loss, history of noise exposure, history of ototoxic medication use, heart disease, diabetes, migraine, and smoking status.

These clinical observations gave rise to the idea that tinnitus from a concussion represents a distinct symptomology and might require different diagnostic approaches and interventions than traditional peripheral tinnitus. Before intervention options can be compared, it was important to compare current clinical diagnostic tools in their ability to detect auditory system changes following a concussion.

Although concussions are known to affect cortical neurons via primary injury, there is no expected sequalae of peripheral symptoms which vary greatly across patients. The incidence of tinnitus as a symptom is generally unknown in part, due to the lack of inclusion of tinnitus on most concussion symptom checklists.

The primary problem examined through this research was whether isolating a subset of people with tinnitus who shared a cortical injury as the source, would allow for objective tinnitus assessment at the cortical level. Objective markers of tinnitus have eluded researchers, and this could be due to the diversity of tinnitus generators included in study populations. Additionally, an aim was to examine whether tinnitus affects the speed and accuracy at which a participant can complete an ERP task. Concussion assessment tools like the Immediate Post Concussion Assessment and Cognitive Testing (ImPACT; (M. Lovell, Collins, Podell, Powell, & Maroon,

2001; M. R. Lovell et al., 2006) utilize auditory stimuli to track injury and recovery, which is problematic if tinnitus alters one's ability to perform such tasks .

To establish whether tinnitus could 1) be generated centrally and 2) influence participants' performance on an auditory cognitive processing exercise, a group with concussion who did not experience tinnitus, a group with concussion and new-onset tinnitus, and a control group were put through peripheral and central auditory diagnostic testing.

Peripheral Findings

The three groups in this study were small, but cohesive in age and gender. It was important to control for normal peripheral auditory function so that differences in central ERP data could be interpreted as related to the central brain injury and not underlying hearing loss. The groups were not found to differ on the puretone audiogram, on a cochlear assessment of outer-hair cell function (DPOAEs), or on MEMR assessment of cranial nerve function.

However, definitive trend was visualized where the participants with tinnitus showed worse high-frequency peripheral hearing. Similarly, MEMR differences approached significance where the group with concussion and tinnitus showed a less steep growth function of the MEMR as the BBN elicitor level increased. It is likely the group experiencing tinnitus did not have normal peripheral auditory function, but the current diagnostic tools used in this study were unable to detect these changes. Without hearing threshold for BBN, there could be no comparison between hearing acuity within the normal range and sensation level of the elicitor. This would be an important contrast in the future if MEMR is going to be examined specifically as an objective assessment of tinnitus via synaptopathy.

Central Findings

The subjective assessment of central auditory function, the Dichotic Digits Test, showed a significant difference where participants with concussion scored significantly worse than controls. However, the presence of tinnitus did not affect DDT scores in a similar manner.

It could indicate the presence of tinnitus is not enough to affect central processing and participants may need to exhibit chronic or more severe tinnitus for effects to be demonstrated. Likewise, the DDT may not represent a cognitively challenging enough task to distinguish abnormal central auditory activity in participants with tinnitus.

Including ERP analysis with the DDT might give insight into whether the task is challenging enough to alter P3 function. Trends might appear where the large amplitudes and relatively short latencies shown for P3 in the simple auditory oddball paradigm move toward smaller amplitudes and/or longer latencies giving an objective measure of the additional resources used to process numbers for participants with concussion to the subjective DDT test.

Interestingly, the right-ear advantage was upheld in participants with concussion and participants with concussion and tinnitus. There is evidence that people with tinnitus perform worse on dichotic testing overall or lose the right-ear advantage (Cuny, Chéry-Croze, Bougeant, & Koenig, 2004; Reiss & Reiss, 2001). There is even data to support that this difference can be remediated through rTMS therapy (Barwood et al., 2013; Cuny et al., 2004). However, these data often represent lateralized tinnitus and may indicate that dichotic listening ear advantage and asymmetrical tinnitus represent the same functional asymmetry in the auditory system. In this study population, all participants experienced bilateral tinnitus, so the right-ear advantage was upheld as expected.

