January 2020

Parametric Study Of Short Latency Vestibular Evoked Potentials In Healthy Young Adults

Sabahet Fatima Rizvi
Wayne State University

PARAMETRIC STUDY OF SHORT LATENCY VESTIBULAR EVOKED POTENTIALS IN HEALTHY YOUNG ADULTS

by

SABAHET F. RIZVI

DISSERTATION

Submitted to the Graduate School

of Wayne State University,

Detroit, Michigan

in partial fulfillment of the requirements

for the degree of

DOCTOR OF PHILOSOPHY

2020

MAJOR: COMMUNICATION SCIENCES AND DISORDERS

Approved by:

_____

Advisor Date

_____

_____

_____

DEDICATION

This is dedicated to all those who helped shape me and taught me to follow my dreams. Firstly, to my parents - my mother and late father - who taught and instilled upon me the secrets of a meaningful life - to never give up and always trust God - through their inner strength, limitless patience, and endless compassion. Secondly, to my brother, Adeel, who has always been a role model for me - I hope to follow a similar path in Academia as you one day; many thanks for being the best big brother and friend since birth. Additionally, this is dedicated to all my family and friends who never quit praying for my health. A special thanks to my organ donor and their selfless family who gave me the gift of life, and without whom I would not be alive today. Finally, this is dedicated to my mentor, Dr. Cacace, and my committee members who were patient as I worked to complete my study, despite multiple setbacks. Many thanks to God for everything!

ACKNOWLEDGEMENTS

First and foremost, I want to thank my committee members for taking an active role in my dissertation. To my mentor, Dr. Anthony Cacace, thank you for supporting my studies. Although his time was limited due to his research, he regularly took the time to respond to any questions or concerns I had related to school or life in general. This study would not have been possible without him, as he allowed me to use his lab and equipment for this and all other studies I had the opportunity to conduct at Wayne State. Dr. Derek Daniels, thanks for keeping on top of paperwork and deadlines. Whenever I had any departmental questions, he was always quick to respond and happy to help. Your kindness is forever noted. Dr. Courtney Stewart, thank you for all your useful feedback; this dissertation definitely would not be the same without your technical knowledge of the anatomy involved in VsEPs and other helpful comments. Dr. Thomas Simpson, you have taught me since my Au.D. studies and I am forever grateful to both you and Dr. Frances Eldis for placing such trust in me to lecture some of your audiology classes. You always made me feel welcome in your classes with your great sense of humor, which definitely helped learn the material more easily. Your feedback, especially during my earlier teaching experiences, helped me gain more confidence in my speaking abilities. Additionally, thank you to Tim Susman for calibrating the equipment used for this VsEP study. Without proper calibration, this study would not be reliable; therefore, it would not have been possible to perform. Last but not least, a very special thanks to the individuals who graciously volunteered their time to come into the lab and be tested. I am forever thankful to you all, as it is the participants who genuinely make research possible.

TABLE OF CONTENTS

LIST OF TABLES

LIST OF FIGURES

CHAPTER 1
INTRODUCTION

The vestibular system consists of both peripheral (inner ear) and central (brainstem and brain) components that are essential for balance. Within the peripheral system, the otolith organs are activated by linear acceleration, whereas the semicircular canals are activated by angular acceleration (Todd, McLean, Paillard, Kluk, & Colebatch, 2014). Although numerous vestibular assessment protocols currently exist in clinical practice, the common aspect of these assessment approaches is that they generally require "observing or quantifying a motor output response" (Jones, 2008, p.379). Therefore, a major limitation of these current assessments is that they are indirect measurements of inner-ear function. However, it is possible to assess the vestibular system more directly by recording short latency evoked potentials (Jones, 2008).

Although the vestibular system can be stimulated with high intensity sounds, motion is required to elicit short latency vestibular evoked potentials (VsEPs) by using transient acceleration stimuli (angular, SCCs; linear, otoliths) that stimulate the vestibular organs, rather than auditory stimuli (Jones & Jones, 2007). In humans, VsEPs can be recorded using surface electrodes on the face and scalp with stimulation of the organs-of-balance. This present VsEP study is an assessment of otolith function, as the stimulus was presented via a bone-conduction vibration (BCV) device that induces linear-acceleration of the skull. VsEP appears to be a valid response of the vestibular system because responses can be seen in deaf individuals with normal vestibular functioning while being absent in

individuals with bilateral vestibular loss (Pyykko, Aalto, Gronfors, Starck, & Ishizaki, 1995).

While VsEP research is limited in humans, studies have shown that various types of stimuli (different durations, frequency, and intensity levels) can elicit VsEP in animals and humans alike (For review, see Brown, Pastras, & Curthoys, 2017). The use of longer latency (cortical) potentials predominates in human research, while a variety of angular (rotational) and linear VsEPs have been studied in animal models using various durations (Jones & Jones, 2007). Several animal studies have used invasive methods to assess VsEPs, such as coupling the head of an animal to a platform using skull screws, while other studies have found ways to test VsEPs using noninvasive procedures, such as coupling the electromechanical shakers directly to the beak in birds (Jones & Jones, 2007). Therefore, VsEPs have been assessed in both anesthetized and non-anesthetized animals, as no behavioral response is required to record VsEPs.

We will evaluate the feasibility of recording VsEPs in healthy humans using BCV and accomplished by evaluating the effects of stimulus frequency, intensity, along with masked and unmasked levels using specialized equipment.

CHAPTER 2
REVIEW OF LITERATURE

In order to better understand vestibular function and create an improved diagnostic tool to assess otolith function, the peripheral and central components of this system will be discussed. Current assessments of otolithic function, including cervical or ocular vestibular evoked myogenic potentials (cVEMPs, oVEMPs) and the novel approach used in this study; the short-latency vestibular evoked potentials (VsEPs) will be reviewed.

Anatomy and Physiology of the Vestibular System

The vestibular system comprises both peripheral and central components. Not only is the vestibular system responsible for maintaining posture and balance, but it also coordinates eye and head movements. Often, the anatomical locations responsible for vestibular and balance dysfunction are relatively straightforward to diagnose specific disorders as being either central or peripheral. However, this approach provides an incomplete picture of the diagnosis, as several central pathways in addition to the various components of the peripheral vestibular system exist (Yagi, 2003).

A review of the complexity of the normal peripheral and central systems is a necessary precursor to understanding when these systems go awry. The bony labyrinth of the inner ear is located within the petrous portion of the temporal bone. The bony labyrinth is a dense shell filled with perilymph, while endolymph fills the membranous labyrinth (Cullen, 2019; Yagi, 2003). Five sensory organs contained within the labyrinth of the inner ear make up the peripheral components of the vestibular system. These five organs include the three semicircular canals (SCCs; anterior, lateral, and posterior) and the two otolith organs (utricle and saccule). The geometric orientation represents an important

consideration. While the saccule is oriented in the vertical parasagittal plane, the utricle is oriented in approximately the same plane as the horizontal SCC (Harsha et al., 2008).

The three SSCs are arranged at right angles to each other, located on the horizontal (lateral SCC), superior (anterior SCC), and posterior planes of reference. The SCCs sense angular acceleration or rotational movements of the head.

The otoliths sense linear acceleration. There are three linear acceleration planes with respect to standing upright, these include up-down (superior-inferior), forwards-backwards (anterior-posterior), and side-to-side movements of the head (Harsha et al., 2008). In addition to linear acceleration, the otoliths also sense pull of gravity due to the weight of the otoconia (calcium-carbonate crystals) that rest on top of the gelatinous matrix; the weight of otoconia is about twice that of the endolymph (Smith, 2019; Harsha et al., 2008).

Vestibular Hair Cells

The vestibular hair cells housed within the membranous labyrinth are surrounded by endolymph fluid. SCCs have an ampulla (small swelling) at one end of each of the three canals that contain a crista (Harsha et al., 2008). While the cristae of the ampulae contain the hair cells in the SCCs, maculae of the otoliths contain the hair cells in the utricle and saccule. Movement of the head causes fluid motion within the membranous labyrinth, which activates or inhibits the hair cells, depending on the whether the stereocilia are bent towards the stationary kinocilium (excitation) or away from the kinocilium (inhibitory response).

Both cochlear and vestibular hair cells are sensitive to bone-conducted vibrations (BCVs) and air-conducted sound (Brown, Pastras, & Curthoys, 2017). In fact, high sound levels can cause not only permanent or temporary hearing loss but can lead to vestibular damage as well (Stewart et al., 2020). This is not surprising since the vestibular organs (SCCs and otoliths) share a continuous endolymph fluid pathway with the cochlea (Harsha et al., 2008). Additionally, the hair cells of the vestibular system are said to be the most critical, yet also the most fragile part of the vestibular system, as these cells can be damaged easily from multiple sources, including but not limited to: trauma (high-intensity noise exposure), infection, vestibulotoxicity, and increased age (Renga, 2019).

There are two types of vestibular hair cells and their stereocilia are surrounded by the endolymphatic fluid, known as Type I and Type II hair cells. It should be noted that Type I and Type II hair cells are found throughout the maculae, not just restricted to the striola or extrastriolar regions. The striola is line that runs through the center of the utricle and saccule and is the line of hair-bundle polarity reversal (Dimiccoli, Girard, Berthoz, & Bennequin, 2013).

The afferent fibers that innervate the two types of hair cells are categorized by the regularity/variability of the firing rate (Goldberg, 2000). While the afferents that innervate the Type I hair cells have a more irregular discharge (high variability), the afferents that innervate Type II hair cells have more regular (low variability) firing rates (Eatock & Songer, 2011).

Firing Rates

Since the extrastriolar regions cover the most surface area of the maculae, the otoliths are associated with more regular firing rates, which have the highest gains and phase leads at lower frequencies, while irregular rates (mostly clustered in the striola) have the higher phase leads and gains in the mid-to-high frequencies (Eatock & Songer, 2011). That is, "the otolith organs receive a low-frequency stimulus causing a fluid shift in the vestibule endolymph" (Renga, 2019, p.7), thus, they are most responsive to low-frequency stimuli.

Additionally, the afferent fibers of the Type II hair cells "show more of a tonic response that is more dependent on the amount of kinocilia deflected", while afferents of the Type I regions "show tonic-phasic responses to stimuli, which increase as the frequency of movement increases. Thus, they are more responsive to the time-rate of deflection" (Harsha et al., 2008, p. 48).

Similar to the shearing force of the stereocilia in the cochlea, the shearing force of the stereocilia bundles in the vestibular system induce either inhibition or excitatory neural transmission to the brain (Duncan, Stoller, Francl, Tissir, Devenport, & Deans, 2017). There are various vestibular reflexes and each have their own neural pathways. Neural transmission from the hair cells to the central nervous system occurs when the stereocilia of the vestibular organ sense movements.

Polarization of Hair Cells

Depending on the tip-links (structural connections that contact the stereocilia), if the bundles of stereocilia are bent towards the kinocilium (stationary), this causes increased

potassium to flow into the cell, which opens up the "mechanoelectrical transducer (MET) channels which then depolarizes the hair cell and initiates synaptic transmission to afferent neurons projecting centrally [via] the eighth cranial nerve" (Duncan et al., 2017, p.126). However, if the vestibular hair cells are bent away from the kinocilium, this causes tip-link tension, which causes an inhibitory response (Duncan et al., 2017).

It is the high potassium content within the endolymph that allows for hair cell and afferent nerve transmission, depending on bending properties of the stereocilia. Specifically, the influx of potassium causes depolarization and excitation (increase release of glutamine), while bending away from the stationary kinocilium content leads to tension and is inhibitory in nature due to hyperpolarization (Casale, Browne, Murray, & Gupta, 2020; Duncan et al., 2017)

Central Components

Various cortical regions are involved with vestibular function. While afferent fibers send sensory signals from the vestibular hair cells to the brain to provide input with respect to body position, gaze, posture, balance, and position, efferent signals allow for motor output of the afferent signals received by the brain. These efferent signals include the reflexes associated with the vestibular system, such as the vestibulospinal and reticulospinal pathways involved with the maintenance of upright head and body postures, through the coordination of the eyes, head movement, and spinal musculature (Rine & Wiener-Vacher, 2013).

The basic components of central processing reflect the most peripheral component, the hair cells located within the SCCs and otoliths of the peripheral vestibular system. Once

stimulated (either through movements, sound, and/or BCV), the afferent flow travels through the vestibulocochlear nerve (CN VIII), contained within "the internal auditory meatus [alongside] the seventh cranial nerve and enters the medulla at its junction with the pons. The central processes terminate within the vestibular and cochlear nuclei in the brainstem" (Wilson-Pauwels, Akesson, Stewart, & Spacey, 2002, p.142).

Vestibular Reflexes

Reflexes are involuntary responses that automatically occur after specific pathways are stimulated, either through physical movements or sensory stimulation. Reflexes can be elicited in multiple ways since there are numerous different types of reflexes; however, regardless of how they are elicited, there is always a receptor and actor. Recall that the hair cells of the vestibular system are the afferent (sensory) receptors for balance, but multiple systems vis-à-vis eyes, ears, and somatosensory components work together to sustain balance. With regards to the vestibular system, there are three main vestibular reflexes, which include: vestibulospinal, vestibulocolic, and vestibulo-ocular reflex (VOR), with the VOR being the most common reflex assessed during specific vestibular tests, specifically the oVEMP (Harsha et al., 2008). Recall that the peripheral and central components of the vestibular system work together to maintain proper postural and balance control and represents a complex multisensory system, that relies on the integration of inputs between multiple sources, such as the inner ears, eyes, spinal cord, skin and joint receptors and brain (Rine & Wiener-Vacher, 2013).

The vestibulo-ocular reflex (VOR) stabilizes the eyes during rapid head movements, which enables control of the head position on the body (Harsha, Phillips, &

Backous, 2008; Rine & Wiener-Vacher, 2013). On a similar note, visual reflexes such as the optokinetic reflex (OKR) can stabilize the eyes during low-frequency head movements, but not with high-frequency movements of the head (Harsha, Phillips, & Backous, 2008).

Again, this is important to mention when describing the purpose of eye closure and light being turned off to test in darkness in this current study; closing the eyes reduces any possible artifacts from the visual system. Additionally, most vestibular assessments are performed in the dark for this reason, as the VOR can stabilize eye gaze in high frequencies, while OKR is able to stabilize gaze in the low frequency range.

Current Diagnostic Vestibular and Balance Assessments

There are multiple vestibular assessment paradigms used clinically, including: electronystagmography, videonystagmography, and oculomotor subtests; caloric assessment, rotational testing, dynamic posturography, and VEMPs (El-Kashlan, & Handelsman, 2008). For the purpose of this study, only the otolith organs are assessed. For this reason, the primary focus moving forward will be to review VEMPs, which are the current method of otolith assessment routinely used in clinical practice.

Current Tests of Otolithic Function

Vestibular evoked myogenic potentials (VEMPs) are closest to the VsEPs being developed and performed in this study. VEMPs can be elicited through both air-conducted sound (ACS) and BCV. Another assessment, known as the Off Vertical Axis Rotation (OVAR) test, assesses the VOR by looking at nystagmus during whole-body off-axis rotation while seated in a rotary chair in a visually restricted environment (chamber). Nevertheless, several limitations exist. With VEMP testing, the final common pathway

requires sustained muscle contraction and this induces considerable variability in the response. With respect to the OVAR, this paradigm is unable to measure each individual otolith organ separately, but rather "provides a global assessment of otolithic function" (Wiener-Vacher, 2001, p.88). However, it should be noted that this assessment is useful for the evaluation of the laterality of the otolithic function by comparing VOR gain between responses (Sugita-Kitajima & Koizuka, 2014). It should be noted that the human body can be rotated in three different axes (x, y, and z-axis). The yaw refers to the movements along the z-axis (vertical plane) and allows for this vertical stabilizer to make left or right movements. With a change in the yaw-axis from the rotations, not only the otoliths, but the SSCs and ocular reflexes are assessed as well, and therefore OVAR is not a specific measure of otolith function (Sugita-Kitajima & Koizuka, 2014).

VEMP

There are two types of VEMP assessments, cervical (cVEMP) and ocular (oVEMP) vestibular evoked myogenic potentials, both of which are said to be short-latency muscle mediated reflexes (Smith McCaslin, Jacobson, & Burkard, 2019). VEMPs can be elicited through a high-intensity auditory stimulus that is presented to the ear via ACS or through BCV. The VEMPs assess otolith function, where the cVEMPs are "thought to reflect the function of the saccule and inferior vestibular nerve" (El-Kashlan & Handelsman, p.13). On the other hand, oVEMPs reflect the activity of the utricle and superior vestibular nerve. To record VEMPs, muscle reflex activity is recorded with surface electrodes, which are typically placed near or on the activated muscles (Smith et al., 2019).

Just as their names suggest, the cervical (cVEMPs) record the neck muscles through the sternocleidomastoid muscle (SCM), with the electrode often referenced at the mid-clavicle or sternal notch (sternoclavicular junction) (El-Kashlan & Handelsman, 2008). The ocular (oVEMPs) record the eye muscles; thus, the electrodes are often placed near the eyes around the inferior oblique muscle (Smith et al., 2019).

While VEMPs allows for individual assessment of the otoliths, there are several limitations that are mentioned below. The purpose of this study was to create a better test of otolith assessment that is able to measure the vestibule directly, rather than through reflexes, as with the current VEMP assessments.

Limitations with Current Assessments of Otolithic Function, Specifically VEMPs

Intense/loud stimuli presentation levels

Intense noise exposure affects hearing and balance, which can lead to temporary and/or permanent threshold shifts (Stewart et al., 2020). That is, just as it is possible to get noise-induced hearing loss, it is also possible to experience peripheral vestibular damage after exposure to loud sounds, which can lead to anatomic and/or physiological changes" (Stewart et al., 2020). In the vestibular system, the otolith organs appear to be the most susceptible to acoustic over stimulation (Stewart et al., 2020). Therefore, possible overstimulation (high intensity of sound used to elicit the VEMPs) and possible damage that may occur as a result of the otolith organs assessed during VEMP testing, particularly oVEMPS , should be of concern.

In a case study by Mattingly and colleagues (2015), cVEMP and oVEMP testing resulted in permanent bilateral sensorineural hearing loss in an elderly patient, whereby the

study authors suggested putting limits on the intensity of sound stimulus levels and the number of repetitions (when multiple trials are used) presented during VEMP tests (Mattingly, Portnuff, Hondorp, & Cass, 2015). It should be noted that the patient in the case study already had a preexisting mild sloping to severe bilateral sensorineural hearing loss. However, post VEMPS, both her speech recognition and pure-tone thresholds worsened significantly, especially between 500 and 6000 Hz. The authors stated that while certain individuals (i.e, those with certain preexisting medical conditions) may be more at risk for permanent damage from overstimulation of acoustic stimuli, it is not always clear-cut to determine beforehand who may be at most risk for permanent damage from VEMP testing and this should be further researched.

Therefore, while VEMPs are common assessments routinely used in clinical practice as part of the vestibular test battery, there is a possibility to induce hearing loss (whether permanent or temporary), and perhaps it is even possible to damage and/or cause additional vestibular issues from overstimulation. However, more research needs to be done in this area because while it is known that intense noise can damage both vestibular and cochlear hair cells, no study thus far has looked into a possibility of additional vestibular damage from the VEMPs themselves.

Further limitations due to age, hearing status, and other factors.

In the elderly, there is a decline in vestibular and auditory function. This is important to note, as certain otolith assessments, namely the VEMPs, are affected by hearing status - both sensorineural and conductive hearing loss. With regards to conductive hearing loss and VEMPs, a group of researchers simulated conductive hearing loss in

healthy participants using an earplug to simulate the conductive loss (Han, Zhang, Chen, Gao, Cheng, Zhang, & Xu, 2016). These researchers assessed both the oVEMPs and cVEMPs prior to (with normal hearing/without temporary earplug blockage) and after simulation of the conductive hearing loss (temporary blockage from the earplug) and found that the conductive hearing loss "significantly impact[ed] oVEMPs and cVEMPs parameters, including: elevated thresholds, prolonged latencies, and attenuated amplitudes" (Han et al., p.194).