As far as utility in identifying auditory central changes from a concussion, the Dichotic Digits test represents a fast, non-invasive tool that correctly separated head injury from controls, at least for this sample. It would be important to repeat testing over time once the concussion is resolved and determine whether these initial differences persist. Also, since tinnitus represents secondary concussion processes, repeat testing out of the acute phase may be the earliest central differences related to the tinnitus can be measured.

A small subset of participants in this study returned for testing after concussion resolution and DD scores were shown to significantly improve. This data was not included due to the extremely small number of repeated measures (n=3) available. Given the likelihood of individual variability in dichotic listening skill, larger numbers and repeated measures would be needed to determine if the DDT would be beneficial to include in a concussion diagnostic toolkit.

The objective central test, the auditory and visual ERPs failed to distinguish participants with tinnitus across conditions and comparisons in terms of reaction time or accuracy. Interestingly, the participants with concussion and tinnitus showed similar P2 and P3 amplitudes as controls during auditory conditions, while the participants with concussion who did not have tinnitus showed larger P2 amplitudes and reduced P3 amplitudes as a group.

This suggests that the presence of tinnitus did not impair participants' ability to correctly identify target tones and may even lead to failed identification of concussion if auditory tests are used in the diagnostic battery for concussion. The abnormal neural activity related to tinnitus perception may mask the differences in cortical responses seen in concussion.

Visual conditions were included for ERP tasks to evaluate whether concussion affects the overall cortical response during an ERP task, or if differences were domain specific. Component analysis included N1, P2, and P3 for comparison with auditory-evoked ERP main effects, with

the addition of P1 for the visual conditions only. The grand average amplitude and latency was not significantly different across groups for the visual ERP task as shown in the auditory task.

The similar amplitude and latency across groups could be related to the central Cz recording location. Although visual ERP amplitude, particularly N1, is shown to be similar across recording sites for standard EEG sensor densities under 20 (Katayama & Polich, 1999), comparing more sites with the HD-EEG (256 channel) system may reveal differences in P1 or N1 amplitude between groups not seen at the central Cz scalp location. The visual N1 response is highly variable on how interesting a target is, and like the auditory N1, it is recruited from neurons throughout the cortex. N1 in particular, is thought to arise from diffuse neurons across the occipito-parietal and occipito-temporal cortex and not strictly from the visual cortex in the occipital lobe (Clark, Fan, & Hillyard, 1994). A comparison of temporal scalp locations may also prove beneficial in further analysis of the auditory ERP components given the auditory cortex location and similar influence of attention which involves more frontal neuron recruitment (Zouridakis, Simos, & Papanicolaou, 1998).

Chapter 5: Conclusions

Central generation of Tinnitus

The current data fail to identify diagnostic tools that separate participants experiencing tinnitus from those who do not following a concussion. Participants with tinnitus also could not be distinguished from controls, and no significant differences shown in this study were related to the presence of tinnitus in any capacity.

Influence of Tinnitus on Auditory ERPs

Auditory ERP data did not separate participants with tinnitus from controls, which presents a potential issue when using auditory stimuli to evaluate concussion at the cortical level. Although the participants in this study had a recent concussion, their auditory ERP findings were similar to the controls which means they would fail to be identified as having a concussion when looking at auditory-evoked potentials. Only the participants with a concussion and no tinnitus showed significant differences in auditory ERP which manifest as increased P2 amplitude and reduced P3 amplitude. Wave latencies were not different between any group, suggesting that normal variability in latency may mask subtle changes, or more likely, that an increased number of participants is needed to see significant latency differences. If this is the case, ERP oddball tasks as a clinical test are likely not sensitive enough for benefit. Additionally, the simple puretone used in the auditory condition, and visually simple grey circle for the visual condition may not tax central processing systems enough for differences to emerge. In the Araneda (2015) paper, the authors included a bimodal task in addition to the unimodal auditory and visual conditions where participants were asked to respond both to rare tones and rare circle targets. Although the unimodal design did not produce differences in these participants with concussion,

the bimodal task may provide the difficulty needed to extract auditory central deficits related to concussion.

To provide a reference comparison in the visual task, participants reporting photophobia were compared on resulting P2/P3 amplitude and latency. There were no significant differences with photophobia, a visual symptom of concussion, as a factor. Although visual ERPs did not appear to be influenced by the presence of a visual symptom, they also failed to separate participants with concussion from controls. This suggests the use of auditory-evoked potentials may be beneficial as an objective, non-invasive tool for diagnosis and recovery monitoring. However, it is suggested that patients be screened for tinnitus prior to any cognitive evaluation that uses auditory stimuli. These data support the idea that tinnitus influences the amplitude of ERP components in a way that makes it more difficult to separate them from normal peers.

Limitations of the Current Study

The project described provides an introductory exploration into ERPs as a clinical tool in the assessment of concussion and specifically, in objective assessment of tinnitus. Data collection began in 2019 and immediately the challenge of recruitment in the concussion clinic was noted. Recruitment of patients with little to no reported noise history and relatively normal puretone audiometric thresholds provided a barrier during initial patient screening. To maintain a focus on central generation models of tinnitus, it was important for the current project, to try and reduce the influence of peripheral noise damage in the cochlea on the ERP data. A large majority of tinnitus research includes populations with noise exposure, so this distinction was the primary emphasis for the current project.

There were additional recruitment issues related to the clinical concussion population and recruitment during the first 4 weeks post-injury. Patients routinely experienced transportation

issues, conflicts with work schedules after being off for extended periods related to their injury, physical pain and limitations related to their concussion, and in general, a lack of desire to participate during their acute injury. It was important to try and recruit during the acute injury period given the high variability in recovery time following concussion and increasing likelihood that symptoms and subsequent ERP changes would resolve over time. It is possible that ERPs change for the worse over time as people shift cognitive resources to account for the neurological changes following concussion. P3 is considered highly cognitive and repeating the same oddball paradigm at intervals during recovery may illustrate this concept if it is the case.

Specific limitations related to the study tools included a lack of resolution for MEMR amplitude recordings with the current clinical MEMR recording device (Otoflex). Data collection was restricted to two decimal places so loudness growth curves could not be compared across groups as in the Wojtczak study as many responses were recorded as 0.00 mmhos using the Otoflex device (M. Wojtczak, J. A. Beim, & A. J. Oxenham, 2017). Additionally, elicitor stimuli were limited to puretone and broadband noise (BBN). Use of click stimuli with contralateral wideband noise is not a method currently available with clinical devices, so further exploration of the MEMR differences seen in this concussion population would require specialized research equipment.

Overall, a small sample likely contributed to the peripheral differences in this study failing to meet significance; not that the groups were peripherally similar. The trends seen in puretone audiometry, DPOAE amplitude, and MEMR amplitude at increasing elicitor level together indicate the auditory periphery may have been abnormal in the group experiencing tinnitus prior to their head injury. It is consistent with current literature on tinnitus where current audiological diagnostic tools are not sensitive enough to separate peripheral auditory damage

from normal function, and these participants could exhibit cochlear synaptopathy despite normal test results (Guest et al., 2017; Kujawa & Liberman, 2009).

For central measures, the Dichotic Digits Test accurately separated participants with concussion from controls, but this test is subjective and would be susceptible to issues with reliability. For the objective central test, ERP recording limitations included varying number of useable channels across subjects as determined through electrode signal-to-noise analysis. Although the EGI system has 256 potential recording channels, neuromuscular artifact and artifact related to poor channel contact with the scalp changed the potential utility and final number of channels for each subject. The ERP setup was modeled after Araneda (2015) to include 440 Hz as the frequent tone with 4kHz or the tinnitus pitch as the rare tone. In retrospect, it would have made sense to use 750 Hz as the low tone given it was the lowest F2 test frequency obtainable using our clinical DPOAE device. These tones still represent distinct regions in the cochlea, which was important for the oddball paradigm, but it would allow for better comparison of the auditory periphery at those specific cochlear sites when aligned with DPOAE F2 stimuli.