Due to the general global decline from aging, all functions, including muscle tone are decreased. cVEMPs require contraction of neck muscles, which are likely impaired, and thus cVEMPs become an invalid measure when a reliable recording cannot take place.

Additionally, studies have found responses from youth also to being affected. In one such study that tested healthy individuals (no conductive hearing loss) from 5-39 years of age to determine if there were any age effects on VEMPs, the researchers found that there was a decrease in amplitude in the younger age participants (Greenwalt, Patterson, Rodriguez, Fitzpatrick, Gordon, & Janky, 2020). People usually consider the decrease in amplitude of responses due to age effects in only the elderly, often failing to realize that youth, especially those who are younger, to have varying effects on electrophysiological responses from their still-developing bodies, both neural connections, and physical statures as well. The decline in amplitude may also be from the stapedial reflex during VEMP assessment, as the reflex may be more sensitive in children; prior research has shown a decrease in magnitude of the stapedial reflex with increased age (Phillips & Marchbanks, 1989) .

Electrophysiological Use in Audiology

Multiple uses of electrophysiology currently exist in audiology clinical practice, not just for assessment of hearing status, but intraoperative monitoring and vestibular assessments as well. While much more information is known about auditory electrophysiology, clinical electrophysiology in the vestibular system is still a work in progress.

Electrophysiological responses used in audiology rely on the transduction of energy from hair cells (stereocilia) of the cochlea for electrocochleography (ECochG) or from stereocilia of the vestibular labyrinth for electrovestibulography (EVestG). The vestibular stereocilia "convert mechanical stimuli triggered by gravity or motion into neural activity [whereby, this] information is conducted centrally to control eye position [and] balance" (Duncan, Stolller, Francl, Tissir, Davenport, & Deans, 2017, p. 127). Both ECochG and EVestG allow for the objective assessment of nerve and hair cell function (Brown et al., 2017).

ECochG is not the name of a response per se, but rather the process of assessing electrical potentials from excitable cochlear cells; ECochG can measure different types of cochlear responses, such as compound action potential (CAP) or cochlear microphonics (CM) and summating potential. Similarly, electrovestibulography (EVestG) assesses vestibular hair cell function, which can take the form of vestibular microphonics (VMs) and/or as VsEPs. VsEPs are analogous to ABRs since both are short latency compound action potentials that arise from synchronous neuronal activity from the nerve and brainstem (Brown et al., 2017).

Both cochlear and vestibular hair cells of the otoliths are sensitive to ACS and BCV. In fact, high-intensity auditory stimulation levels can produce not only permanent hearing loss but can result in damage to the vestibular system as well, particularly to the highly sensitive otolith organs (Stewart et al., 2020).

While basic vestibular anatomy states that the otolith organs respond to linear acceleration, the use of ACS and BCV can evoke responses to both the auditory and vestibular system. According to Brown et al. (2017), VsEPs were first studied in pigeons as far back as 1949 (Bleeker & De Vries, 1949). Additional vestibular electrophysiological studies using other bird species such as chickens, canaries, and quail occurred in the 1980s and the 1990s. VsEPs in reptiles (bullfrogs) and fish, along with various rodents (mouse, chinchilla, guinea pig) and other mammals, such as cats, rhesus monkeys, and humans, have also been studied. However, the majority of VsEP studies have been conducted in animals rather than in humans (Brown et al., 2017). With respect to recording methodology, in animals, the non-inverting electrode has often been placed at the vertex.

It should be noted that we presume that the latency of the first peak indicates it arises from the vestibulocochlear nerve, since it occurs ~1.5 ms post stimulation. With regards to the central component, it has been found that neurotoxic and neural blocking agents eliminate VsEP responses (Chihara, Wang, & Brown, 2013). In one study, VsEPs were performed on guinea pigs using a neural blocker (tetrodotoxin; TTX) that was applied to either the round window or the utricle, which resulted in a gradually decrease in VsEP responses, while application of the TTX to the inner ear fluids completely extinguished the VsEP (Chihara, Wang, & Brown, 2013). Additionally, it is well known that VsEPs do not

rely on the cochlea and therefore are direct measurements of the vestibular system since even deaf individuals with normal balance functions have been found to produce VsEP responses (Rosengren & Colebatch, 2006).

Benefits of Electrophysiological Assessments

There are several benefits to the use of electrophysiological assessments, including but not limited to the ability to test a more diverse patient population with respect to age and abilities, mobility (some electrophysiological assessments can be performed at bedside if needed), noninvasiveness, relatively objective, and where no behavioral response is needed, etc., (Hall, 2007). We would argue that the VsEP is thought to be similar to the ABR, despite difference in stimuli and the potential for similar widespread use.

According to Chihara and colleagues (2013), numerous benefits of VsEP testing exist, such as ease of measurement (relatively simple to obtain), which can be useful for monitoring drug toxicity as well.

VsEP Assessment

Use of BCV

BCV are used to elicit direct responses of the vestibular system through direct stimulation of the vestibular organs, either by using angular (assess SCCs) or linear (assess otoliths) acceleration. Recall from the Introduction chapter that VsEP are elicited through motion and not auditory stimuli (Jones & Jones, 2007). Traditional tests of otolith function that are currently available, specifically cVEMPs, use ACS. One of the downsides previously noted about VEMPs is that they are indirect measures of otolith function, particularly if using ACS, as ACS relies on normal soundwave transmissions to the inner

ear to record properly; if there is a middle ear problem due to any conductive hearing loss (i.e., middle-ear effusions, otosclerosis, etc.), then ACS will not give an accurate response (such as an attenuated/decreased/reduced response), unlike BCV, which by contrast, are not impacted by the middle ear (Renga, 2019). Thus, this is a benefit of VsEPs being able to directly assess the otoliths via linear acceleration of the BCV.

Low Frequencies Tested

This study assessed only a lower and a low-mid frequency at 500 and 1000 Hz, as electrophysiological recordings have been found to have more diagnostic value with lower frequency recordings due to the anatomical properties of the otoliths (Renga, 2019). Additionally, lower frequencies would be tested for this study based on the fact that current clinical VEMP, which similar to the VsEPs, also assesses otolith function, and utilize low frequencies (500 Hz) to measure (Fujimoto et al., 2017).

Use of Masking

Similar to the auditory system, the vestibular system is responsive to both ACS and BCV (Brown, Pastras, & Curthoys, 2017). Subsequently, the specificity of VsEP responses becomes a challenge due to the possibility of cochlear responses contaminating vestibular responses (Böhmer, Hoffman, & Honrubia, 1995). Since not much is known about the use of acoustic masking in vestibular assessments in humans, the use of unilateral (ipsilateral) and bilateral masking utilized in this study will add to the knowledge base in this area . Contralateral masking would not be attempted in this study due to the already low number of participants and a limited time-frame to test all participants properly, but should be

conducted in the future to determine if it can aid with assessment of laterality in individuals with unilateral dysfunction, rather than just for the purpose of minimizing noise artifacts.

Supine Position Testing

Prior studies have indicated that VsEPs arise from the otolith organs, though the exact location may vary depending upon electrode placements and stimulation used (Brown, Pastras, Curthoys, 2017). The anatomical orientation of the utricle and saccule are positioned at right angles to each other (Smith, 2019). The VsEPs in this study were recorded in a supine position. Most VsEP recordings, even in animals, measure VsEP responses laying in the supine position, similar to how caloric testing measures the horizontal SCCs in a supine position, but at a specific 30-degree angle due to the positioning of the horizontal SCC in each ear. This is interesting to note since the horizontal SCC is parallel to the utricle, and the utricle is oriented in approximately the same plane as the horizontal SCC (Harsha et al., 2008). Thus, the horizontal supine position was used for the VsEPs recorded in this study, especially considering that this is the same supine position used in several prior VsEP animal studies (Brown et al., 2017).

While the exact location of VsEP generation is still controversial, some studies appear to indicate that VsEP responses almost entirely arise from the utricle when using linear acceleration impulses (Chihara, Wang, & Brown, 2013). However, as Brown et al. (2017) mentioned, specific VsEP generators vary based on stimuli used and electrode placements; thus, currently cannot say much on where the VsEPs generated in this study stem from, but it is likely the utricle , though it depends upon the plane of stimulation as well.

Electrode Montage

Several electrophysiological responses utilize electrodes to convert biologic responses to electrical recordings (Burkard & Secor, 2002). Electrode placement is an important component to recording responses. Typically, three-electrode leads are used for each recording channel, which are known as the non-inverting (active/positive), inverting (reference/negative), and common (ground) leads (Burkard & Secor, 2002). This specific study was recorded using a single-channel, which is described in the Methods chapter.

The use of various techniques to record VsEPs (e.g., change in electrode placements and recording stimulus) changes not only the different characteristics of the waveforms (latency, amplitude, waveform shape.) but measures different peripheral and central locations as well (Brown et al., 2017). For example, the use of the BCV placed at the nasion elicits a different response than when the BCV is placed at the vertex (Todd et al., 2014; Brown et al., 2017). This study is therefore unique as no study has assessed VsEPs in the same manner prior to this study; thus, not much is currently known about where the best placement of electrodes is to get the strongest VsEP recordings.

Research Question

Will there be any difference in VsEPs when using varying stimuli (frequency, masking, and intensity levels) with regard to VsEP amplitude and latency responses?

Expected Outcomes

Since this is a parametric and feasibility study using a novel approach, especially with regards to electrode placements, use of a wick electrode, and BCV that have not been tested exactly in the same manner prior to this study, not much is known regarding these

VsEPs. Therefore, null hypotheses are stated instead of listing hypotheses in a traditional manner.

Null Hypotheses

There will be no difference with regards to the waveform amplitudes and latencies in the VsEP recordings across the various conditions tested, regardless of the frequency (500 and 1000 Hz), the intensity of the stimuli (115, 105, 95, and 85dB SPL), and masking used (no masker, 100, 90, and 80dB HL).

CHAPTER 3

METHODS

The primary purpose of this parametric study was to evaluate the feasibility of developing vestibular short-latency evoked potentials (VsEPs) in humans by obtaining fundamental characteristics of VsEP responses in healthy young adults in response to various stimulus parameters.

Subjects

Eleven healthy adults ranging in age from 19 – 39 years (mean age = 23.1 years; SD = 6.9 years; 5 females and 6 males) participated in this study. Prior to any testing, all participants provided written informed consent. The instructions were given in written form then reiterated verbally (Appendix A). The Institutional Review Board at Wayne State University (Detroit, Michigan) approved this study. Participants were recruited through direct face-to-face recruitment and snowball non-probabilistic sampling.

Inclusion and Exclusion Criteria

Inclusion criteria included individuals with a negative history of hearing, balance, neurological, and cognitive issues. Exclusion criteria included individuals with a history of acoustic trauma (e.g., workplace noise or blast exposure), ototoxic/vestibulotoxic drug treatment, middle ear pathology, and any cognitive issues.

Vision Screening

Once consent forms were reviewed and signed by each participant, a Snellen chart was used to ensure normal or corrected-to-normal vision, as the ocular system is known to play a role in balance (Black and Pesznecker, 2003). For this portion, participants stood at

a marked line on the floor that was 9 feet away from the chart and read the smallest intelligible line with one eye at a time and then both eyes to ensure both eyes had similar perception; use of corrective lenses was permitted.

Auditory Thresholds

Standard pure-tone audiometric threshold testing was performed to ensure clinically normal hearing (0.25-8 kHz, bilaterally; <25 dB HL) in a commercial sound-attenuating test booth using a standard audiometer (Grason-Stadler; GSI 61) and insert earphones (Etymōtic Research; ER-3A).

Electrophysiological Recordings

Participants were taken into another sound attenuated test booth for the VsEP assessments. For this portion, participants were told to relax/close their eyes and remain quiet throughout this test since they would not have to respond in any way and to ensure minimal artifacts.

Instructions

For VsEPs, as in any other assessment performed on any patient, for consistently successful measurements, individuals who are testing (researchers and clinicians alike) must master basic technical skills (i.e., proper electrode placement; check impedance before beginning as well if required, as with VsEPs) and be able to properly operate the evoked response system - such as being sure program and all devices are turned on, not only electrodes - but inserts for masking hooked and connected correctly in proper channels, and be able to fix any encountered problems such as noisy recordings and the like (Hall III, 2007).

The instructions given to participants, just as with any test, should not be taken lightly. It is through proper instruction that participants are able to understand their task and remain calm. Many of the participants were concerned about the wick electrode placement, as most were unfamiliar except with the standard surface electrodes; in order to make participants feel comfortable, the words used during directions and reinstructions as needed were very gentle and simple to understand - such as the wick electrode going down the ear canal might tickle like a piece of spaghetti, but it should not hurt. Electrode placement, including wick placement, was straight forward especially with the use of the operation microscope and nasal speculum to open up the ear canal for better TM visualization. Really, the main concern was boredom and fatigue that caused some individuals to move, but that was easily corrected through reinstruction.

Special Instrumentation

Mini-shaker

A special mini-shaker (Bruel & Kjaer, model 4810) was used to present stimuli for this study. The mini-shaker is the bone vibrating apparatus that caused linear movements of the skull. The B&K mini-shaker was connected to the power amplifier, which was securely held in place by an adjustable metal rod (Figure 1A).

NeuroScan

The VsEP electrophysiological recordings were made using a NeuroScan evoked potential system (Stim and Scan) inside a commercial test booth, located in the Hearing Science Lab (room 045), Horace H. Rackham Educational Memorial Building on the campus of Wayne State University (Detroit, Michigan). All VsEPs were recorded and data

saved on a desktop computer (Dell Optiplex-760). The two Dell desktop computers each had special programs designed for stimulus generation, signal averaging, saving the VsEP responses and quantifying the latency and amplitude of the data. The stimulation program on one of the computers allowed the tester to select the stimulus frequency and level.

Electrodes

Standard gold cup surface electrodes were used to record the VsEP responses. Electrode gel and tape were used to hold the surface electrodes in place. A commercially available wick electrode (Lilly wick electrode) was placed on the left tympanic membrane with the direct visualization with the aid of an operating microscope; analogous to what is used in single-channel extra-tympanic electrocochleography recordings (Figure 1). The use of the wick electrode was to record early electrical activity as close as possible to the otolith organs. These recordings were non-invasive and safe.

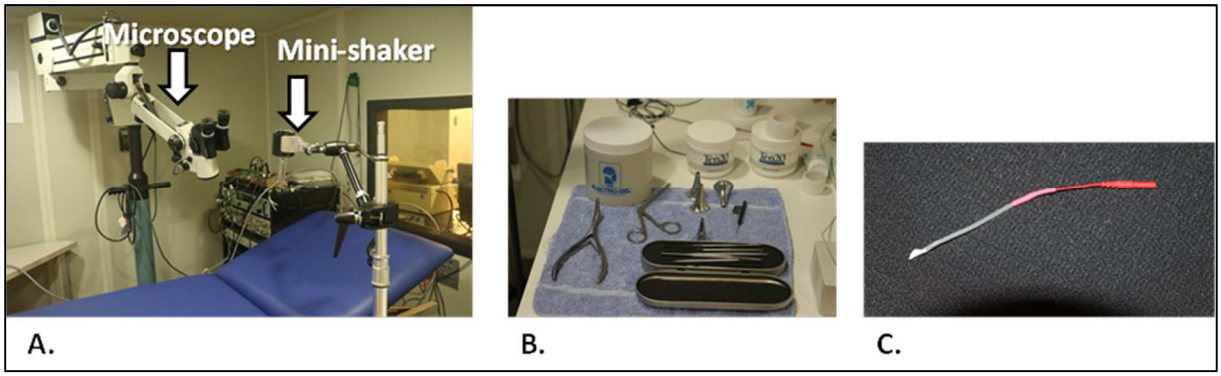


Figure 1: Special equipment for VsEPs A) operating microscope, examination table, and mini-shaker attached to an articulating stand B) tools to enhance TM visualization and placement (i.e., nasal speculum, electrode gel, etc) C) Lily Wick electrode

Electrode Montage and Insert Earphone Placement

The researcher scrubbed and attached surface electrodes to each participant in order to get a low impedance value. The active cotton wick electrode was placed on each participants' left tympanic membrane (TM). An insert earphone Etymōtic (ER-3A) was

then placed into the left ear canal to ensure that the cotton wick electrode maintained its position during testing and for presenting masking noise.

This current study was performed using a single-channel, where the reference electrode was placed on the Fpz (forehead), ground on the mastoid process of the left ear (M2), and the active wick electrode was placed inside the ear canal on the left TM (Figure 2).

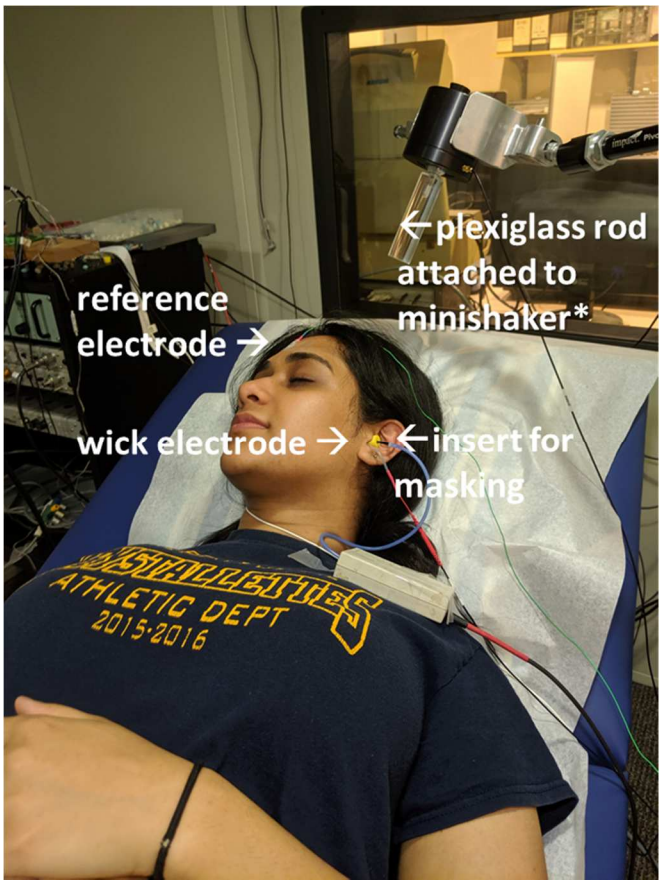


Figure 2: Mini-shaker and placement of electrodes. Please note ground electrode (M2; left mastoid process) is not shown in this image.

Calibration

For calibration (Figure 3), acceleration measures were obtained with a custom designed Triaxial accelerometer. A plexiglass-rod from the mini-shaker was applied to the

artificial mastoid (B&K Model: 4930) and sound-pressure levels were obtained from a Precision Impulse Sound-Level Meter (B&K Model: 2209), while the load cell measured the amount of force from the mini-shaker.