Eight of the twenty-four participants could not be analyzed for the visual ERP waveform analysis due to errors within their raw EEG files. The lack of differences between groups for visual ERPs could be related to the reduced sample size in this condition compared to the auditory condition. However, 5 of the 8 participants were from the tinnitus group which did not show significant differences from controls in the auditory ERP tasks. Three participants from the control group were excluded and their data might have significantly contributed to the grand average response and ultimate differences shown in the auditory ERP conditions.

Additionally, there was an apparent ceiling effect for behavioral ERP reaction time and accuracy measures. Increasing the difficulty of the task may better distinguish participants with

tinnitus by challenging their attentional systems in a way that competes with tinnitus compensatory strategies. Increased difficulty could include lower presentation level, shorter ISIs, shorter tone presentations, or even multimodal paradigms where participants are asked to respond to visual and auditory targets in tandem.

Future Directions

Auditory ERPs as an Objective Assessment of Tinnitus

The data discussed in this paper failed to demonstrate the utility of auditory ERPs as an objective assessment of tinnitus. At this point, it cannot be determined if audiology training programs should look to expand content and clinical practice with EEG so future clinical providers are comfortable and competent utilizing this non-invasive, objective tool more regularly. For tinnitus, it does not appear to offer objective diagnostic value, at least with the current oddball task difficulty. A more complex design may stress the attention and memory systems implicated in concussion and tinnitus to a degree where changes in performance or resulting ERP amplitude/latency are found.

For concussion, the question remains. Next steps should include examination of ERP components for individuals with concussion and unresolved tinnitus > 4 months post-concussion and a comparison of ABR and ERPs as objective assessment tools in concussion regardless of tinnitus report. ABR is already a common diagnostic tool in audiology and there is ample data to support that concussion alters the central auditory cortex. With the differences seen in MEMR amplitudes across elicitor levels in this study, it would be valuable to include ABR as a contrasting objective tool in evaluation of the auditory nerve and connections with higher brainstem centers.

There is evidence that ABR may provide an indirect, but objective look at cochlear synaptopathy in humans where some ears with normal audiograms exhibit a reduced Wave I amplitude (Tepe, Smalt, Nelson, Quatieri, & Pitts, 2017; Xiong et al., 2013). However, the data are mixed on whether Wave I is consistently reduced in humans with tinnitus, and comparison of the N1/P2 slope or interpeak intervals may provide better estimation of underlying noise damage (Cartocci et al., 2012; Guest et al., 2017; Meehan, Hebert, Deru, & Weaver, 2019). Wave V might also show beneficial comparisons given it is the last stop before the cortex, which was the focus of this study. There is emerging evidence that ABR comparisons might be useful in identifying central auditory dysfunction following a head injury as well, so future work related to tinnitus and specifically tinnitus from a concussion, should include ABR given its ability to objectively assess function at the auditory nerve (CN VII), and the auditory brainstem (Meehan et al., 2019).

Auditory ERPs to Monitor Concussion Recovery

Auditory ERPs have been utilized in monitoring treatment effect for auditory training therapies related to Auditory Processing Disorders (APD) as well as treatments related to tinnitus and concussion recovery (Alonso & Schochat, 2009; Reches et al., 2017; Yang et al., 2013).

Specifically, long-latency ERPS like the auditory P3 are useful as they represent cognitive functions like attention and memory which are known to be impaired in all three of these populations (Hudac, Cortesa, Ledwidge, & Molfese, 2018; N. Kraus et al., 1995; Milner et al., 2020; Tai & Husain, 2019). P3 wave latency has well-established norms, and additionally, normative data representing latency reduction following auditory discrimination therapy (Didoné et al., 2016; Tremblay et al., 2001). Although this data failed to distinguish participants with

tinnitus, the lack of separation is interesting given the concussion group without tinnitus performed consistently worse and with lower response amplitude across central tests.

The differences seen only in participants with concussion and no tinnitus, reinforce the idea that tinnitus, at the very minimum, needs to be included on all concussion symptom checklists. A non-finding in this data was an unexpected and alarming discovery. Altered activity in the cortex related to tinnitus representation may lead to wrongful interpretation of auditory evoked potentials following a concussion. The tinnitus group in this study performed similarly to controls in terms of reaction speed and accuracy, also presenting with similar latency and amplitudes of auditory N1, P2, and P3 components despite having a recent concussion. A next step might be to compare a variety of auditory signals for use in cortical evaluation following concussion and determine if choice of stimuli impacts the ability to correctly identify who has a concussion, who has tinnitus, and who is a control participant.