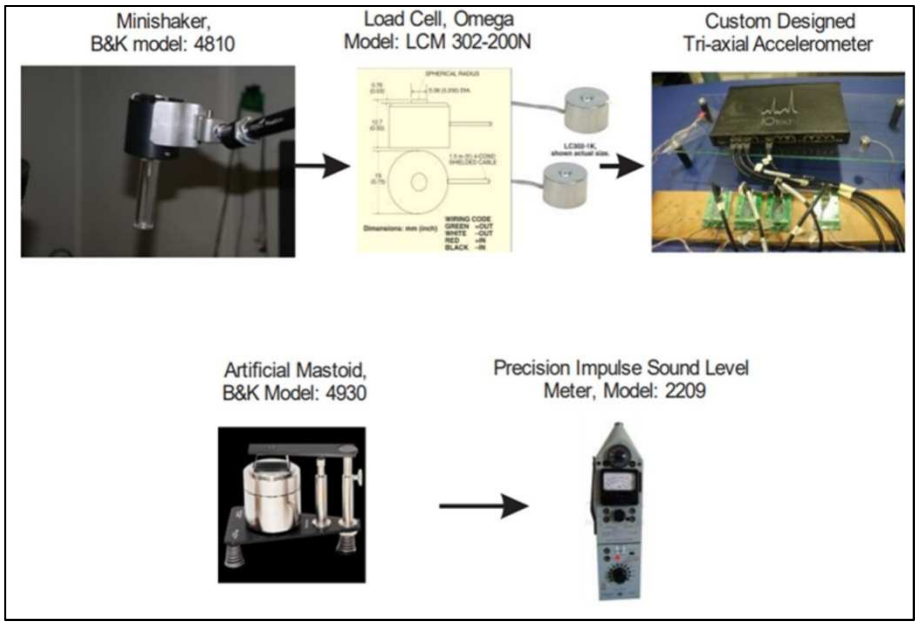


Figure 3: Signal path for calibration of the B&K mini-shaker

Stimuli

Stimuli were presented to the skull via a plexiglass rod attached to the B&K mini-shaker. This mini-shaker was placed on the frontal part of the head/scalp. Stimuli consisted of 4 ms, 500 and 1000 Hz Blackman-windowed tone bursts presented at a rate of 3/s, and at a level approximating 80 dB re: 0.2 g's of force obtained via a force/load cell. Stimuli were presented with and without ipsilateral air conduction masking noise to eliminate potential cochlear participation in the VsEP measurement.

Testing assessed the two frequencies (500 and 1000 Hz) at four intensity levels (115, 105, 95, and 85 dB SPL), and three masking levels (100, 90, and 80 dB HL) along

with unmasked levels. Due to time constraints, only on one side (left) was tested (Table 1). However, two participants were also tested with bilateral masking.

VsEP Testing Protocol @ 500 & 1000 Hz		
INTENSITY (dB SPL)	*NON-MASKING*	*MASKING (dB HL)*
115	YES	NO
105	YES	80
		90
		100
95	NO	90
85	NO	90

Table 1: VsEP testing parameters for both 500 and 1000 Hz. Masking levels were randomized.

Masking

The purpose of using acoustic masking noise was to ensure that the VsEP responses were of vestibular, not auditory, origin. Therefore, acoustic masking was a way eliminate any possible contamination from the auditory portion of the inner ear.

Analyses

VsEP data was saved onto the desktop in specific coded files without any personal identifiers. An editing program (Waveboard) on the Scan computer was used to quantify peak latencies and amplitudes of the individual waveforms. Data was analyzed with a repeated measures analysis-of-variance (ANOVA) to evaluate the effects of frequency, intensity, and masking. Power analysis was not possible since effect sizes could not be determined due to the limited literature in this area on humans. All graphs were plotted using SigmaPlot software and statistical analysis was obtained from Statistica software.

CHAPTER 4

RESULTS

VsEP Waveforms

A total of 11 participants (6 males and 5 females) ranging in age from 19-39 years (mean: 23.1 years; SD: 6.9 years) met the inclusion criteria and completed testing; of the 11 included in the analysis, only two participants also underwent binaural masking conditions at 105 dB SPL under three different masker intensity levels (100 dB HL, 90 dB HL, and 80 dB HL) due to time constraints. All participants had VsEPs conducted and analyzed at both 500 and 1000 Hz. There were no adverse effects of testing.

Figure 4 shows representative waveforms of the VsEP responses at 1000 Hz (Figure 4A) and 500 Hz (Figure 4B), respectively. Waveforms were labeled using a polarity (P = positive voltage; N = negative voltage) latency (time; milliseconds, ms) nomenclature.

Figure 4: General Waveforms at 500 and 1000 Hz

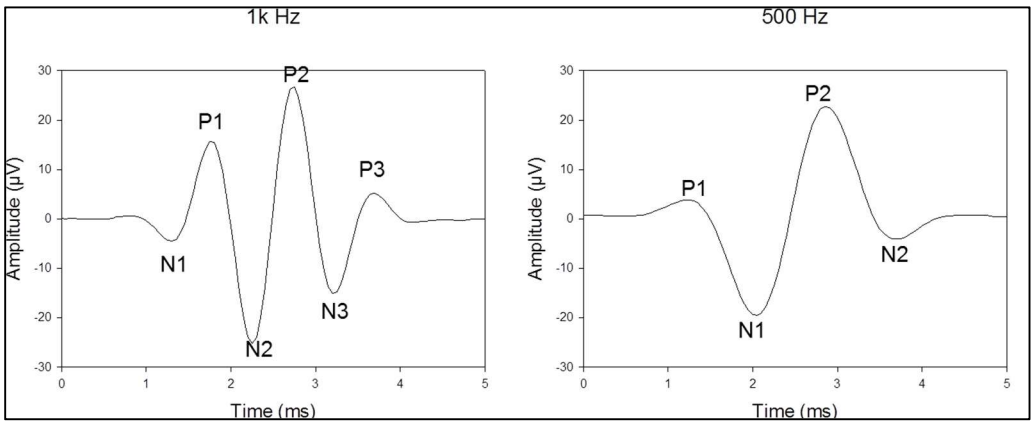


Figure 4A **Figure 4B**

Figure 4: Typical waveform responses in healthy individuals at 1000 Hz (Fig. 4A) and 500 Hz (Fig. 4B)

In Figure 4, the peaks (P) and valleys (N) of a typical healthy/normal VsEP waveform response at 1000 Hz (Figure 4A) and 500 Hz (Figure 4B), where the y-axis represents amplitude (microvolts. uV) and the x-axis represents time (milliseconds, ms). Numerical data are provided in the Appendices for all conditions. All participants' unmasked VsEPs are shown in Figure 5 and Figure 6 below.

Figure 5: 1000 Hz data for all participants at all unmasked and monaural masking conditions tested

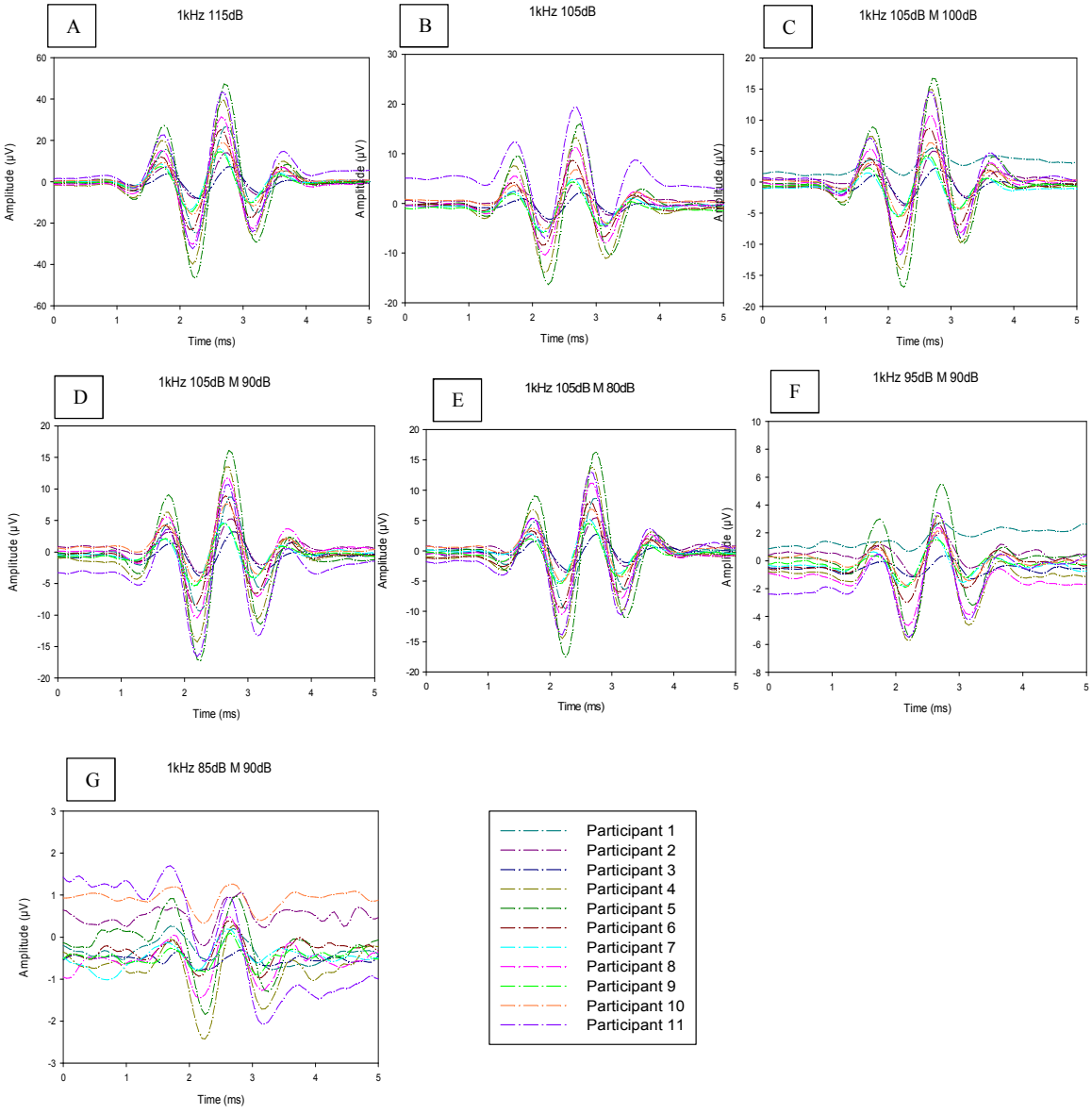


Figure 5: 1000 Hz waveform data for all participants for all unmasked and monaural masking conditions: A) 115 dB SPL, B) 105 dB SPL C) 105 dB SPL with 100 dB HL masker, D) 105 dB SPL with 90 dB HL masker, E) 105 dB SPL with 80 dB HL masker, F) 95 dB SPL with 90 dB HL masker, G) 85 dB SPL with 90 dB HL masker

Figure 6: 500 Hz data for all participants at all unmasked and monaural masking conditions tested

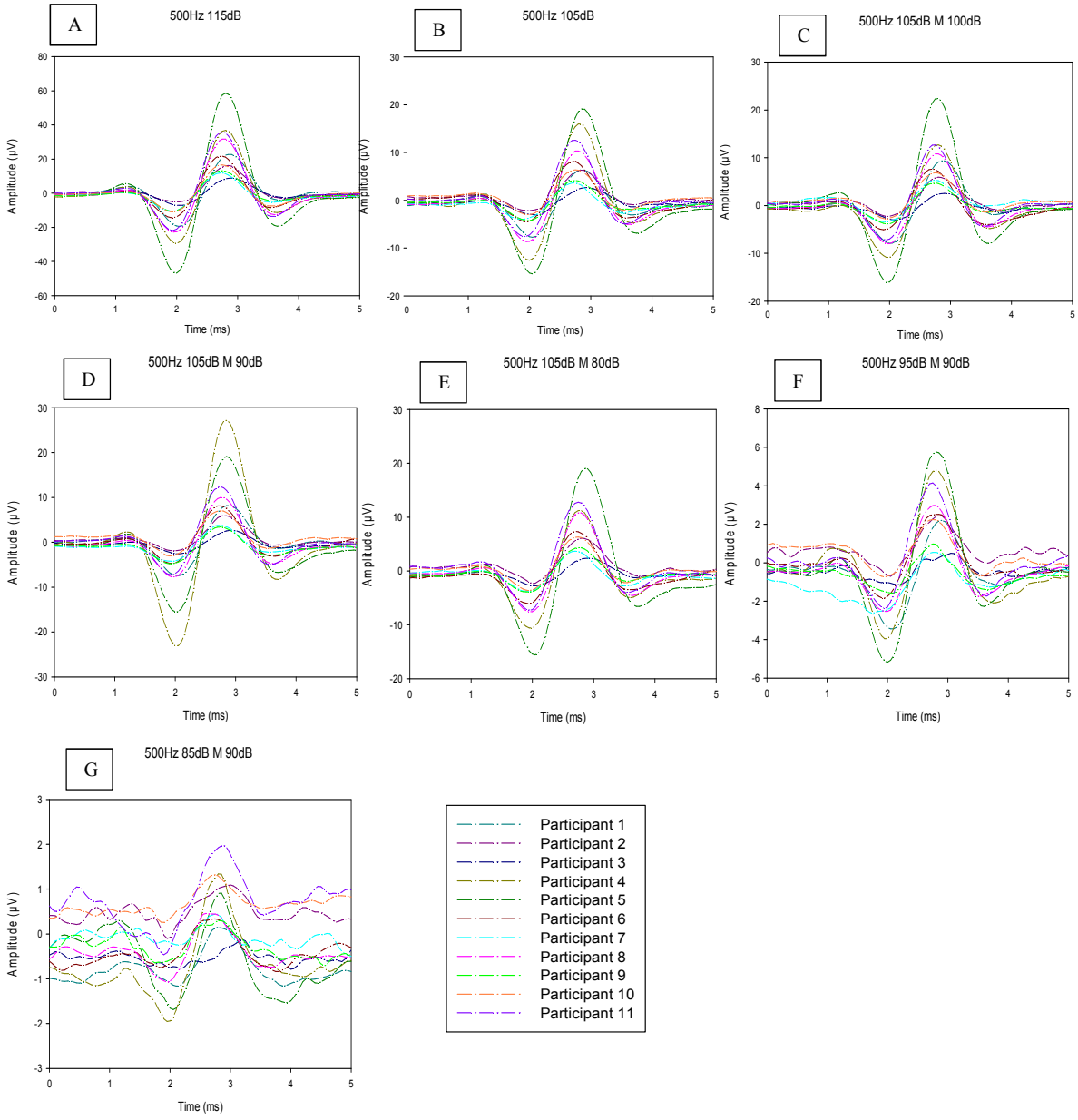


Figure 6: 500 Hz waveform data for all participants for all unmasked and monaural masking conditions: A) 115 dB SPL, B) 105 dB SPL C) 105 dB SPL with 100 dB HL masker, D) 105 dB SPL with 90 dB HL masker, E) 105 dB SPL with 80 dB HL masker, F) 95 dB SPL with 90 dB masker, G) 85 dB SPL with 90 dB HL masker

As can be seen in the above figures, response waveforms were generally reproducible. However, since the majority of responses are noisy at the 90 dB HL masker condition at 85 dB SPL stimulus intensity (Figures 5G and 6G) with very small amplitudes (Tables 4A and 4C, condition 3), the artifacts may indeed be from masking noise. However, what can be inferred from the data is that the use of the mini-shaker stimuli intensity at 85 dB SPL and even 95 dB SPL (Table 4, condition 2) is not high enough to elicit a strong VsEP response based on the smaller amplitude size compared to responses produced at 115 dB SPL and 105 dB SPL (Figures 7A and 7C), although, latency remains unaffected regardless of the condition (Figures 7B and 7D).

Figure 7: Unmasked and masked VsEP amplitude and latencies with SD (error bars) at 500 and 1000 Hz

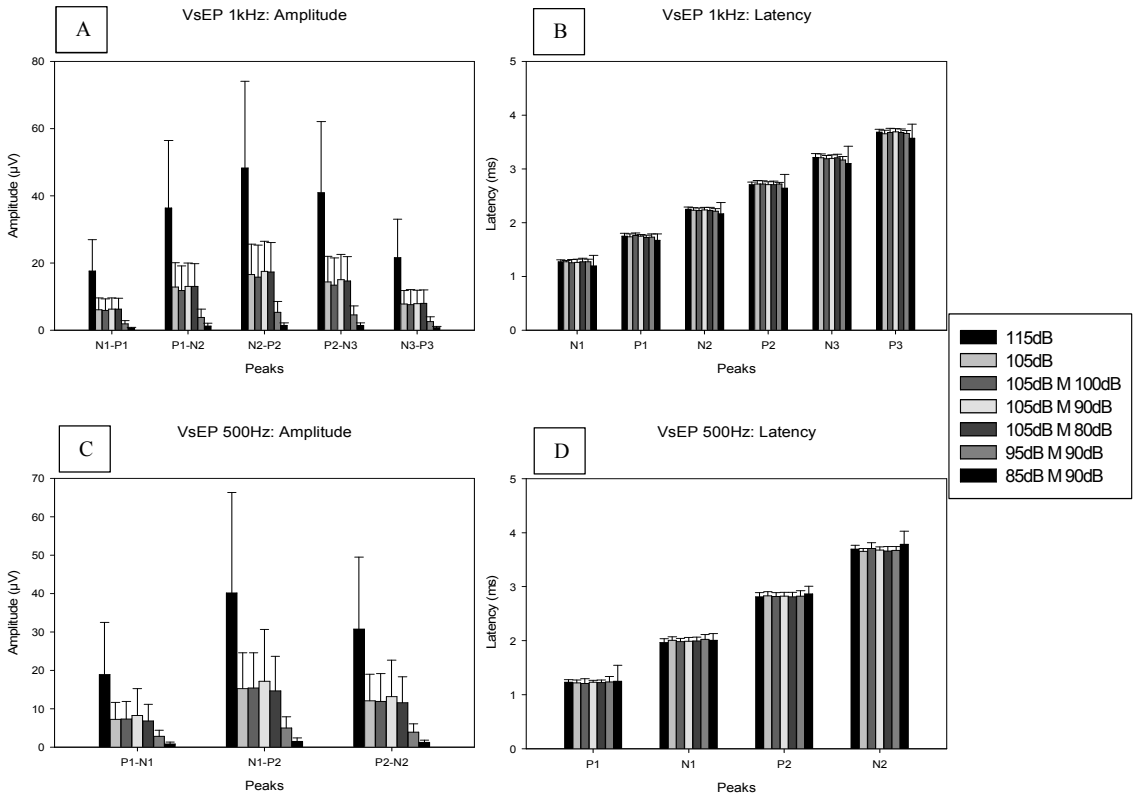


Figure 7: Bar graphs of unmasked and ipsilateral masking (amplitude and latency effects) with SD at a varying BCV stimulus (115 dB SPL and 105 dB SPL unmasked) and masking intensities (100 dB HL masker at 105 dB SPL; 80 dB HL masker at 105 dB SPL; and 90 dB HL masker at 105 dB SPL, 95 dB SPL, & 85 dB SPL); Fig 7A) Amplitude effects

of the varying unmasked and masked stimulus and masking intensities at 1000 Hz, Fig. 7B) Latency effects at 1000 Hz, Fig. 8C) Amplitude effects at 500 Hz, and Fig. 8D) Latency effects at 500 Hz

Figure 8: Binaural masking VsEP amplitude and latencies with SD (error bars) at 500 and 1000 Hz