Finally, the data presented here make a case that concussion affects the auditory system without obvious symptomology, which was not the intended question, but raises an alarming new question. It is possible that lasting central auditory changes are occurring with concussion, but our current standard of care does not include diagnostic evaluation, or even inclusion of these deficits on symptom checklists, yet alone protocols for appropriate remediation and care. Better initial identification of auditory symptoms will lead to increased awareness of these symptoms for concussion providers outside of audiology. It is an imperative step in better understanding the underlying neural mechanisms responsible for the deficits shown in this data, and ultimately, for helping to improve recovery options for our patients.

Appendix

Appendix A

Tinnitus Handicap Inventory (Newman et al., 1996)

Instructions: The purpose of this questionnaire is to identify problems your tinnitus may be causing you. Check **Yes, Sometimes,** or **No** for each question. Do not skip a question.

		Yes (4)	Sometimes (2)	No (0)
1F.	Because of your tinnitus is it difficult for you to concentrate?	___	___	___
2F.	Does the loudness of your tinnitus make it difficult for you to hear people?	___	___	___
3E.	Does your tinnitus make you angry?	___	___	___
4F.	Does your tinnitus make you feel confused?	___	___	___
5C.	Because of your tinnitus do you feel desperate?	___	___	___
6E.	Do you complain a great deal about your tinnitus?	___	___	___
7F.	Because of your tinnitus do you have trouble falling to sleep at night?	___	___	___
8C.	Do you feel as though you cannot escape your tinnitus?	___	___	___
9F.	Does your tinnitus interfere with your ability to enjoy social activities (such as going out to dinner, to the movies)?	___	___	___
10E.	Because of your tinnitus do you feel frustrated?	___	___	___
11C.	Because of your tinnitus do you feel that you have a terrible disease?	___	___	___
12F.	Does your tinnitus make it difficult for you to enjoy life?	___	___	___
13F.	Does your tinnitus interfere with your job or household responsibilities?	___	___	___
14F.	Because of your tinnitus do you find that you are often irritable?	___	___	___
15F.	Because of your tinnitus is it difficult for you to read?	___	___	___
16E.	Does your tinnitus make you upset?	___	___	___
17E.	Do you feel that your tinnitus problem has placed stress on your relationship with members of your family and friends?	___	___	___
18F.	Do you find it difficult to focus your attention away from your tinnitus and on other things?	___	___	___
19C.	Do you feel that you have no control over your tinnitus?	___	___	___
20F.	Because of your tinnitus do you often feel tired?	___	___	___
21E.	Because of your tinnitus do you feel depressed?	___	___	___
22E.	Does your tinnitus make you feel anxious?	___	___	___
23C.	Do you feel that you can no longer cope with your tinnitus?	___	___	___
24F.	Does your tinnitus get worse when you are under stress?	___	___	___
25E.	Does your tinnitus make you feel insecure?	___	___	___

F denotes an item on the functional subscale; E, an item on the emotional subscale; and C, an item on the catastrophic response subscale.

Appendix B

1-Minute Noise Screen

Name: _____ Date: _____

DURING THE PAST YEAR (12 months),	
1.	How often were you around or did you shoot firearms such as rifles, pistols, shotguns, etc.? ☐ Never ☐ Every few months ☐ Monthly ☐ Weekly ☐ Daily
2.	How often were you exposed to loud sounds while working on a paid job? By loud sounds, we mean sounds so loud that you had to shout or speak in a raised voice to be heard at arm's length. ☐ Never ☐ Every few months ☐ Monthly ☐ Weekly ☐ Daily
3.	How often were you exposed to any other types of loud sounds, such as power tools, lawn equipment, or loud music? By loud sounds, we mean sounds so loud that you had to shout or speak in a raised voice to be heard at arm's length. ☐ Never ☐ Every few months ☐ Monthly ☐ Weekly ☐ Daily
	Noise exposure score: _____

How to Score Your

1-Minute Noise Screen

First, give yourself the following number of points for your answer to each question:

	Never	Every Few Months	Monthly	Weekly	Daily
Question 1.	0	1	2	3	4
Question 2.	0	1	2	3	4
Question 3.	0	1	2	3	4

Then, add your three individual scores together to get your total Noise Exposure Score. Enter this total number of points in the box in the lower right corner of your card.