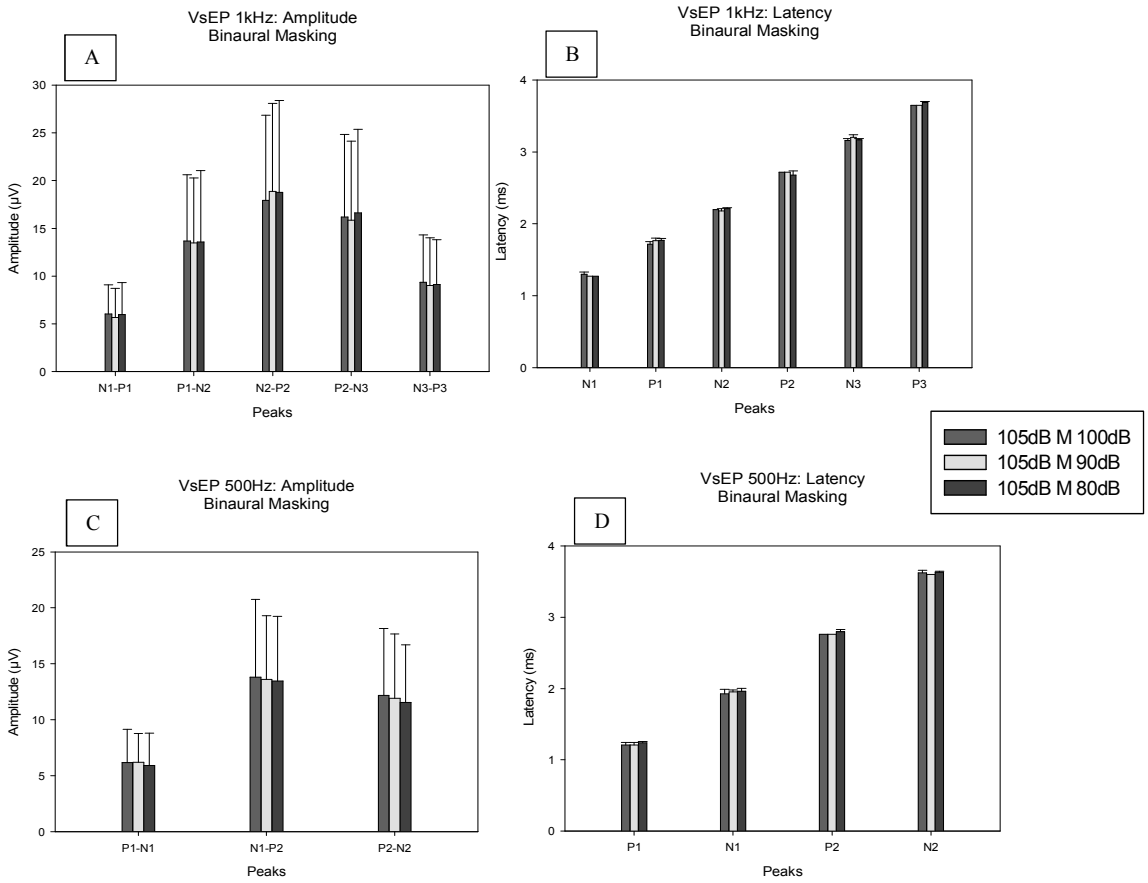


Figure 8: Bar graphs of binaural masking (amplitude and latency effects) with SD at a constant BCV stimulus intensity of 105 dB SPL at 3 different masker levels (100 dB HL, 90 dB HL, and 80 dB HL masking noise); Fig 8A) Amplitude effects of binaural masking at 1000 Hz, Fig. 8B) Latency effects at 1000 Hz, Fig. 8C) Amplitude effects at 500 Hz, and Fig. 8D) Latency effects at 500 Hz

Unmasked Conditions

A one-way ANOVA was conducted to determine whether the frequency and/or the stimulation intensity of the mini-shaker used to elicit the VsEPs would impact the responses. With regards to the intensity levels for the unmasked conditions, both 115 dB SPL and 105 dB SPL were compared by looking at both the amplitudes and latencies of the VsEP responses (Tables 2A-2D) at 500 and 1000 Hz. Results indicate that the

amplitudes of the VsEPs are significantly impacted ($p<.05$) by the intensity of the unmasked conditions, regardless of the frequency tested. On the other hand, no significant effects of the unmasked intensity conditions on any of the VsEPs latencies at the $p<.05$ level were found for either of the intensity (115 dB SPL and 105 dB SPL) conditions tested at both frequencies tested (Table 2B. and Table 2D). All post-hoc analyses are described at the end of this chapter, as well as in the tables found in Appendix E.

All of the mean amplitudes at both 500 and 1000 Hz were significantly impacted by the stimulus intensity, with the higher intensity (115 dB SPL) having higher mean amplitudes than at 105 dB SPL. The mean amplitudes, along with the standard deviation and standard error scores can be found in the tables below (Table 2A and Table 2C).

It should be noted that one less participant was tested at the 105 dB SPL stimulus (N = 10) intensity condition than at 115 dB SPL (N = 11). However, results across all conditions are consistent; thus, one less participant will not be enough to be of any statistical significance for the unmasked latencies and amplitudes data.

Table 2A.
Summary of ANOVA VsEPs amplitudes for unmasked conditions (115 dB and 105 dB SPL) at 1000 Hz

1kHz Amplitude	Effect	SS	DF	MS	F	P	Conditions	Mean	SD	Std.Err.	-Std.Err	+Std.Err	N
N1/P1	unmasked	692.5	1	692.5	13.43	.002*	1	17.57	9.32	2.17	15.40	19.73	11
							2	6.07	3.52	2.27	3.80	8.34	10
P1/N2	unmasked	2882	1	2882	12.11	.003*	1	36.30	20.11	4.65	31.65	40.95	11
							2	12.84	7.27	4.88	7.97	17.72	10
N2/P2	unmasked	5263	1	5263	13.49	.002*	1	48.25	25.84	5.96	42.29	54.20	11
							2	16.55	9.03	6.25	10.30	22.80	10
P2/N3	unmasked	3694	1	3694	14.07	.001*	1	40.92	21.14	4.89	36.03	45.80	11
							2	14.36	7.61	5.12	9.24	19.48	10
N3/P3	unmasked	991.4	1	991.4	13.01	.002*	1	21.54	11.44	2.63	18.91	24.18	11
							2	7.79	3.94	2.76	5.02	10.55	10

Table 2A: Main effects of amplitude for unmasked conditions at 1000 Hz. BCV stimulus presented in 2 conditions: condition 1) 115 dB SPL and condition 2) 105 dB SPL

Table 2B.
Summary of ANOVA VsEPs latencies for unmasked conditions (115 dB and 105 dB SPL) at 1000 Hz

1kHz Latency	Effect	SS	DF	MS	F	P	Conditions	Mean	SD	Std.Err.	-Std.Err	+Std.Err	N
N1	unmasked	0	1	0	0.019	0.892	1	1.27	0.04	0.01	1.26	1.28	11
							2	1.27	0.03	0.01	1.26	1.28	10
P1	unmasked	0.001	1	0.001	0.273	0.607	1	1.75	0.05	0.02	1.73	1.76	11
							2	1.73	0.05	0.02	1.72	1.75	10
N2	unmasked	0.002	1	0.002	1.078	0.312	1	2.25	0.04	0.01	2.24	2.26	11
							2	2.23	0.05	0.01	2.22	2.24	10
P2	unmasked	0.001	1	0.001	0.169	0.685	1	2.71	0.05	0.02	2.69	2.72	11
							2	2.72	0.06	0.02	2.70	2.74	10
N3	unmasked	0	1	0	0.09	0.768	1	3.22	0.07	0.02	3.19	3.24	11
							2	3.21	0.07	0.02	3.18	3.23	10
P3	unmasked	0.004	1	0.004	1.274	0.273	1	3.68	0.05	0.02	3.67	3.70	11
							2	3.65	0.07	0.02	3.64	3.67	10

Table 2B: Main effects of latencies for unmasked conditions at 1000 Hz. BCV stimulus presented in 2 conditions: condition 1) 115 dB SPL and condition 2) 105 dB SPL

Table 2C.
Summary of ANOVA VsEPs amplitudes for unmasked conditions (115 dB and 105 dB SPL) at 500 Hz

500Hz Amplitude	Effect	SS	DF	MS	F	P	Conditions	Mean	SD	Std.Err.	-Std.Err	+Std.Err	N
P1/N1	unmasked	745.8	1	745.8	7.32	.014*	1	18.87	13.56	3.04	15.82	21.91	11
							2	7.22	4.45	3.04	4.18	10.26	11
N1/P2	unmasked	3405	1	3405	8.799	.008*	1	40.13	26.21	5.93	34.20	46.06	11
							2	15.25	9.32	5.93	9.32	21.18	11
P2/N2	unmasked	1925	1	1925	9.594	.006*	1	30.73	18.78	4.27	26.46	35.00	11
							2	12.02	6.96	4.27	7.75	16.29	11

Table 2C: Main effects of amplitude for unmasked conditions at 500 Hz. BCV stimulus presented in 2 conditions: condition 1) 115 dB SPL and condition 2) 105 dB SPL

Table 2D.
Summary of ANOVA VsEPs latencies for unmasked conditions (115 dB and 105 dB SPL) at 500 Hz

500Hz Latency	Effect	SS	DF	MS	F	P	Conditions	Mean	SD	Std.Err.	-Std.Err	+Std.Err	N
P1	unmasked	0.001	1	0.001	0.451	0.509	1	1.23	0.05	0.02	1.22	1.25	11
							2	1.22	0.05	0.02	1.20	1.23	11
N1	unmasked	0.009	1	0.009	2.211	0.153	1	1.97	0.07	0.02	1.95	1.99	11
							2	2.01	0.06	0.02	1.99	2.03	11
P2	unmasked	0.002	1	0.002	0.305	0.587	1	2.82	0.07	0.02	2.79	2.84	11
							2	2.83	0.07	0.02	2.81	2.85	11
N2	unmasked	0.009	1	0.009	2.364	0.14	1	3.69	0.07	0.02	3.67	3.71	11
							2	3.65	0.05	0.02	3.63	3.67	11

Table 2D: Main effects of latencies for unmasked conditions at 500 Hz. BCV stimulus presented in 2 conditions: condition 1) 115 dB SPL and condition 2) 105 dB SPL

Monaural Masking

Monaural Masking Conditions at Varying Intensities at 105 dB SPL

A one-way ANOVA was conducted to compare the effects of unilateral masking at three different levels (100 dB HL, 90 dB HL, and 80 dB HL) at a single VsEP stimulation intensity of 105 dB SPL. Based on the statistical analysis (Tables 3A-3D), no significant effects of the masker level at any of the three conditions analyzed were found at any of the VsEP amplitudes or latencies for either of the frequencies (500 and 1000 Hz) tested.

However, it should be noted that one less participant (N = 10) was tested at the 105 dB SPL stimulus intensity with 80 dB HL masker condition at 500 Hz (Tables 3C-3D, condition 3). Based on the data, it can be stated that the level of masker does not significantly impact the amplitude nor latency of VsEPs in healthy young adults at a single stimulation intensity, at least for the masking levels analyzed with a 105 dB SPL VsEP stimulus level.

Table 3A.
Summary of ANOVA VsEPs amplitudes for 105 dB SPL monaural masking conditions (100 dB, 90 dB, & 80 dB HL) at 1000 Hz

1kHz Amplitude	Effect	SS	DF	MS	F	P	Conditions	Mean	SD	Std.Err.	-Std.Err	+Std.Err	N
N1/P1	Masker conditions	1.187	2	0.594	0.053	0.948	1	5.83	3.49	1.01	4.83	6.84	11
							2	6.26	3.28	1.01	5.25	7.26	11
							3	6.21	3.25	1.01	5.20	7.21	11
P1/N2	Masker conditions	11.39	2	5.695	0.115	0.891	1	11.79	7.33	2.12	9.67	13.91	11
							2	13.04	6.94	2.12	10.92	15.16	11
							3	13.03	6.79	2.12	10.91	15.15	11
N2/P2	Masker conditions	19.6	2	9.799	0.118	0.889	1	15.74	9.52	2.74	13.00	18.49	11
							2	17.45	9.00	2.74	14.70	20.19	11
							3	17.30	8.77	2.74	14.56	20.05	11
P2/N3	Masker conditions	15.74	2	7.87	0.135	0.874	1	13.39	8.09	2.30	11.09	15.69	11
							2	14.99	7.57	2.30	12.69	17.28	11
							3	14.67	7.19	2.30	12.37	16.97	11
N3/P3	Masker conditions	1.246	2	0.623	0.036	0.965	1	7.53	4.50	1.26	6.28	8.79	11
							2	7.86	4.01	1.26	6.61	9.12	11
							3	8.00	3.96	1.26	6.74	9.25	11

Table 3A: Main effects of amplitude for monaural masking conditions at 1000 Hz. BCV stimulus presented at a single/constant intensity of 105 dB SPL in 3 different masker conditions: 1) 100 dB HL, 2) 90 dB HL, and 3) 80 dB HL

Table 3B.
Summary of ANOVA VsEPs latencies for 105 dB SPL monaural masking conditions (100 dB, 90 dB, & 80 dB HL) at 1000 Hz

1kHz Latency	Effect	SS	DF	MS	F	P	Conditions	Mean	SD	Std.Err.	-Std.Err	+Std.Err	N
N1	Masker conditions	0.001	2	0.001	0.181	0.835	1	1.25	0.06	0.02	1.24	1.27	11
							2	1.26	0.06	0.02	1.24	1.28	11
							3	1.27	0.07	0.02	1.25	1.29	11
P1	Masker conditions	0.007	2	0.004	2.091	0.141	1	1.76	0.05	0.01	1.74	1.77	11
							2	1.75	0.03	0.01	1.74	1.76	11
							3	1.72	0.04	0.01	1.71	1.74	11
N2	Masker conditions	0.001	2	0.001	0.274	0.762	1	2.22	0.05	0.02	2.21	2.24	11
							2	2.24	0.05	0.02	2.22	2.25	11
							3	2.22	0.06	0.02	2.21	2.24	11
P2	Masker conditions	0.001	2	0	0.094	0.91	1	2.72	0.06	0.02	2.70	2.73	11
							2	2.71	0.06	0.02	2.69	2.72	11
							3	2.71	0.06	0.02	2.69	2.73	11
N3	Masker conditions	0.002	2	0.001	0.25	0.78	1	3.19	0.06	0.02	3.17	3.21	11
							2	3.19	0.06	0.02	3.17	3.21	11
							3	3.21	0.07	0.02	3.19	3.22	11
P3	Masker conditions	0.001	2	0	0.089	0.915	1	3.68	0.07	0.02	3.66	3.70	11
							2	3.69	0.06	0.02	3.67	3.71	11
							3	3.68	0.07	0.02	3.66	3.70	11

Table 3B: Main effects of latencies for monaural masking conditions at 1000 Hz. BCV stimulus presented at a single/constant intensity of 105 dB SPL in 3 different masker conditions: 1) 100 dB HL, 2) 90 dB HL, and 3) 80 dB HL

Table 3C.
Summary of ANOVA VsEPs amplitudes for 105dB SPL monaural masking conditions (100 dB, 90 dB, & 80 dB HL) at 500Hz

500Hz Amplitude	Effect	SS	DF	MS	F	P	Conditions	Mean	SD	Std.Err.	-Std.Err	+Std.Err	N
P1/N1	Masker conditions	10.92	2	5.462	0.182	0.834	1	7.32	4.53	1.65	5.67	8.97	11
							2	8.23	7.03	1.65	6.58	9.88	11
							3	6.82	4.36	1.73	5.08	8.55	10
N1/P2	Masker conditions	36.55	2	18.27	0.156	0.856	1	15.36	9.16	3.26	12.11	18.62	11
							2	17.16	13.49	3.26	13.91	20.42	11
							3	14.61	8.99	3.42	11.20	18.03	10
P2/N2	Masker conditions	13.46	2	6.731	0.106	0.9	1	11.91	7.24	2.41	9.50	14.32	11
							2	13.08	9.55	2.41	10.68	15.49	11
							3	11.57	6.76	2.52	9.05	14.10	10

Table 3C: Main effects of amplitude for monaural masking conditions at 500 Hz. BCV stimulus presented at a single/constant intensity of 105dB SPL in 3 different masker conditions: 1) 100 dB HL, 2) 90 dB HL, and 3) 80 dB HL

Table 3D.
Summary of ANOVA VsEPs latencies for 105 dB SPL monaural masking conditions (100 dB, 90 dB, & 80 dB HL) at 500 Hz

500Hz Latency	Effect	SS	DF	MS	F	P	Conditions	Mean	SD	Std.Err.	-Std.Err	+Std.Err	N
P1	Masker conditions	0.005	2	0.002	0.639	0.535	1	1.20	0.09	0.02	1.19	1.22	11
							2	1.23	0.03	0.02	1.21	1.25	11
							3	1.23	0.05	0.02	1.21	1.25	10
N1	Masker conditions	0	2	0	0.045	0.956	1	1.98	0.06	0.02	1.96	2.00	11
							2	1.99	0.07	0.02	1.97	2.01	11
							3	1.99	0.07	0.02	1.97	2.01	10
P2	Masker conditions	0	2	0	0.028	0.972	1	2.82	0.07	0.02	2.80	2.84	11
							2	2.82	0.07	0.02	2.80	2.84	11
							3	2.81	0.08	0.02	2.79	2.84	10
N2	Masker conditions	0.012	2	0.006	0.877	0.427	1	3.71	0.10	0.02	3.68	3.73	11
							2	3.68	0.06	0.02	3.65	3.70	11
							3	3.66	0.08	0.03	3.63	3.69	10

Table 3D: Main effects of latencies for monaural masking conditions at 500 Hz. BCV stimulus presented at a single/constant intensity of 105 dB SPL in 3 different masker conditions: 1) 100 dB HL, 2) 90 dB HL, and 3) 80 dB HL

Monaural 90 dB HL Masking Conditions

In addition to analyzing the use of the various masking levels at a single intensity, a one-way ANOVA was also conducted in this study to determine whether the use of a masker consistently at 90 dB HL at three different VsEP stimulation intensities (105 dB SPL, 95 dB SPL, and 85 dB SPL) would have any significant effects on the VsEPs responses at 500 and 1000 Hz. Results indicate that the amplitudes of the VsEPs are significantly impacted ($p<.05$) by the 90 dB HL masked intensity conditions at both frequencies (500 and 1000 Hz) tested, while there are no significant effects of the 90 dB HL masked intensity conditions on any of the VsEPs latencies for both frequencies tested (Table 4B and Table 4D).

All of the mean amplitudes at both 500 and 1000 Hz were significantly impacted by the stimulus intensity, with the higher BCV VsEP stimulus intensity levels (ie, 105 dB SPL) having higher mean amplitudes than those with a smaller VsEP stimulation intensity

(95 dB SPL and 85 dB SPL). The mean amplitudes, along with the standard deviation and standard error scores can be found in the tables below (Table 4A. and Table 4C.).

Table 4A.
Summary of ANOVA VsEPs amplitudes for varying intensity conditions (105 dB, 95 dB, & 85 dB SPL) with 90 dB HL masker at 1000 Hz

1kHz Amplitude	Effect	SS	DF	MS	F	P	Conditions	Mean	SD	Std.Err	-Std.Err	+Std.Er	N
N1/P1	90dB monaural masker	195.2	2	97.59	25.12	.000*	1	6.26	3.28	0.59	5.66	6.85	11
							2	1.87	0.92	0.59	1.27	2.46	11
							3	0.58	0.27	0.59	-0.02	1.17	11
P1/N2	90dB monaural masker	852.6	2	426.3	23.28	.000*	1	13.04	6.94	1.29	11.75	14.33	11
							2	3.74	2.48	1.29	2.45	5.03	11
							3	1.22	0.81	1.29	-0.07	2.51	11
N2/P2	90dB monaural masker	1543	2	771.3	25.26	.000*	1	17.45	9.00	1.67	15.78	19.11	11
							2	5.33	3.16	1.67	3.66	6.99	11
							3	1.38	0.79	1.67	-0.29	3.04	11
P2/N3	90dB monaural masker	1120	2	560.2	25.86	.000*	1	14.99	7.57	1.40	13.58	16.39	11
							2	4.50	2.67	1.40	3.09	5.90	11
							3	1.36	0.78	1.40	-0.05	2.76	11
N3/P3	90dB monaural masker	291.8	2	145.9	23.11	.000*	1	7.86	4.01	0.76	7.11	8.62	11
							2	2.51	1.45	0.76	1.75	3.27	11
							3	0.77	0.31	0.79	-0.02	1.56	10

Table 4A: main effects of amplitude for monaural masking conditions at 1000 Hz. Masker presented with a constant 90 dB HL noise in 3 different BCV stimulus intensity conditions: 1) 105 dB SPL, 2) 95 dB SPL, and 3) 85 dB SPL

Table 4B.
Summary of ANOVA VsEPs latencies for varying intensity conditions (105 dB, 95 dB, & 85 dB SPL) with 90 dB HL masker at 1000 Hz

1kHz Latency	Effect	SS	DF	MS	F	P	Conditions	Mean	SD	Std.Err	-Std.Err	+Std.Er	N
N1	90dB monaural masker	0.039	2	0.02	1.333	0.279	1	1.26	0.06	0.04	1.22	1.30	11
							2	1.27	0.05	0.04	1.23	1.31	11
							3	1.19	0.20	0.04	1.16	1.23	11
P1	90dB monaural masker	0.04	2	0.02	3.117	0.059	1	1.75	0.03	0.02	1.72	1.77	11
							2	1.73	0.06	0.02	1.71	1.76	11
							3	1.67	0.12	0.02	1.64	1.69	11
N2	90dB monaural masker	0.031	2	0.015	0.936	0.403	1	2.24	0.05	0.04	2.20	2.28	11
							2	2.21	0.05	0.04	2.17	2.25	11
							3	2.16	0.21	0.04	2.13	2.20	11
P2	90dB monaural masker	0.039	2	0.02	0.824	0.448	1	2.71	0.06	0.05	2.66	2.75	11
							2	2.72	0.03	0.05	2.67	2.76	11
							3	2.64	0.26	0.05	2.59	2.69	11
N3	90dB monaural masker	0.054	2	0.027	0.732	0.489	1	3.19	0.06	0.06	3.14	3.25	11
							2	3.17	0.07	0.06	3.11	3.22	11
							3	3.10	0.32	0.06	3.04	3.16	11
P3	90dB monaural masker	0.078	2	0.039	1.668	0.206	1	3.69	0.06	0.05	3.64	3.73	11
							2	3.66	0.06	0.05	3.61	3.71	11
							3	3.57	0.26	0.05	3.52	3.62	10

Table 4B: main effects of latency for monaural masking conditions at 1000 Hz. Masker presented with a constant 90 dB HL noise in 3 different BCV stimulus intensity conditions: 1) 105 dB SPL, 2) 95 dB SPL, and 3) 85 dB SPL

Table 4C.
Summary of ANOVA VsEPs amplitudes for varying intensity conditions (105 dB, 95 dB, & 85 dB SPL) with 90 dB HL masker at 500 Hz

500Hz Amplitude	Effect	SS	DF	MS	F	P	Conditions	Mean	SD	Std.Err	-Std.Err	+Std.Err	N
P1/N1	90dB monaural masker	320.5	2	160.3	8.443	.001*	1	8.23	7.03	1.31	6.92	9.55	11
							2	2.83	1.52	1.54	1.29	4.37	8
							3	0.80	0.53	1.31	-0.51	2.11	11
N1/P2	90dB monaural masker	1488	2	744.1	11.69	.000*	1	17.16	13.49	2.41	14.76	19.57	11
							2	4.99	2.86	2.41	2.58	7.40	11
							3	1.50	0.85	2.41	-0.91	3.90	11
P2/N2	90dB monaural masker	853.6	2	426.8	13.29	.000*	1	13.08	9.55	1.71	11.37	14.79	11
							2	3.85	2.16	1.71	2.14	5.56	11
							3	1.22	0.60	1.71	-0.49	2.93	11

Table 4C: main effects of amplitude for monaural masking conditions at 500 Hz. Masker presented with a constant 90 dB HL noise in 3 different BCV stimulus intensity conditions: 1) 105 dB SPL, 2) 95 dB SPL, and 3) 85 dB SPL

Table 4D.
Summary of ANOVA VsEPs latencies for varying intensity conditions (105 dB, 95 dB, & 85 dB SPL) with 90 dB HL Masker at 500 Hz

500Hz Latency	Effect	SS	DF	MS	F	P	Conditions	Mean	SD	Std.Err	-Std.Err	+Std.Err	N
P1	90dB monaural masker	0.001	2	0.001	0.021	0.98	1	1.23	0.03	0.06	1.18	1.29	11
							2	1.24	0.10	0.07	1.17	1.31	7
							3	1.25	0.29	0.06	1.19	1.31	11
N1	90dB monaural masker	0.01	2	0.005	0.505	0.609	1	1.99	0.07	0.03	1.96	2.02	11
							2	2.03	0.09	0.03	2.00	2.06	10
							3	2.01	0.12	0.03	1.98	2.04	11
P2	90dB monaural masker	0.012	2	0.006	0.538	0.59	1	2.82	0.07	0.03	2.79	2.85	11
							2	2.83	0.10	0.03	2.80	2.87	10
							3	2.87	0.14	0.03	2.84	2.90	11
N2	90dB monaural masker	0.081	2	0.04	1.715	0.198	1	3.68	0.06	0.05	3.63	3.73	11
							2	3.67	0.07	0.05	3.62	3.72	10
							3	3.78	0.25	0.05	3.74	3.83	11

Table 4D: main effects of latency for monaural masking conditions at 500 Hz. Masker presented with a constant 90 dB HL noise in 3 different BCV stimulus intensity conditions: 1) 105 dB SPL, 2) 95 dB SPL, and 3) 85 dB SPL

Binaural Masking

Only two out of the 11 participants in this study had binaural masking performed and analyzed. Similar to the monaural masking testing conditions at 105 dB SPL, a one-way ANOVA was conducted to compare the effects of bilateral masking at three different masking levels (100 dB HL, 90 dB HL, and 80 dB HL) at a single VsEP stimulation intensity of 105 dB SPL. Upon statistical analysis of the results (Tables 5A-5D), no significant effects of the masker level at any of the three conditions analyzed were found

at any of the VsEP amplitudes or latencies for either of the frequencies (1000 Hz and 500 Hz) tested, besides at the P3 latency at 1000 Hz (Table 5C). It should be noted again, however, that only two participants were tested with binaural masking, thus, not much can be said about this binaural masking data besides that the individual data for monaural and binaural masking is similar (Figure 6), and more participants need to be tested and compared.

Table 5A.
Summary of ANOVA VsEPs amplitudes for 105 dB SPL binaural masking conditions (100 dB, 90 dB, & 80 dB HL) at 1000 Hz

1kHz Amplitude	Effect	SS	DF	MS	F	P	Conditions	Mean	SD	Std.Err	Std.Err	Std.Err	N
N1/P1	binaural masking	0.147	2	0.073	0.007	0.993	1	6.03	3.07	2.23	3.80	8.27	2
							2	5.67	3.04	2.23	3.44	7.91	2
							3	5.97	3.36	2.23	3.73	8.20	2
P1/N2	binaural masking	0.051	2	0.026	0.001	0.999	1	13.69	6.92	5.01	8.68	18.70	2
							2	13.46	6.81	5.01	8.45	18.47	2
							3	13.57	7.50	5.01	8.56	18.58	2
N2/P2	binaural masking	1.058	2	0.529	0.006	0.994	1	17.93	8.94	6.55	11.38	24.48	2
							2	18.87	9.22	6.55	12.32	25.41	2
							3	18.77	9.61	6.55	12.23	25.32	2
P2/N3	binaural masking	0.606	2	0.303	0.004	0.996	1	16.18	8.66	6.05	10.12	22.23	2
							2	15.87	8.28	6.05	9.82	21.93	2
							3	16.64	8.75	6.05	10.59	22.70	2
N3/P3	binaural masking	0.122	2	0.061	0.003	0.997	1	9.35	4.98	3.46	5.89	12.81	2
							2	9.01	5.01	3.46	5.55	12.46	2
							3	9.13	4.68	3.46	5.68	12.59	2

Table 5A: Main effects of amplitude for binaural masking conditions at 1000 Hz. BCV stimulus presented at a single/constant intensity of 105 dB SPL in 3 different masker conditions: 1) 100 dB HL, 2) 90 dB HL, and 3) 80 dB HL

Table 5B.
Summary of ANOVA VsEPs latencies for 105 dB SPL binaural masking conditions (100 dB, 90 dB, & 80 dB HL) at 1000 Hz

1kHz Latency	Effect	SS	DF	MS	F	P	Conditions	Mean	SD	Std.Err	-Std.Er	+Std.Er	N
N1	binaural masking	0.001	2	0	1	0.465	1	1.30	0.04	0.01	1.28	1.31	2
							2	1.27	0.00	0.01	1.26	1.28	2
							3	1.27	0.00	0.01	1.26	1.28	2
P1	binaural masking	0.004	2	0.002	1.682	0.324	1	1.72	0.04	0.02	1.69	1.74	2
							2	1.77	0.04	0.02	1.74	1.79	2
							3	1.77	0.03	0.02	1.75	1.79	2
N2	binaural masking	0.001	2	0	1.4	0.372	1	2.20	0.00	0.01	2.19	2.21	2
							2	2.18	0.03	0.01	2.17	2.19	2
							3	2.21	0.01	0.01	2.20	2.22	2
P2	binaural masking	0.002	2	0.001	1	0.465	1	2.72	0.00	0.02	2.70	2.74	2
							2	2.72	0.00	0.02	2.70	2.74	2
							3	2.68	0.06	0.02	2.66	2.70	2
N3	binaural masking	0.002	2	0.001	1.489	0.356	1	3.16	0.03	0.02	3.14	3.18	2
							2	3.21	0.04	0.02	3.19	3.22	2
							3	3.17	0.01	0.02	3.15	3.19	2
P3	binaural masking	0.002	2	0.001	16	.025*	1	3.65	0.00	0.01	3.64	3.66	2
							2	3.65	0.00	0.01	3.64	3.66	2
							3	3.69	0.01	0.01	3.68	3.70	2

Table 5B: Main effects of latency for binaural masking conditions at 1000 Hz. BCV stimulus presented at a single/constant intensity of 105 dB SPL in 3 different masker conditions: 1) 100 dB HL, 2) 90 dB HL, and 3) 80 dB HL

Table 5C.
Summary of ANOVA VsEPs amplitudes for 105 dB SPL binaural masking conditions (100 dB, 90 dB, & 80 dB HL) at 500 Hz

500Hz Amplitude	Effect	SS	DF	MS	F	P	Conditions	Mean	SD	Std.Err	-Std.Er	+Std.Er	N
P1/N1	binaural masking	0.09	2	0.045	0.006	0.994	1	6.15	2.99	2.00	4.15	8.15	2
							2	6.18	2.59	2.00	4.18	8.18	2
							3	5.91	2.89	2.00	3.91	7.91	2
N1/P2	binaural masking	0.121	2	0.06	0.002	0.998	1	13.80	6.94	4.36	9.45	18.16	2
							2	13.61	5.67	4.36	9.26	17.97	2
							3	13.45	5.78	4.36	9.10	17.81	2
P2/N2	binaural masking	0.384	2	0.192	0.006	0.994	1	12.17	5.98	3.98	8.19	16.15	2
							2	11.92	5.75	3.98	7.93	15.90	2
							3	11.56	5.14	3.98	7.57	15.54	2

Table 5C: Main effects of amplitude for binaural masking conditions at 1000 Hz. BCV stimulus presented at a single/constant intensity of 105 dB SPL in 3 different masker conditions: 1) 100 dB HL, 2) 90 dB HL, and 3) 80 dB HL

Table 5D.
Summary of ANOVA VsEPs latencies for 105 dB SPL binaural masking conditions (100 dB, 90 dB, & 80 dB HL) at 500 Hz

500Hz Latency	Effect	SS	DF	MS	F	P	Conditions	Mean	SD	Std.Err	-Std.Er	+Std.Er	N
P1	binaural masking	0.002	2	0.001	0.907	0.492	1	1.21	0.04	0.02	1.18	1.23	2
							2	1.21	0.04	0.02	1.18	1.23	2
							3	1.24	0.01	0.02	1.22	1.26	2
N1	binaural masking	0.001	2	0.001	0.293	0.765	1	1.93	0.06	0.03	1.89	1.96	2
							2	1.95	0.03	0.03	1.92	1.98	2
							3	1.96	0.04	0.03	1.93	1.99	2
P2	binaural masking	0.002	2	0.001	1.96	0.285	1	2.76	0.00	0.01	2.75	2.77	2
							2	2.76	0.00	0.01	2.75	2.77	2
							3	2.80	0.04	0.01	2.78	2.81	2
N2	binaural masking	0.001	2	0.001	1.069	0.446	1	3.63	0.04	0.02	3.61	3.64	2
							2	3.60	0.00	0.02	3.58	3.62	2
							3	3.63	0.01	0.02	3.61	3.65	2

Table 5D: Main effects of latency for binaural masking conditions at 500 Hz. BCV stimulus presented at a single/constant intensity of 105 dB SPL in 3 different masker conditions: 1) 100 dB HL, 2) 90 dB HL, and 3) 80 dB HL

In comparison to monaural masking means (Table 3), there is no significant difference with binaural masking as can be seen in Table 5 and Figure 9.

Figure 9: monaural and binaural masking amplitude and latency comparisons at 500 and 1000 Hz

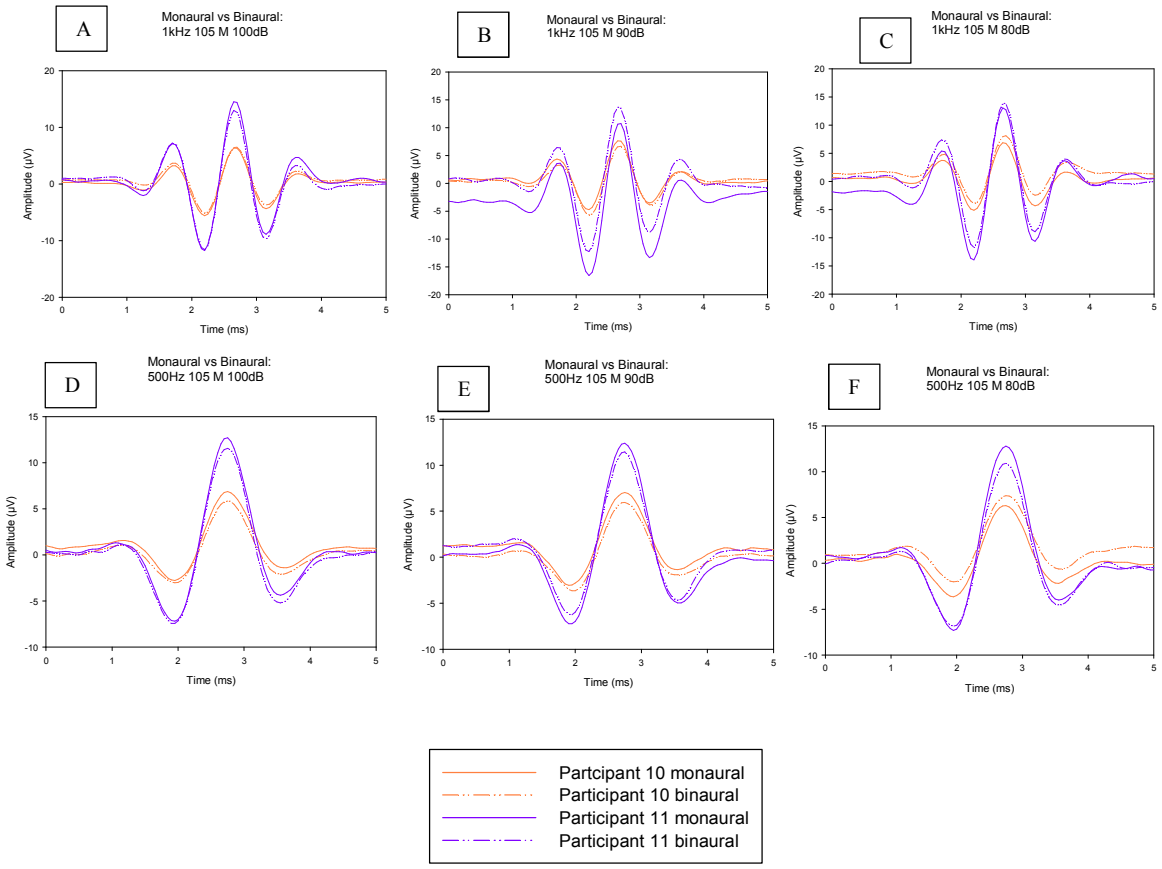


Figure 9: Monaural and binaural masking comparison between 1000 Hz and 500 Hz waveform data for the two participants tested with binaural masker: 100 Hz waveforms at A) 105 dB SPL with 100 dB HL masker, B) 105 dB SPL with 90 dB HL masker, C) 105 dB SPL with 80 dB HL masker; 500 Hz waveforms at D) 105 dB SPL with 100 dB HL masker, E) 105 dB SPL with 90 dB HL masker, F) 105 dB SPL with 80 dB HL masker

Analyses of Possible Interaction Effects of Main Effects

Monaural masking (100 dB HL, 90 dB HL, & 80 dB HL) at 105 dB SPL: interaction of latency and amplitude at 1000 Hz

No interaction effects between latency and amplitudes at the BCV stimulus at 105 dB SPL at 1000 Hz were found (Appendix E1), regardless of the three monaural masking conditions assessed (100 dB HL, 90 dB HL, and 80 dB HL). The mean latency for all 3

conditions was around 2ms, while the mean amplitude was about 11 microvolts (μV) in condition 1 (100 dB HL masker) and 12 μV in conditions 2 and 3 (90 dB HL and 80 dB HL masking).

Monaural masking (100 dB HL, 90 dB HL, & 80 dB HL) at 105 dB SPL: interaction of latency and amplitude at 500 Hz

No interaction effects between latency and amplitude at the BCV stimulus at 105 dB SPL at 500 Hz were found in the three monaural masking conditions assessed (100 dB HL, 90 dB HL, and 80 dB HL). For the 105 dB SPL monaural masking conditions at 500 Hz (Appendix E2), the mean latency was about 2ms for all 3 masking conditions, while mean amplitude was about 12 μV in conditions 1 and 2 (100 dB HL and 90 dB HL masker, respectively) and 11 μV in condition 3 (80 dB HL masking).

Latencies between 1000 and 500 Hz at 105 dB SPL with monaural masking (100 dB HL, 90 dB HL, & 80 dB HL): interaction of latency and frequency

Regardless of the frequency and the 3 masker levels assessed, all latencies at both 1000 Hz and 500 Hz remained consistent at with a mean of about 2ms. Therefore, latency was not impacted by masker levels, nor the frequency tested (Appendix E3).

Amplitudes between 1000 Hz and 500 Hz at 105 dB SPL with monaural masking (100 dB HL, 90 dB HL, & 80 dB HL): interaction of amplitude and frequency

The mean amplitudes at both 1000 Hz and 500 Hz also remained consistent, regardless of frequency, with the mean amplitude around 11 μV and 12 μV across both frequencies and the 3 masker levels assessed. Thus, no interaction effects between amplitude and frequency were noted (Appendix E4).

Varying intensity conditions (105 dB SPL, 95 dB SPL, & 85 dB SPL) with 90 dB HL masker: interaction of latency and amplitude at 1000 Hz

There was a significant interaction found (p = .002) between the mean amplitude and the 3 varying intensities, where the mean amplitude was found to be the smallest in the third condition (85 dB SPL stimulus with the 90 dB HL masker) and the mean amplitude increased with increase in the stimulus level. When the 90 dB HL masker remained constant throughout all 3 intensity conditions tested (105 dB SPL, 95 dB SPL, and 85 dB SPL), the higher intensity had the highest mean amplitude (105 dB SPL, condition 1) at around 12 μV, while the mean amplitudes were around 4 μV and 1 μV for conditions 2 and 3 (95 dB SPL and 85 dB SPL). This change in amplitude with varying stimulus levels can be observed not only in the corresponding table analysis (Appendix E9), but looking at the general waveforms in both the waveforms in the results chapter across participants and across individual participants (Appendix D) as well. However, regardless of the conditions, the mean latency remained consistent at about 2ms.