See the reverse side of this sheet for an explanation of your Noise Exposure Score and suggestions for how to manage your risk of developing noise-induced hearing loss.

Example:

1-Minute Noise Screen

Name: ***Example*** Date: ***07/01/2015***

DURING THE PAST YEAR (12 months),

1.	How often were you around or did you shoot firearms such as rifles, pistols, shotguns, etc.? ☐ Never ☐ Every few months ☑ ~~Monthly~~ ☐ Weekly ☐ Daily ***Score: 0 1 2 3 4***
2.	How often were you exposed to loud sounds while working on a paid job? By loud sounds, we mean sounds so loud that you had to shout or speak in a raised voice to be heard at arm's length. ☐ Never ☐ Every few months ☐ Monthly ☑ Weekly ☐ Daily ***Score: 0 1 2 3 4***
3.	How often were you exposed to any other types of loud sounds, such as power tools, lawn equipment, or loud music? By loud sounds, we mean sounds so loud that you had to shout or speak in a raised voice to be heard at arm's length. ☐ Never ☑ Every few months ☐ Monthly ☐ Weekly ☐ Daily ***Score: 0 1 2 3 4***

Noise exposure score: *6*

1-Minute Noise Screen/University of Kansas Medical Center/Hearing & Speech Department/© 2016

1-Minute Noise Screen: Recommendations

If your Noise Score is in this range:	Then your Noise Risk is:	Explanation
0 to 4	Lower Risk	Based on your noise experiences during the past year, your risk of developing noise-induced hearing loss is relatively low if you continue to experience similar levels of noise in the future. However, if your noise exposures increase, your risk of developing hearing loss will increase as well. Everyone is different in their tolerance to noise, and it is difficult to predict your individual susceptibility. Still, it is important to remember that risk increases: the louder the sounds, the longer you spend around them, and the more often you are exposed. See the following tips for how you can manage your risk of developing noise-induced hearing loss. **Special note for firearm users**: If you use firearms, you are at high risk of hearing loss, even if you only use firearms every few months and have a low risk score on the 1-Minute Noise Screen. See the following tips for things you can do to manage your risk.
5 and above	Higher Risk	Based on your noise experiences during the past year, you are at risk of developing noise-induced hearing loss if you continue to experience similar or higher levels of noise in the future. Everyone is different in their tolerance to noise, and it is difficult to predict your individual susceptibility. Still, it is important to remember that risk increases: the louder the sounds, the longer you spend around them, and the more often you are exposed. See the following tips for how you can manage your risk of developing noise-induced hearing loss.

What You Can Do To Manage Your Risk:

- **Avoid loud noise when you can:** This may go without saying, but avoiding loud noise is a first step toward conserving your hearing for a lifetime. Remember, when you feel the need to shout to be heard by someone just a few feet away, the background noise levels are probably in a hazardous range. Look for quieter products when you buy noisy appliances or tools such as leaf blowers and lawn mowers. And turn down the volume when using electronic devices such as cell phones and music players.
- **Wear hearing protection whenever you are around loud noise**: When you can't avoid loud noise, be sure to wear well-fitted earplugs or earmuffs, even if your noise experiences are only occasional. Hearing protectors can be purchased at many pharmacies, and convenience, hardware, and sporting goods stores. Be sure you have proper training in the use and care of your hearing protectors, and replace them as needed. Proper and consistent use of hearing protection can lower your risk. This is especially true if you shoot firearms, where even one exposure to gunfire can damage your hearing if you are not wearing hearing protection.
- **Get regular hearing tests:** Keep an eye on your ears! Get a routine hearing test, once a year if you are in the higher risk category listed above or if you experience any increase in your exposure to noise. Keep track of your hearing test results and ask your audiologist to compare annual tests to your earliest test to look for any significant changes that may signal a concern.
- **Take care of your ears:** See your doctor if you notice problems such as sudden changes in hearing, or pain, "fullness," or ringing in your ears.