Varying intensity conditions (105 dB SPL, 95 dB SPL, & 85 dB SPL) with 90 dB HL masker: interaction of latency and amplitude at 500 Hz

Again, there was a significant interaction found (p = .03) with amplitude and the 3 varying intensities, however, no interaction between latency and amplitudes was found with the constant 90 dB HL masking noise conditions. The mean latency remained around 2ms across all conditions, while the amplitude decreased with decreased stimulus intensity. Similar to 1000 Hz, with assessment at 500 Hz, the mean amplitudes were around 1 μV, 4

μV, and 13 μV at 85 dB SPL, 95 dB SPL, and 105 dB SPL BCV stimulus conditions, respectively (Appendix E10).

Latencies between 1000 and 500 Hz at varying intensity conditions (105 dB SPL, 95 dB SPL, & 85 dB SPL) with 90 dB HL masker: interaction of latency and frequency

Surprisingly, a significant interaction effect between frequency and mean latency was found ($p = .0046$) (Appendix E11). Although it appears to be insignificant, the above p value proves otherwise. The mean latencies at 500 Hz were around 2.4ms, while the mean latencies at 1000 Hz were all in the 1.9 ms range (close to 2ms). This makes sense considering that the vestibular system responds best at lower frequencies (Renga, 2019).

Amplitudes between 1000 and 500 Hz at varying intensity conditions (105 dB SPL, 95 dB SPL, & 85 dB SPL) with 90 dB HL masker: interaction of amplitude and frequency

There was a significant interaction found ($p = .03$) with amplitude and the 3 varying intensities at 500 Hz and 1000 Hz. Again, this might have been due to noise and not necessarily due to frequency effects, as the mean amplitudes were similar at both frequencies in the same conditions, with conditions 2 and 3 (95 dB SPL and 85 dB SPL BCV stimuli) intensities having a mean amplitude of 4 μV and 1 μV, respectively, at both 500 Hz and 1000 Hz. The 105 dB SPL with 90 dB HL masker (condition 1) had a higher mean amplitude, with the mean being around 13 μV at 500 Hz and 12 μV at 1000 Hz. However, this difference in mean amplitude across conditions may actually be due to noise/overmasking and not due to any frequency interaction, since higher intensity conditions also had higher standard error scores (Appendix E12). This might seem counterintuitive, but in actuality, the error scores in the lower stimulus conditions might

possibly be low due to the difficulty in observation of the positive and negative peaks due to the noise, especially with the 85 dB SPL with 90 dB HL masker (condition 3), as can be observed in the general waveforms as well.

Unmasked conditions (115 dB SPL and 105 dB SPL): interaction of latency and amplitude at 1000 Hz

While latencies remained similar (about 2ms) across conditions, there was a significant difference between the mean amplitude between the two conditions ($p = .0379$). Again, this amplitude difference is not due to any interaction with latency, as latency remained consistent regardless of BCV stimulus level; rather, it is likely a direct result of the stimulus intensity, with the louder condition (unmasked BCV at 115 dB SPL) having a mean amplitude of around 33 μV, while condition 2 (unmasked BCV at 105 dB SPL) had a mean amplitude of about 12 μV (Appendix E13).

Unmasked conditions (115 dB SPL and 105 dB SPL): interaction of latency and amplitude at 500 Hz

No significant difference was found between the latencies and amplitudes at 500 Hz ($p = .146$). The mean latencies at both intensity conditions remained around 2 ms, while again the higher intensity BCV stimulus (115 dB SPL) had a higher mean amplitude (about 30 μV) compared to the mean amplitude of about 11 μV at BCV stimulus at 105 dB SPL (Appendix E4).

Latencies between 1000 and 500 Hz at unmasked conditions (115 dB SPL and 105 dB SPL): interaction of latency and frequency

No significant difference was found between the latencies and conditions at either frequency at 1000 Hz and 500 Hz (Appendix E15). The latencies remained consistent, with the mean around 2 ms, with low error scores across all conditions as well.

Amplitudes between 1000 and 500 Hz at unmasked conditions (115 dB SPL and 105 dB SPL): interaction of amplitude and frequency

There was no significant difference ($p = .186$) found between frequencies tested and the mean amplitudes (Appendix E16). Condition 1 (115 dB SPL) had higher mean amplitudes regardless of frequency (34 μV and 30 μV) at 1000 Hz and 500 Hz, respectively, while the mean amplitude was around 12 μV (1000 Hz) and 11 μV (500 Hz). However, it should be noted that while the amplitudes are larger in the high intensity conditions, the error scores are also larger with the louder BCV stimulus (115 dB SPL) compared with condition 2 (105 dB SPL), regardless of the frequency (1000 Hz and 500 Hz) tested.

CHAPTER 5

DISCUSSION

Relatively few studies have been conducted in humans using VsEPs. Most VsEP studies have used animal models, particularly birds and small mammals (rodents and cats). The VsEPs recorded in this study were therefore unique since they were non-invasive, required no effort on the part of the participant, other than to remain relaxed, quiet, and keep their eyes closed.

In this study, fundamental characteristics of VsEP responses in healthy young adults were obtained and analyzed by evaluating the effects of stimulus frequency, intensity, along with masked and unmasked response levels. The 500 Hz responses were characterized as having two positive (P1, P2) and two negative (N1, N2) peaks; the 1000 Hz responses were characterized as having three positive (P1,P2,P3) and three negative (N1, N2, N3) peaks. Amplitude and latency did not appear to be influenced by the frequency tested (Appendix E).

Stimuli used to elicit these VsEPS were bone conducted vibrations that presumably cause linear acceleration of the skull and therefore stimulate the otolith organs. Based on the morphology of VsEPs and results of the ANOVAs, response amplitude but not latency were primarily affected by stimulus intensity.

Latency remained constant throughout all conditions, regardless of frequency, stimulus and masker intensity levels tested. However, the amplitudes likely were influenced by the intensity levels of the stimulus and/or masker, rather than any other possible interaction effects from frequency. The results, found in Appendix E, indicate that

the higher BCV intensity conditions were found to have higher mean amplitude responses. However, it should be noted that greater levels of error (SD) were observed at the higher (115 dB SPL) BCV stimulus than at lower intensity levels. It would therefore make sense to further test intensities below 115 dB SPL, not only due to SD concerns, but possible damage from an excessive stimulus levels, which can cause not only temporary and/or permanent hearing thresholds shifts, but cause damage to vestibular function as well (Stewart et al., 2020). It should be noted that the study by Stewart and colleagues (2020) used free-field (air-conduction) noise, rather than BCV used in this study. However, since the vestibular hair cells are similar to the hair cells in the cochlea, overstimulation of these hair cells regardless of stimulation type (BCV or ACS) is possible because the inner ear (cochlear and vestibular) hair cells are responsive/sensitive to both BCV and ACS (Brown, Pastras, & Curthoys, 2017).

Frequency did not seem to impact any of the responses in general; although, at the constant masking noise of 90 dB HL presented at varying BCV stimulus intensity conditions (105 dB HL, 95 dB HL, & 85 dB SPL), the probability values did show a statistically significant interaction ($p = .0046$) between the frequency tested and latencies (Appendix 11E). However, this makes sense considering that the vestibular system responds best at lower frequencies due to the endolymphatic fluid found within the labyrinth (Renga, 2019). For this reason, it would be worthwhile to assess additional lower frequencies (perhaps 250 Hz and 750 Hz) in future studies to see if these make any difference to the VsEPs, such as possibly higher amplitudes. The issue with the lower frequency recordings in auditory tests (as much is still unknown regarding vestibular

electrophysiological recordings) seems to be the amount of artifacts, since low frequencies require less intensity to attenuate/crossover the skull to the non-test ear.

With regards to masking, it does appear that overmasking is possible, due to the noisy recordings when the stimulus was closest to the masker level (i.e., BCV at 85 dB SPL with 90 dB HL masker). Therefore, the BCV stimulus intensity should be higher than the masking noise to decrease the possibility of noisy recordings.

Additionally, binaural masking should be performed on all individuals, as the general consensus of participants was that the monaural masker was annoying. Although binaural masking was performed only on two participants, the feedback received indicated the binaural masker felt more comfortable. Since binaural masker did not cause noisy recordings or any similar issues in this study, it would definitely be worthwhile to explore the use of a binaural masker in future studies, especially since auditory masking should not affect the VsEPs. However, ipsilateral and contralateral monaural masking should also be compared to binaural since additional normative data is needed to know the extent to which masking might play a role in the VsEP responses.

Limitations and Future Directions of the Current Study

The most obvious weakness of the study was that very few individuals were tested and therefore, more participants are needed to be assessed. Part of this limitation was due to the Hearing Science Lab and the Department of Communication Sciences and Disorders being moved to a different building on campus. As a consequence, it would take an inordinate amount of time to reconstruct the lab and recalibrate the necessary instrumentation.

Besides the number of participants tested, a more diverse sample should be studied in the future. Different ethnic groups could be analyzed in future studies to determine whether VsEPs might be impacted by race. It is well known that there is a higher incidence of certain vestibular disorders in specific groups of people with known disease states, like Meniere's disease. For example, Meniere's disease, which requires a vestibular component for diagnosis, is known to have a higher incidence in Caucasians than in other racial groups (Simo, Yang, Qu, Preis, Nazzal, & Baugh, 2015). The current VsEP study tested mainly individuals of South Asian and Middle Eastern descent. Of the eleven individuals studied, only one individual was African American, one was Caucasian, and one was East Asian. Thus, without additional testing of a more diverse and larger sample, little can be said with respect to ethnicity and VsEP recordings.

Additionally, age effects would also be important to study, due to well-known age related changes to sensory systems, including mechanisms related to gait and balance related effects. While the cutoff for inclusion in this study was 40 years, it is hypothesized that approximately "6% of hair cells per decade are lost between 40-90 years.... (About 5 percent) of nerve fibers are lost between the ages of 40 to 90 years" (Fattal, Hansen, & Fritzsch, 2018, p.327).

Hearing Status

Presently, it remains to be determined if there will be similar VsEP waveforms in those with normal vestibular functioning but with hearing loss, as only healthy/normal hearing young adults were tested (thresholds <25 dB HL). However, prior research indicates that VsEPs are true vestibular responses, where hearing status alone would have

minimal or no forbearance on the outcomes/VsEP waveforms. VsEPs in individuals with hearing loss have been found to be present, which indicates direct/reliance on vestibular activation. A review by Brown and colleagues (2017) discussed various studies regarding VsEPs (Brown, Pastras, & Curthoys, 2017). One study mentioned that the first positive peak of the VsEP, which were elicited by brief linear BCV, reflected activity of the peripheral vestibular nerve (Pyykko, Aalto, Gronfors, Stark, & Ishizaki, 1995). Additionally, these researchers found the VsEPs to be true vestibular responses, as the responses were present in deaf subjects, but not in those with bilateral vestibular loss nor in cadaver heads (Pyykko et al., 1995).This supports the notion that VsEPs are indeed vestibular responses and are not affected by cochlear function/hearing status, as they are not present in those with bilateral vestibular dysfunction, but are still observable in those with hearing loss.

Since the main purpose of this study was for the development of VsEPs for possible use in clinical settings, it would be important to test people with known vestibular disorders and determine whether VsEPs are able to give the proper diagnosis and laterality of the disorder both accurately and consistently, for diagnostic reliability, specificity, and validity purposes. With regards to being able to diagnose the side (in single-sided disorders), testing using wick placements on both sides with the use of a masker would be most beneficial.

Masking

Based on the results of this study, it appears 105 dB SPL will be the best to further test in future studies, along with 95 dB SPL without masking and/or possibly with no more 80 dB HL masking. Also, feedback received once testing was complete from many of the

participants was that the use of masking was rather annoying in one ear, but both individuals who were tested using binaural masking said that felt more comfortable than the unilateral masker alone.

Although additional testing should be completed on more subjects, for now, this study indicated no significant effects of masking at 105dB SPL regardless of the masking level used and regardless of whether only ipsilateral (for unilateral masker) or bilateral masking was used. Furthermore, binaural masking should be employed for all participants.

Additional Parameters

While more than one frequency and intensity level were tested in this study, additional stimulus durations, masking conditions, along with mini-shaker and electrode placements should be performed in future VsEP studies.

In order to optimize this VsEP assessment, placement of the mini-shaker would be one of the added parameters that should be studied to help determine what the best mini-shaker placements would be for the most robust VsEP responses. Additionally, one of the limitations of this study was that only one side was tested, with placement of the wick electrode in the left ear for all participants tested.

Future Application of VsEPs for Eventual Clinical Use

Once these VsEPs are able to be translated into clinical use after additional testing, there will still be a need for use of multiple assessments, as a single assessment is not enough to get a clear picture of the problem, especially since vestibular disorders are often very complex to diagnose (Brown, Pastras, & Curthoys, 2017).

Disorders of the vestibular system are diverse, as such disorders can be central or peripheral, with peripheral vertigo being more common than central dysfunction (Casale, Browne, Murray, & Gupta, 2020; Shin & Jensen, 2010). Additionally, a vestibular disorder can be unilateral or bilateral. A unilateral vestibular dysfunction typically causes vertigo, while a bilateral dysfunction can be perceived as an imbalance or lightheadedness (Renga, 2019). This is important to know, as many people may think lightheadedness may be due from low blood sugar and other factors, when in actuality, it may be a symptom of bilateral vestibular dysfunction. However, generally speaking, the symptom of vertigo predominates in peripheral lesions of the vestibular system (Renga, 2019). Additionally, it is not uncommon for "hearing loss, tinnitus, and ear fullness" to occur on the side of the peripheral lesion, while "fluctuation in visual acuity and oscillopsia" can also occur in individuals with vestibular dysfunction (Renga, 2019, p. 6).

Just as there are multiple symptoms associated with vestibular dysfunction, vestibular disorders can be due to various other issues (e.g., vestibular migraine, vestibular neuritis, vestibular schwannomas, etc.). The three most common vestibular etiologies include benign paroxysmal positional vertigo (BPPV), Meniere's disease, and viral labyrinthitis (Smith, 2019; Casale et al., 2020). However, it should be noted that in addition to these disorders, damage to the vestibular system can also occur from high-intensity noise exposure, as the hair cells in both the cochlea and otoliths are sensitive to noise (Curthoys, 2010). Regardless of the cause of balance disturbances, even if not due to vestibular pathology, balance disorders can be quite disturbing and impact daily life activities.

Quality of Life (QOL) of Individuals with Balance Disorders

In general, individuals with vestibular dysfunction may become fearful of falling; thus, they are more likely to avoid being in any position that may cause them to become dizzy. Avoidance of certain positions may lead to poor posture and/or increased inactivity (Fattal, Hansen, & Fritzsch, 2018, Renga, 2019). This is a considerable concern, since the common saying of 'use it or lose it'- when associated with the elderly, the lack of physical activity may lead muscle mass to decrease along with an increase in risk for bed sores and pulmonary embolism, leading to a quick downhill progression to death (Fattal et al., 2018). On the other hand, children with vestibular disorders may have delayed development; however, in some instances, without timely intervention, children may never reach certain milestones related to normal motor development (Rine & Wiener-Vacher, 2013). While the vestibular system is known to play a role in learning and memory, more research is being conducted to further knowledge in this area since many aspects of the vestibular pathways are currently unknown (Cullen, 2019).

Additionally, QOL may be affected by comorbid issues and annoying symptoms, such as tinnitus. One study compared fatigue levels in individuals with and without hearing loss (Burke & Naylor, 2020). The researchers found that those with tinnitus, regardless of hearing status (even those with normal hearing), experienced higher fatigue rates than those without tinnitus. This is interesting to note, as there is a high associated tinnitus rate in individuals with certain vestibular disorders, such as Menieres Disease.

Pediatric

Similar to childhood hearing loss, the earlier the diagnosis with proper treatment and management of a vestibular disorder, there is an increased likelihood of better outcomes. At birth or shortly after birth, any vestibular impairments are difficult to diagnose and manage, especially if there are no cofounding disorders or syndromes present in a pediatric patient. This becomes an issue, as early intervention produces the best outcomes. The vestibular system relies on various integrated sensory functions (e.g., vision), thus "disruption of vestibular function prior to maturation can be more debilitating than adult-onset vestibular dysfunction" (Rine & Wiener-Vacher, 2013, p.508).

The reason for increased disability outcomes in the young compared to the elderly with a vestibular disorder may, for example, be due to a child being unable to properly focus due to issues with gaze, where their instability may lead to motor issues and learning disorders due to the association of the vestibular system with learning (Wiener-Vacher, Quarez, & Le Priol, 2018). A proper gaze is required for reading skills. So much is still unknown regarding the vestibular system's role in learning and memory, not just balance; thus, there may be neurological disorders that may result primarily due to a vestibular disturbance in children that currently remain unknown (Cullen, 2019; Rine & Wiener-Vacher, 2013).

Additionally, balance disorders are likely to be undiagnosed or misdiagnosed, therefore underestimated in many children, as some children may be asymptomatic and/or younger children appear to tolerate, or rather either the child and/or their caregivers don't realize that a young child is experiencing dizziness, rather may think they are a late walker

or clumsy when compared to older children and adults. Similarly, young children tend not to complain about their unsteadiness, either because they may be unable to put their symptoms into words/unclear in their description of feeling off-balance, or unless their daily activities become limited (Wiener-Vacher, Quarez, & Le Priol, 2018). Still, some children may remain undiagnosed due to the limited vestibular assessments currently available, which may require a child to be mature enough to follow specific directions. Some children may also be misdiagnosed due to overlapping symptoms or inability to adequately convey their symptoms (Wiener-Vacher, Quarez, & Le Priol, 2018).

Elderly

The elderly often have global/multisensory issues due to the physiological changes associated with aging, along with a greater likelihood of exposure to various pharmaceutical agents and a higher rate of chronic health issues that come with increased age (Kim, Wilson, & Wiet, 2008). Any sensory impairment will often result in a generally decreased quality of life. While hearing loss is the most common neurosensory disorder due to aging, more focus/emphasis should be placed upon vestibular issues as well, since the quality of life is very much affected by balance.

In general, the elderly are at the highest risk for falls and lifelong issues that may come with falls, such as hospitalization in long-term care facilities (Fattal et al., 2018). Additionally, recent research has shown that the increase in falls in the elderly may be due to aging factors associated with impaired otolith function due to reduced numbers and function of the otoconia and vestibular hair cells (Fattal et al., 2018). This decline in vestibular function, especially with the otoliths, has been associated with an increased risk

of impaired cognition and dementia (Smith, 2019). That is to say that a loss of vestibular function (not just hearing loss) is found to play a role in cognition and dementia (Dobbels, Peetermans, Boon, Martens, Van de Heyning, & Van Rompaey, 2019).

Dobbels and colleagues (2019) studied 126 patients with known bilateral vestibulopathy and found that individuals have cognitive limitations and not just balance issues, especially a decline in spatial navigation. Therefore, it comes as no surprise that the hippocampus, which is known to play a role in memory, is impaired in those with reduced spatial reasoning/memory (Smith, 2019). Specifically, it has been found that the size of the hippocampus "positively correlates with the performance during navigation and spatial memory tasks" (Cullen, 2019, p.358). It should be noted that the "hippocampus is one of the first regions to degenerate during Alzheimer's disease, and [that] postural imbalance, as well as spatial disorientation and wandering, are common features of the disease" (Cullen, 2019, p.358). This is not to imply any cause and effect from vestibular dysfunction in the elderly, as not all causes of balance disturbances are due to dementia; however, clinicians should keep this in mind when giving testing instructions, as well as for proper referrals as needed to possibly help delay a fast decline. On a positive note, recall that the VsEP assessment is non-invasive and well suited for a pediatric and an elderly population. This protocol requires no active participation from an individual being tested; therefore such an assessment can easily be performed.

Summary

In addition to assessing and treating auditory disorders, the field of audiology plays a vital role in the diagnosis and management of individuals with balance disorders. Recall

the only tests available clinically today to assess utricle and saccule function are the VEMP protocols, which require active participation; i.e., lifting the neck (cVEMP) or maintaining eye positions. Therefore, with regards to vestibular electrophysiological assessments, the VsEPs seem promising for future clinical use, especially for their ability to be tested in a wider/more diverse range of patients who are most vulnerable for falls and delays with cognition (i.e., pediatric, elderly, and others with certain physical and/or mental/cognitive disabilities); possibly the only exceptions may be young infants or those with seizure disorders, as the mini-shaker might be too much pressure/forceful, especially on an infant's delicate skull. Nevertheless, VsEPs will one day be added to our vestibular armamentarium. Although this is just a single study, VsEPs look promising for potential clinical use in the future due to the ease of measurement and analysis. This study showed consistency across all participants in most conditions. While additional studies are necessary to explore other parameters and recording techniques, the future seems bright with respect to translating VsEPs for eventual clinical use.

Lastly, it is becoming increasingly apparent that intense noise exposure and blast overpressures affect balance function. In fact, which can lead to temporary and/or permanent otolith dysfunction and threshold shifts to these sensory receptors (Stewart et al., 2018; Stewart et al., 2020a; Stewart et al., 2020b; Stewart et al., in press). That is, just as it is possible to get noise-induced hearing loss, recent compelling data implies that it is possible to experience "peripheral vestibular damage after exposure to loud sounds, which "can lead to anatomic and/or physiological changes" (Stewart et al., 2020, p. 658). In fact,

otolith organs appear to be most susceptible to acoustic over stimulation (Stewart et al., 2020).

Conclusion

This study supports general findings from prior VsEP research. That is, the VsEPs recorded from the tympanic membrane appear to be valid responses since the onset latencies are >1.0 ms and do not appear to be artifact. Artifactual responses would coincide with the stimulus onset (0 ms). With regards to the reliability of VsEPs, the recordings from this study were consistent across participants; most conditions were tested twice for participants at random to see if any difference could be found between trials. It should be noted that all trial results showed similar results in participants, but results were averaged whenever multiple (2 trials) per condition were tested.

Overall, results indicate that while there are no significant differences in waveform shape and latency in healthy adults across both frequencies (500 Hz and 1000 Hz) and in all conditions tested, the amplitude of the VsEP responses were significantly impacted by the level-of-stimulation.

Similar to the auditory system, the vestibular system has sensitivity to both high-level sounds and bone-conduction vibrations (Brown, Pastras, & Curthoys, 2017). Nevertheless, the specificity of VsEP responses becomes a challenge due to the possibility of cochlear responses contaminating vestibular responses (Böhmer, Hoffman, & Honrubia, 1995). This study supports the findings of the Böhmer et al (1995), which found that "acoustic masking with white noise did not affect the VsEP in most previous experiments. Only [. . .] did acoustic masking influence the amplitude of some response components"

(Böhmer, Hoffman, & Honrubia, 1995; p. 498). Presently, it remains to be determined if there will be similar VsEP waveforms in those with peripheral hearing loss, as only healthy/normal hearing (thresholds <25 dB HL) young adults were tested. Although additional studies are needed to determine reliability and validity of testing across a more diverse group (healthy and those with otolith disorders, various age groups, etc), this study shows great promise for future use of VsEPs in clinical practice due to the consistency of recordings across all participants assessed in this study.

Appendix A: Consent Form

Medical Research Informed Consent

Title of Study: Parametric Study of Short Latency Vestibular Evoked Potentials (VsEPs) in Healthy Young Adults

Principal Investigator (PI): Sabahet F. Rizvi
Communication Sciences and Disorders

Purpose

You are being asked to be in a research study to assist in the development of a short latency vestibular evoked potentials (VsEP) because you are a healthy adult with a negative history of hearing, balance, or cognitive problems and are between the ages of 18 to 40 years. This study is being conducted at WayneStateUniversity, in the Hearing Science Laboratory of Dr. Anthony T. Cacace. The Laboratory is located in the basement of the RackhamMemorialBuilding, room 045, 60 Farnsworh Street, Detroit, MI. A total of 30 participants will be enrolled in this study. **Please read this form and ask any questions you may have before agreeing to be in the study.**

In this research study, we plan to record electrical responses from balance receptors located in the inner ear (utricle and saccule) with disposable adhesive disks which will be placed on the top of the head and behind your ear. The disks are similar to those used when your doctor measures your heartbeat. Another cotton wick electrode will be placed in your ear canal. Then, an ear-bud like earphone will be placed in the ear canal and this will hold the cotton wick electrode in place so it doesn't move. A vibrator will be placed on different areas of your head to see where we get the best response. Participants in the study will be healthy young male and female adults, between the ages of 18 to 40 years.

Study Procedures

If you agree to take part in this research study, you will be asked to come to the Hearing Science Laboratory, located in the basement of the RackhamBuilding (room 045) at WayneStateUniversity. Prior to taking part in any of the assessments for this study, we want to ensure that your hearing and vision are clinically normal. For the vision screening, you will read letters from a chart on the wall in a well lit room. Each eye will be tested separately. For the hearing test, you will listen to tones presented to earphones in a sound booth and you will respond to the lowest sound you hear for different low and high pitched sounds. Each ear will be tested separately. The vision and hearing tests will take about 10 minutes.

After the hearing test, you will be taken into another sound booth for the VsEP assessment. For this test, you will be asked to lay comfortably on a bed-type recliner. The researcher will attach electrodes to your head (or use an electrode cap, depending on your hair type/thickness) and place a cotton wick inside your ear canal. The earphone, consisting of a soft spongy material, will be placed in the ear canal. The soft foam earphone will ensure that the cotton wick electrode does not move during testing. In some conditions, a noise from the earphone will be presented which sounds like a shower running. The purpose for this masking noise is to ensure that your VsEP responses are not coming from the hearing portion of your ear, but rather from the balance receptors. For the testing, you will need to relax and remain quiet. You will not have to respond in any way. All testing is simple and painless. The VsEP assessment should take about 1.5 hours. Therefore, total testing time will take about 2 hours or less, which includes testing and filling out and signing the consent form.

Benefits

As a participant in this research study, there will be no direct benefit for you; however, information from this study may benefit other people now or in the future.

Risks

By taking part in this study, you may experience the following risks:

The application of the electrodes on the head may cause some minor irritation, which should resolve after the test.

The cotton wick-electrode may also cause temporary irritation, but this is not typical and should resolve quickly. Both electrode types are used routinely in audiology clinics on a routine basis.

It is possible, but not likely, that stimulation from the vibrator could cause temporary dizziness or even a mild headache. If this occurs, testing will be stopped immediately until these conditions resolve.

There may also be risks involved from taking part in this study that are not known to researchers at this time.

Alternatives

The only alternative for participation in this study is to <u>not</u> to participate in the study.

Study Costs

Participation in this study will be of no cost to you.

Compensation

You will not be paid for taking part in this study.

Confidentiality

All information collected about you during the course of this study will be kept confidential to the extent permitted by law. You will be identified in the research records by a code name or number. Information that identifies you personally will not be released without your written permission. However, the study sponsor, the Institutional Review Board (IRB) at Wayne State University, or federal agencies with appropriate regulatory oversight [e.g., Food and Drug Administration (FDA), Office for Human Research Protections (OHRP), Office of Civil Rights (OCR), etc.) may review your records.

When the results of this research are published or discussed in conferences, no information will be included that would reveal your identity.

Voluntary Participation/Withdrawal

Taking part in this study is voluntary. You have the right to choose not to take part in this study. You are free to only answer questions that you want to answer. You are free to withdraw from participation in this study at any time. Your decisions will not change any present or future relationship with WayneStateUniversity or its affiliates, or other services you are entitled to receive.

The PI may stop your participation in this study without your consent. If you have any side effects that are very serious or if you become ill during the course of the research study you may have to drop out, even if you would like to continue. The PI will make the decision and let you know if it is not possible for you to continue. The decision that is made is to protect your health and safety, or because it is part of the research plan that people who develop certain conditions or do not follow the instructions from the study doctor may not continue to participate.

Questions

If you have any questions about this study now or in the future, you may contact Dr. Rizvi or one of her research team members at the following phone number [redacted]. If you have questions or concerns about your rights as a research participant, the Chair of the Institutional Review Board can be contacted at [redacted]. If you are unable to contact the research staff, or if you want to talk to someone other than the research staff, you may also call the Wayne State Research Subject Advocate at ([redacted] to discuss problems, obtain information, or offer input.

Consent to Participate in a Research Study

To voluntarily agree to take part in this study, you must sign on the line below. If you choose to take part in this study you may withdraw at any time. You are not giving up any of your legal rights by signing this form. Your signature below indicates that you have read, or had read to you, this entire consent form, including the risks and benefits, and have had all of your questions answered. You will be given a copy of this consent form.

_____	_____
Signature of participant	Date
_____	_____
Printed name of participant	Time
_____	_____
Signature of witness**	Date
_____	_____
Printed of witness**	Time
_____	_____
Signature of person obtaining consent	Date
_____	_____
Printed name of person obtaining consent	Time

**Use when participant has had this consent form read to them (i.e., illiterate, legally blind, translated into foreign language).

_____	_____
Signature of translator	Date
_____	_____
Printed name oftranslator	Time

Appendix B1: Air-Conduction (AC) Audiometric Thresholds

Right Ear (AD) AC Thresholds

Participant #	250	500	1k	2k	4k	8k	PTA
1	5	5	5	5	10	0	5
2	10	10	10	5	10	5	8.333333
3	10	10	15	10	15	5	11.66667
4	15	20	20	20	20	10	20
5	10	10	10	5	5	0	8.333333
6	15	10	5	5	5	0	6.666667
7	15	0	5	5	0	0	3.333333
8	5	5	5	5	5	0	5
9	20	15	5	10	5	0	10
10	10	15	15	10	5	20	13.33333
11	10	15	10	5	10	5	10
							9.242424

Left Ear (AS) AC Thresholds

Participant #	250	500	1k	2k	4k	8k	PTA
1	0	0	0	10	5	0	3.333333
2	10	10	5	10	10	5	8.333333
3	10	10	10	15	10	10	11.66667
4	15	20	20	20	20	10	20
5	10	15	10	5	5	0	10
6	10	5	5	5	5	5	5
7	20	15	5	10	0	0	10
8	10	5	0	5	10	0	3.333333
9	20	15	5	10	10	0	10
10	20	20	10	15	5	0	15
11	15	15	5	0	10	0	6.666667
							9.393939

Pure-tone average across all participants was about 9 dB HL for both AD (9.24 dB) and AS (9.39 dB) ears

Appendix B2: Age and Gender Demographics of Participants*

*****_labeled by participant number below each age and gender category_

AGE	
>25	**<25**
10	1
11	2
	3
	4
	5
	6
	7
	8
	9

GENDER	
Male	**Female**
4	1
5	2
6	3
7	8
10	9
11	

Total of 11 participants; 2 participants were older than 25 years, while 9 were 25 years and under; 6 participants were male, while 5 were female.

Appendix C1: Raw VsEP Data for 500 Hz

	Partcipant #	1	2	3	4	5	6	7	8	9	10	11		
INTENSITY	MASKING													
115	no masking												Mean	SD
	Latency													
	P1	1.27	1.23	1.32	1.23	1.13	1.23	1.18	1.27	1.23	1.23	1.23	1.231818	0.048748
	N1	2.07	1.97	2.11	1.97	1.94	1.93	1.88	1.97	1.93	1.93	1.93	1.966364	0.066974
	P2	2.9	2.9	2.95	2.81	2.85	2.76	2.76	2.76	2.76	2.76	2.76	2.815455	0.072161
	N2	3.74	3.74	3.84	3.7	3.76	3.6	3.65	3.65	3.65	3.65	3.65	3.693636	0.069609
	amplitude													
	P1/N1	23.381	6.7	7.523	32.79	51.72	15.85	10.318	24.32	10.964	11.78	12.17	18.86509	13.56364
	N1/P2	42.06	20.84	15.82	65.89	104.36	36.07	21.956	54.53	23.713	27.5	28.676	40.12864	26.21115
	P2/N2	26.531	18.823	11.315	47.92	76.24	29.96	16.991	44.14	17.647	23.929	24.487	30.72573	18.78452

	Partcipant #	1	2	3	4	5	6	7	8	9	10	11		
105	no masking												Mean	SD
	Latency													
	P1	1.23	1.17	1.3	1.18	1.24	1.21	1.27	1.23	1.27	1.13	1.16	1.217273	0.052743
	N1	2.07	1.97	2.11	2.03	2.03	1.99	1.88	2.02	2.02	2.02	1.94	2.007273	0.061982
	P2	2.9	2.91	2.96	2.87	2.87	2.76	2.72	2.81	2.76	2.81	2.79	2.832727	0.074578
	N2	3.7	3.66	3.68	3.71	3.75	3.58	3.6	3.65	3.65	3.6	3.6	3.652727	0.054239
	amplitude													
	P1/N1	8.555	3.026	3.033	12.978	16.698	5.505	3.469	8.986	4.193	4.526	8.458	7.220636	4.449414
	N1/P2	14.042	8.348	5.772	28.481	34.53	12.524	7.573	18.925	8.383	9.309	19.829	15.24691	9.322009
	P2/N2	9.39	7.125	4.08	20.644	26.004	11.758	6.163	15.37	6.056	8.461	17.148	12.01809	6.95683

	Partcipant #	1	2	3	4	5	6	7	8	9	10	11		
105	100 masking												Mean	SD
	Latency													
	P1	1.2	1.32	1.27	1.27	1.23	1.23	1.02	1.27	1.18	1.18	1.08	1.204545	0.088472
	N1	2.05	1.97	2.11	2.02	1.97	1.93	1.93	1.97	1.97	1.95	1.95	1.983636	0.055186
	P2	2.9	2.81	2.95	2.81	2.9	2.72	2.8	2.81	2.76	2.8	2.74	2.818182	0.071249
	N2	3.79	3.84	3.93	3.7	3.65	3.7	3.67	3.65	3.6	3.65	3.61	3.708182	0.103133
	amplitude													
	P1/N1	8.352	3.352	3.046	10.799	18.688	5.828	4.997	8.372	4.235	4.305	8.509	7.316636	4.529483
	N1/P2	17.206	8.205	5.478	23.543	36.643	12.722	8.517	18.738	8.554	9.508	19.899	15.36482	9.157236
	P2/N2	11.152	6.864	3.903	17.39	28.466	11.623	5.208	15.177	6.098	8.127	16.985	11.90845	7.237394

	Partcipant #	1	2	3	4	5	6	7	8	9	10	11		
105	90 masking												Mean	SD
	Latency													
	P1	1.23	1.23	1.27	1.23	1.27	1.23	1.23	1.27	1.17	1.2	1.23	1.232727	0.030361
	N1	2.07	1.97	2.07	2.06	2.07	2.02	1.88	1.97	1.93	1.92	1.93	1.99	0.070711
	P2	2.9	2.81	2.95	2.89	2.9	2.76	2.76	2.81	2.74	2.76	2.76	2.821818	0.074541
	N2	3.7	3.74	3.74	3.73	3.74	3.65	3.65	3.65	3.65	3.57	3.65	3.679091	0.055037
	amplitude													
	P1/N1	8.35	2.886	2.63	25.34	17.168	5.399	3.266	8.081	4.332	4.618	8.482	8.232	7.025348
	N1/P2	15.62	7.841	5.263	49.67	34.24	12.742	7.943	17.671	8.164	10.075	19.584	17.16482	13.49487
	P2/N2	9.587	6.493	3.918	34.91	25.464	11.24	5.922	14.661	6.208	8.349	17.162	13.08309	9.554244

	Partcipant #	1	2	3	4	5	6	7	8	9	10	11		
105	80 masking												Mean	SD
	Latency													
	P1	DID NOT	1.32	1.19	1.18	1.23	1.23	1.23	1.27	1.23	1.23	1.15	1.226	0.047188
	N1	TEST	2.07	2.07	2.02	2.11	1.93	1.93	2.02	1.93	1.93	1.91	1.992	0.074356
	P2	N/A	2.9	2.96	2.81	2.9	2.76	2.72	2.81	2.76	2.76	2.76	2.814	0.079331
	N2		3.84	3.71	3.65	3.74	3.65	3.6	3.65	3.6	3.56	3.61	3.661	0.082523
	amplitude													
	P1/N1		3.537	2.608	11.368	16.305	5.456	3.773	8.114	3.805	4.36	8.832	6.8158	4.361161
	N1/P2		8.056	5.061	21.827	34.191	13.311	7.412	18.299	8.231	9.86	19.896	14.6144	8.993467
	P2/N2		6.696	3.598	16.094	25.576	10.747	6.35	15.315	6.152	8.477	16.71	11.5715	6.759643

Partcipant #	1	2	3	4	5	6	7	8	9	10	11		
95 90 masking												Mean	SD
Latency													
P1	1.37	1.04	1.32	1.23	1.22	1.28		1.23			1.23	1.24	0.096806
N1	2.12	2.11	2.18	2.02	1.98	1.93	1.88	2.02	2.07	2.02	1.93	2.023636	0.091353
P2	2.96	2.86	3.05	2.81	2.78	2.78	2.76	2.81	2.76	2.76	2.76	2.826364	0.095632
N2	3.81	3.65	3.68	3.65	3.68	3.62	3.79	3.6	3.65	3.6	3.65	3.670909	0.069348
amplitude													
P1/N1	2.994	1.414	1.004	4.667	5.415	2.067		2.5			2.564	2.828125	1.520565
N1/P2	5.575	3.066	1.633	8.771	10.934	4.331	3.074	5.513	2.567	2.948	6.475	4.989727	2.855964
P2/N2	3.3	2.494	1.168	6.778	7.868	3.176	1.762	4.665	2.383	2.898	5.894	3.853273	2.162552

Partcipant #	1	2	3	4	5	6	7	8	9	10	11		
85 90 masking												Mean	SD
Latency													
P1	1.27	1.37	1.18	1.27	1.23	1.46	1.51	1.23	1.14	1.6	0.48	1.249091	0.293273
N1	2.16	1.97	2.16	2.02	2.11	1.88	2.16	2.02	1.85	1.88	1.88	2.008182	0.124725
P2	2.9	3	3.18	2.81	2.9	2.72	2.76	2.72	2.89	2.76	2.9	2.867273	0.137411
N2	3.88	3.7	4.02	4.21	3.93	3.84	3.28	3.65	3.84	3.6	3.65	3.781818	0.245919
amplitude													
P1/N1	0.543	0.776	0.392	1.172	1.935	0.335	0.341	0.727	0.768	0.332	1.473	0.799455	0.525824
N1/P2	1.273	1.198	0.645	3.28	2.451	1.087	0.682	1.499	0.899	1.064	2.398	1.497818	0.845216
P2/N2	1.273	0.782	0.664	2.294	2.332	1.145	0.682	1.189	0.843	0.74	1.496	1.221818	0.6032

BINAURAL MASKING at 105 100 dB masker

Partcipant #	10	11		
Latency			Mean	SD
P1	1.23	1.18	1.205	0.035355
N1	1.97	1.88	1.925	0.06364
P2	2.76	2.76	2.76	0
N2	3.6	3.65	3.625	0.035355
amplitude				
P1/N1	4.039	8.268	6.1535	2.990355
N1/P2	8.891	18.712	13.8015	6.944496
P2/N2	7.947	16.397	12.172	5.975052