Appendix C

Sample Post-Concussion Symptom Checklist from the KU CCM O2 Electronic Medical Record

Symptoms		
Headache	2	3
Nausea	3	1
Vomiting	0	0
Balance Problem	2	2
Dizziness	4	3
Fatigue	3	3
Trouble Falling Asleep	5	5
Sleeping more than usual	0	3
Sleeping less than usual	3	5
Drowsiness	0	5
Sensitivity To Light	3	4
Sensitivity To Noise	0	4
Irritability	5	6
Sadness	5	6
Nervousness	5	5
More Emotional	5	6
Numbness or tingling and/or neck pain	5	3
Feeling Slowed Down	0	4
Feeling Mentally Foggy	5	6
Difficulty Concentrating	5	5
Difficult Remembering	5	5
Visual Problems	5	4
Neck Pain	1	0
Total Number Of Symptoms		
Total Symptoms Score	71	88

Appendix D

Dichotic Digits Double Pairs Sample

DICHOTIC DIGITS
Double Pairs

Standard Version

Name Jane Doe				Age 8		Date August 17, 2020					
Results: 78 % Correct Left Ear				72 % Correct Right Ear							
Channel	1	2		Number Correct		Channel	1	2		Number Correct	
Trial	Left	Right	Response	Left	Right	Trial	Left	Right	Response	Left	Right
1	4,1	6,8	4,1,6,8	2	2	26	2,1	4,8	2,1,8	2	1
2	5,8	4,3	8,5,3,4	2	2	27	6,8	9,4	9,4,6,8	2	2
3	3,9	6,5	3,6,5,9	2	2	28	1,5	4,2	1,5,4,2	2	2
4	4,5	8,1	4,8,1	1	2	29	9,4	2,5	9,4,5	2	1
5	2,6	3,9	2,4,9,3	1	2	30	1,9	6,2	6,2	0	2
6	6,4	1,2	6,4,1	2	1	31	6,2	5,8	5,8	0	2
7	4,9	8,6	4,9,8,6	2	2	32	4,9	2,6	4,9,6	2	1
8	2,4	5,1	2,5,1,4	2	2	33	3,1	5,9	3,5,9	1	2
9	5,2	4,9	5,4,9,2	2	2	34	8,4	3,6	8,4,3	2	1
10	2,6	9,1	9,1,2,6	2	2	35	2,3	8,6	2,3,8	2	1
11	8,5	2,6	8,5,2,6	2	2	36	3,6	1,9	3,6,1,9	2	2
12	6,4	9,2	6,4,9	2	1	37	8,1	6,5	1	1	0
13	9,5	1,3	9,5	2	0	38	5,2	9,1	5,2,9,1	2	2
14	6,3	4,8	6,3,4,8	2	2	39	4,8	3,1	1	0	1
15	6,8	3,2	6,8,3	2	1	40	9,5	8,3	9,5,8	2	1
16	9,1	6,3	3,6,9	1	2	41	4,2	5,9	5	0	1
17	5,6	1,8	5,1,8	1	2	42	1,5	6,2	1,5	2	0
18	1,9	2,5	1,2,5	1	2	43	3,6	8,4	3,6,8,4	2	2
19	1,3	8,4	1,3,8,4	2	2	44	9,3	2,1	9,3,2	2	1
20	3,8	5,9	3,8,5,9	2	2	45	5,4	3,8	5,4,3	2	1
21	8,6	1,4	8,6,1,4	2	2	46	9,6	5,2	9,6	2	0
22	3,4	8,5	8,5	0	2	47	9,2	1,8	1,8	0	2
23	5,6	9,3	5,6	2	0	48	4,5	6,3	4	1	0
24	4,8	5,4	4,8,5	2	1	49	4,8	9,5	4,8,9,5	2	2
25	1,3	6,2	1,3,6	2	1	50	6,1	2,3	2	0	1
			Column A Sum	43	41				Column B Sum	35	31
Column A Sum for Left Ear 43 + Column B for Left Ear 35 = 78 % Correct Left Ear											
Column A Sum for Right Ear 41 + Column B for Right Ear 31 = 72 % Correct Right Ear											

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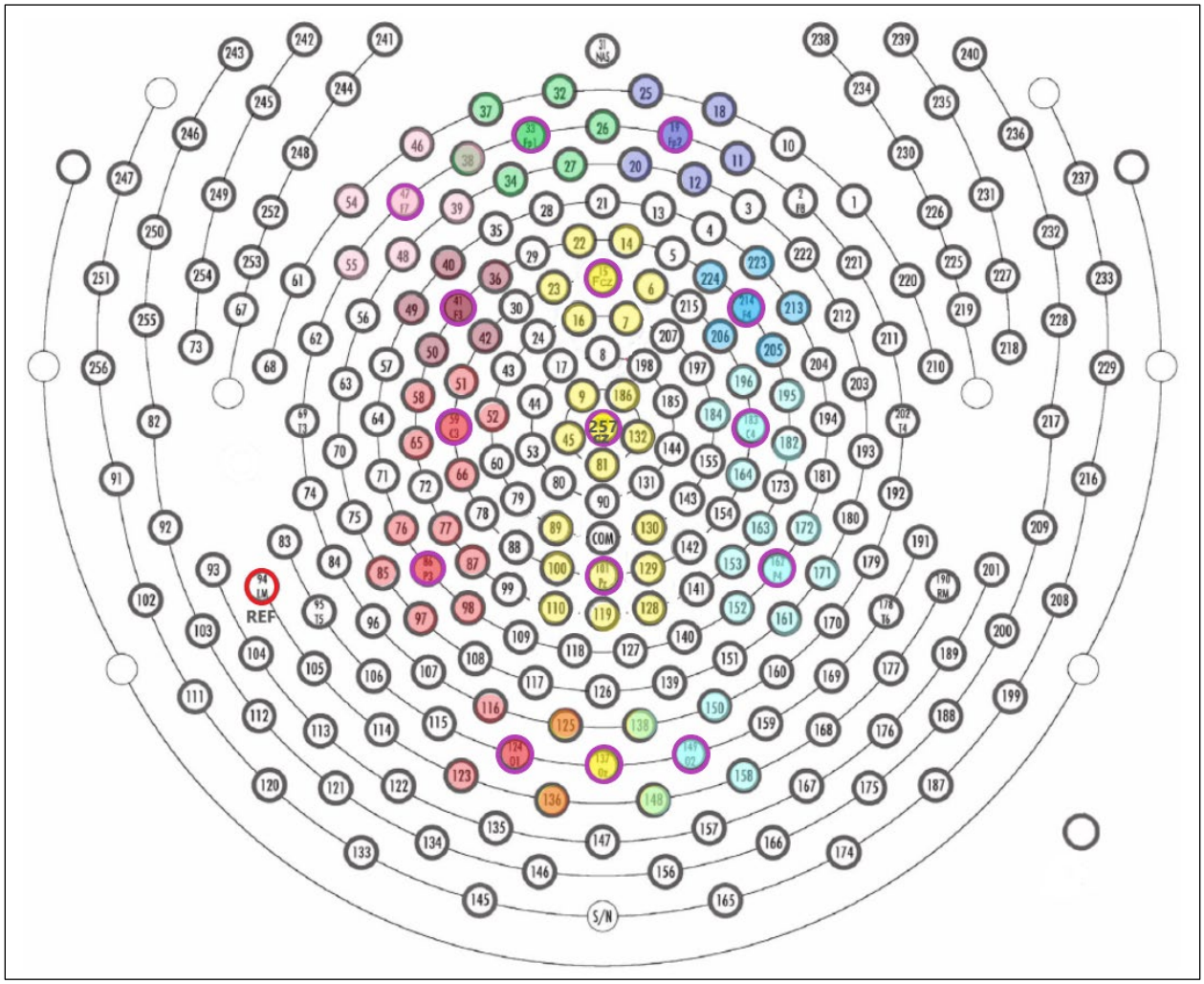
Appendix E

EGI High Density 256 Channel Sensor Map



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