BINAURAL MASKING at 105 90 dB masker

Partcipant #	10	11		
Latency			Mean	SD
P1	1.18	1.23	1.205	0.035355
N1	1.97	1.93	1.95	0.028284
P2	2.76	2.76	2.76	0
N2	3.6	3.6	3.6	0
amplitude				
P1/N1	4.355	8.012	6.1835	2.585889
N1/P2	9.602	17.62	13.611	5.669582
P2/N2	7.853	15.98	11.9165	5.746657

BINAURAL MASKING at 105 80 dB masker

Partcipant #	10	11		
Latency			Mean	SD
P1	1.25	1.23	1.24	0.014142
N1	1.99	1.93	1.96	0.042426
P2	2.77	2.82	2.795	0.035355
N2	3.64	3.62	3.63	0.014142
amplitude				
P1/N1	3.865	7.955	5.91	2.892067
N1/P2	9.365	17.544	13.4545	5.783426
P2/N2	7.922	15.188	11.555	5.137838

Appendix C2: Raw VsEP Data for 1000 Hz

Partcipant #		1	2	3	4	5	6	7	8	9	10	11		
INTENSITY	**MASKING**													
115	**no masking**												**Mean**	**SD**
Latency														
	N1	1.32	1.31	1.33	1.26	1.27	1.26	1.24	1.26	1.22	1.27	1.24	1.270909	0.035058
	P1	1.79	1.81	1.85	1.74	1.74	1.69	1.67	1.74	1.7	1.76	1.72	1.746364	0.053716
	N2	2.25	2.31	2.31	2.22	2.27	2.21	2.2	2.22	2.22	2.3	2.25	2.250909	0.041099
	P2	2.76	2.76	2.78	2.65	2.74	2.68	2.68	2.71	2.65	2.7	2.68	2.708182	0.045567
	N3	3.28	3.31	3.35	3.18	3.22	3.2	3.12	3.19	3.17	3.14	3.21	3.215455	0.070903
	P3	3.7	3.75	3.74	3.66	3.74	3.63	3.6	3.72	3.65	3.68	3.64	3.682727	0.050812
Amplitude														
	N1/P1	19.95	9.188	5.659	27.57	35.87	16.46	10.48	20.72	10.3	11.46	25.58	17.567	9.319077
	P1/N2	40.67	14.886	12.112	59.71	74	35.04	21.49	45.14	21.62	21.56	53.07	36.29982	20.11245
	N2/P2	51.94	21.628	15.498	79.15	93.16	46.83	27.718	60.99	28.8	31.16	73.84	48.24673	25.84156
	P2/N3	41.52	19.731	12.015	64.33	75.75	39.27	24.306	51.97	24.47	30.48	66.24	40.91655	21.13655
	N3/P3	20.08	8.457	5.468	35.08	37.08	22.37	13.803	27.15	12.66	17.12	37.71	21.54345	11.43814

Partcipant #		1	2	3	4	5	6	7	8	9	10	11		
105	**no masking**												**Mean**	**SD**
Latency														
	N1	DID NOT	1.3	1.32	1.26	1.28	1.24	1.25	1.28	1.26	1.27	1.23	1.269	0.027264
	P1	TEST	1.82	1.84	1.73	1.74	1.67	1.72	1.71	1.72	1.69	1.7	1.734	0.05461
	N2	N/A	2.24	2.31	2.21	2.27	2.25	2.2	2.23	2.14	2.2	2.26	2.231	0.046774
	P2		2.81	2.78	2.64	2.75	2.68	2.72	2.75	2.6	2.72	2.73	2.718	0.06321
	N3		3.28	3.3	3.21	3.32	3.17	3.1	3.18	3.12	3.18	3.2	3.206	0.073515
	P3		3.75	3.68	3.64	3.74	3.65	3.53	3.65	3.58	3.65	3.67	3.654	0.065524
Amplitude														
	N1/P1		2.6	1.783	10.52	12.2	5.533	4.099	7.537	3.742	3.932	8.74	6.0686	3.515734
	P1/N2		6.381	4.111	21.53	25.96	11.446	7.955	15.916	7.788	8.802	18.55	12.8439	7.266857
	N2/P2		8.453	5.331	27.2	32.36	15.376	10.099	20.528	10.088	11.947	24.12	16.5502	9.030037
	P2/N3		6.767	4.29	23.94	25.35	14.646	8.802	18.05	8.859	10.691	22.21	14.3605	7.612485
	N3/P3		3.524	2.142	12.24	12.16	8.204	5.263	10.37	4.857	6.157	12.94	7.7857	3.944097

Partcipant #		1	2	3	4	5	6	7	8	9	10	11		
105	**100 masking**												**Mean**	**SD**
Latency														
	N1	1.28	1.25	1.41	1.27	1.25	1.2	1.21	1.19	1.27	1.23	1.24	1.254545	0.059391
	P1	1.74	1.82	1.83	1.69	1.82	1.72	1.73	1.78	1.74	1.75	1.71	1.757273	0.048185
	N2	2.27	2.25	2.3	2.2	2.29	2.2	2.2	2.21	2.16	2.17	2.19	2.221818	0.04792
	P2	2.74	2.77	2.77	2.72	2.82	2.63	2.66	2.75	2.67	2.64	2.71	2.716364	0.060708
	N3	3.22	3.29	3.29	3.18	3.2	3.16	3.13	3.19	3.09	3.16	3.14	3.186364	0.062333
	P3	3.65	3.81	3.8	3.65	3.72	3.59	3.6	3.68	3.6	3.68	3.67	3.677273	0.074578
Amplitude														
	N1/P1	2.485	3.07	2.326	10.64	12.07	6.042	3.195	7.411	3.514	4.249	9.15	5.832	3.486142
	P1/N2	2.565	6.657	4.468	21.45	24.13	12.606	6.572	16.253	7.574	8.481	18.91	11.78782	7.33404
	N2/P2	4.392	8.816	5.743	29.02	30.61	17.439	8.934	20.5	9.916	11.61	26.2	15.74364	9.520438
	P2/N3	2.791	7.17	4.771	24.36	24.9	15.488	8.006	17.182	8.57	10.697	23.32	13.38682	8.093165
	N3/P3	1.611	3.777	2.62	12.33	14.04	8.781	4.71	10.472	4.885	6.061	13.58	7.533364	4.500854

Partcipant #		1	2	3	4	5	6	7	8	9	10	11		
105	**90 masking**												**Mean**	**SD**
Latency														
	N1	1.25	1.28	1.37	1.27	1.29	1.2	1.15	1.23	1.24	1.3	1.28	1.26	0.057096
	P1	1.77	1.78	1.79	1.74	1.77	1.73	1.72	1.71	1.73	1.72	1.77	1.748182	0.02822
	N2	2.23	2.28	2.31	2.2	2.25	2.21	2.14	2.23	2.26	2.23	2.27	2.237273	0.045407
	P2	2.75	2.78	2.78	2.72	2.73	2.64	2.61	2.7	2.65	2.7	2.71	2.706364	0.055186
	N3	3.27	3.23	3.3	3.14	3.21	3.13	3.09	3.22	3.13	3.21	3.2	3.193636	0.064385
	P3	3.73	3.78	3.77	3.65	3.68	3.65	3.61	3.7	3.62	3.63	3.74	3.687273	0.060678
Amplitude														
	N1/P1	6.706	3.542	2.793	10.657	12.46	5.468	3.174	7.411	3.45	4.306	8.87	6.257909	3.276917
	P1/N2	14.115	6.495	5.38	20.621	26.31	12.107	7.399	16.063	6.692	8.641	19.62	13.04027	6.935469
	N2/P2	18.086	8.573	7.154	27.78	33.36	17.109	10.048	22.159	9.066	11.843	26.73	17.44618	8.999883
	P2/N3	14.299	7.306	5.861	24.13	27.61	15.462	8.793	18.39	8.363	10.891	23.73	14.985	7.569385
	N3/P3	6.962	3.719	2.664	13.04	13.824	8.457	4.913	10.06	4.704	5.415	12.75	7.864364	4.01355

Partcipant #	1	2	3	4	5	6	7	8	9	10	11		
105 80 masking												Mean	SD
Latency													
N1	1.28	1.37	1.4	1.23	1.32	1.25	1.24	1.23	1.2	1.25	1.2	1.27	0.066483
P1	1.75	1.76	1.78	1.69	1.76	1.72	1.67	1.76	1.64	1.7	1.72	1.722727	0.044066
N2	2.32	2.25	2.3	2.2	2.3	2.19	2.2	2.24	2.14	2.18	2.15	2.224545	0.062026
P2	2.75	2.75	2.82	2.72	2.79	2.66	2.64	2.68	2.63	2.67	2.67	2.707273	0.062943
N3	3.27	3.28	3.3	3.23	3.24	3.13	3.12	3.21	3.13	3.2	3.15	3.205455	0.065017
P3	3.7	3.77	3.77	3.7	3.73	3.59	3.65	3.65	3.57	3.64	3.67	3.676364	0.065616
Amplitude													
N1/P1	7.104	3.148	2.331	9.87	12.301	5.952	3.344	7.07	3.684	4.08	9.38	6.205818	3.251215
P1/N2	14.067	6.453	4.95	21.24	25.845	12.706	7.639	15.18	7.348	8.859	19.02	13.02791	6.78675
N2/P2	17.816	9.015	5.944	28.3	31.938	17.554	10.071	21	9.993	11.989	26.69	17.30091	8.768816
P2/N3	14.868	7.627	4.515	22.2	26.109	14.991	8.933	18.62	8.819	11.007	23.64	14.66627	7.190618
N3/P3	7.895	3.957	2.381	11.33	13.588	8.858	4.623	10.14	5.259	5.794	14.12	7.995	3.959775

Partcipant #	1	2	3	4	5	6	7	8	9	10	11		
95 90 masking												Mean	SD
Latency													
N1	1.32	1.32	1.23	1.23	1.32	1.2	1.23	1.32	1.23	1.31	1.27	1.270909	0.047844
P1	1.76	1.75	1.83	1.69	1.79	1.67	1.65	1.69	1.74	1.69	1.79	1.731818	0.057761
N2	2.24	2.31	2.25	2.2	2.2	2.19	2.16	2.16	2.16	2.25	2.2	2.210909	0.047213
P2	2.71	2.74	2.76	2.72	2.76	2.66	2.67	2.72	2.72	2.72	2.72	2.718182	0.031247
N3	3.14	3.21	3.28	3.14	3.28	3.13	3.09	3.14	3.09	3.19	3.14	3.166364	0.066374
P3	3.67	3.68	3.74	3.65	3.7	3.59	3.6	3.65	3.56	3.71	3.7	3.659091	0.055938
Amplitude													
N1/P1	1.75	0.897	0.848	2.796	3.735	1.968	1.417	2.277	0.954	1.28	2.606	1.866182	0.919264
P1/N2	0.655	2.215	1.038	7.135	8.202	4.01	2.451	5.016	2.194	2.548	5.717	3.743727	2.483165
N2/P2	2.04	3.033	1.506	9.019	10.864	5.729	3.483	6.887	3.315	3.857	8.867	5.327273	3.157408
P2/N3	1.007	2.475	1.622	7.867	8.568	4.724	3.187	6.213	2.634	3.568	7.589	4.495818	2.665909
N3/P3	0.671	1.654	0.932	4.605	4.103	2.7	1.7	3.3	1.478	1.808	4.679	2.511818	1.45293

Partcipant #	1	2	3	4	5	6	7	8	9	10	11		
85 90 masking												Mean	SD
Latency													
N1	1.03	1.06	1.22	1.2	1.37	1.31	0.71	1.27	1.41	1.27	1.27	1.192727	0.197033
P1	1.74	1.49	1.41	1.78	1.65	1.74	1.6	1.69	1.69	1.81	1.74	1.667273	0.123458
N2	2.34	2.21	1.55	2.21	2.31	2.17	2.16	2.2	2.16	2.24	2.25	2.163636	0.211673
P2	2.76	2.84	1.88	2.69	2.78	2.7	2.62	2.67	2.72	2.71	2.67	2.64	0.259075
N3	3.32	3.22	2.16	3.27	3.29	3.13	3.09	3.14	3.09	3.18	3.18	3.097273	0.32044
Amplitude													
N1/P1	0.753	0.429	0.093	0.749	0.994	0.46	0.869	0.566	0.356	0.34	0.733	0.576545	0.268147
P1/N2	0.816	0.924	0.207	2.332	2.622	0.847	0.626	1.429	0.533	0.859	2.216	1.219182	0.812963
N2/P2	0.724	1.235	0.299	2.691	2.761	1.271	0.96	1.916	0.836	0.92	1.526	1.376273	0.790574
P2/N3	0.93	0.802	0.458	1.916	2.208	1.302	0.804	1.752	0.925	0.823	3.011	1.357364	0.775086

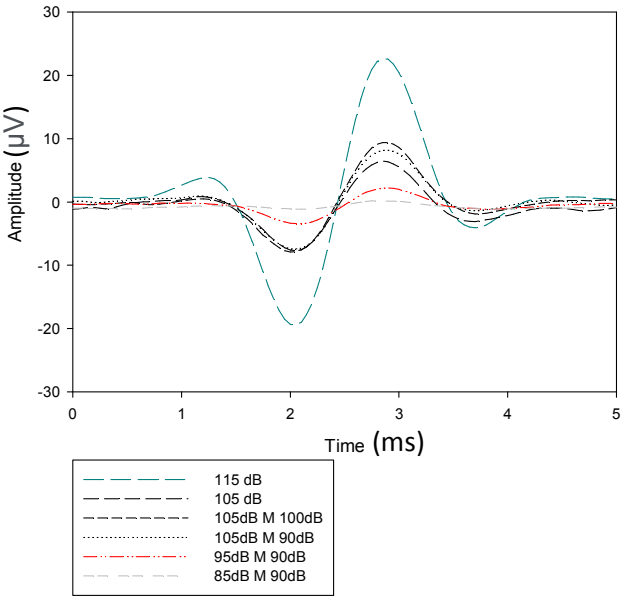
BINAURAL MASKING at 105 dB	100 dB masker			
Partcipant #	10	11		
Latency			Mean	SD
N1	1.32	1.27	1.295	0.035355
P1	1.69	1.74	1.715	0.035355
N2	2.2	2.2	2.2	0
P2	2.72	2.72	2.72	0
N3	3.18	3.14	3.16	0.028284
P3	3.65	3.65	3.65	0
Amplitude				
N1/P1	3.862	8.2	6.031	3.067429
P1/N2	8.795	18.58	13.6875	6.91904
N2/P2	11.614	24.25	17.932	8.935001
P2/N3	10.057	22.3	16.1785	8.657108
N3/P3	5.833	12.87	9.3515	4.97591

BINAURAL MASKING at 105 dB	90 dB masker			
Partcipant #	10	11		
Latency			Mean	SD
N1	1.27	1.27	1.27	0
P1	1.79	1.74	1.765	0.035355
N2	2.2	2.16	2.18	0.028284
P2	2.72	2.72	2.72	0
N3	3.23	3.18	3.205	0.035355
P3	3.65	3.65	3.65	0
Amplitude				
N1/P1	3.522	7.824	5.673	3.041973
P1/N2	8.643	18.279	13.461	6.813681
N2/P2	12.346	25.385	18.8655	9.219965
P2/N3	10.019	21.723	15.871	8.275978
N3/P3	5.461	12.55	9.0055	5.01268

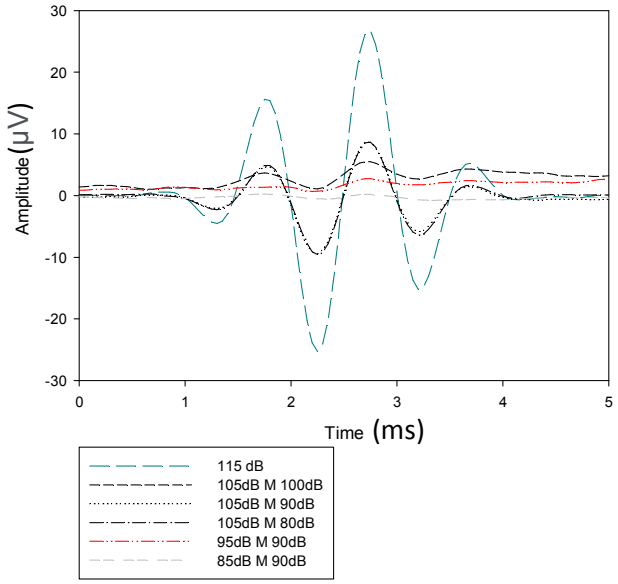
BINAURAL MASKING at 105 dB	80 dB masker			
Partcipant #	10	11		
Latency			Mean	SD
N1	1.27	1.27	1.27	0
P1	1.79	1.75	1.77	0.028284
N2	2.2	2.22	2.21	0.014142
P2	2.72	2.64	2.68	0.056569
N3	3.18	3.16	3.17	0.014142
P3	3.7	3.68	3.69	0.014142
Amplitude				
N1/P1	3.592	8.347	5.9695	3.362293
P1/N2	8.262	18.871	13.5665	7.501696
N2/P2	11.977	25.568	18.7725	9.610288
P2/N3	10.459	22.829	16.644	8.746911
N3/P3	5.826	12.441	9.1335	4.677511

Appendix D1: Participant 1 all conditions

500 Hz:
Participant 1

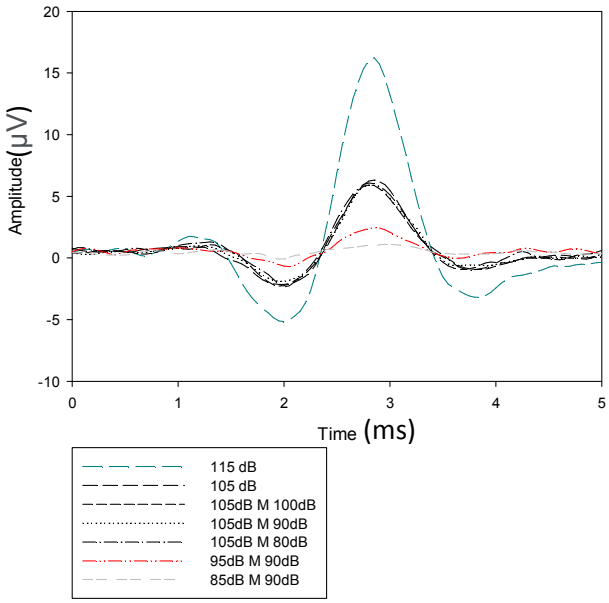


1k Hz:
Participant 1

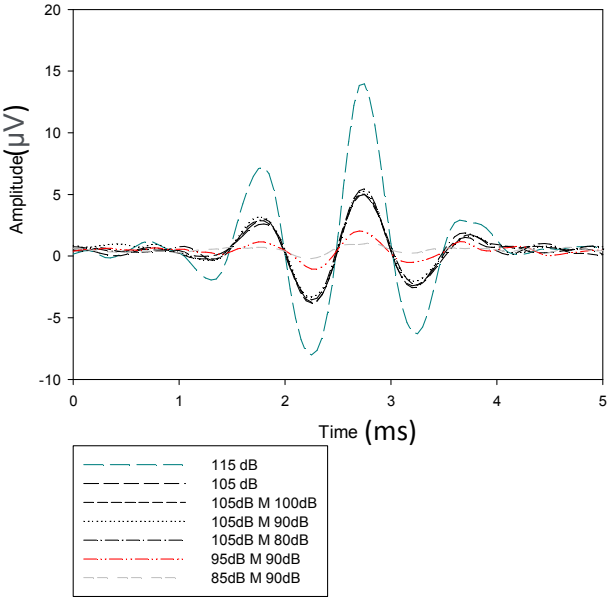


Appendix D2: Participant 2 all conditions

500 Hz:
Participant 2

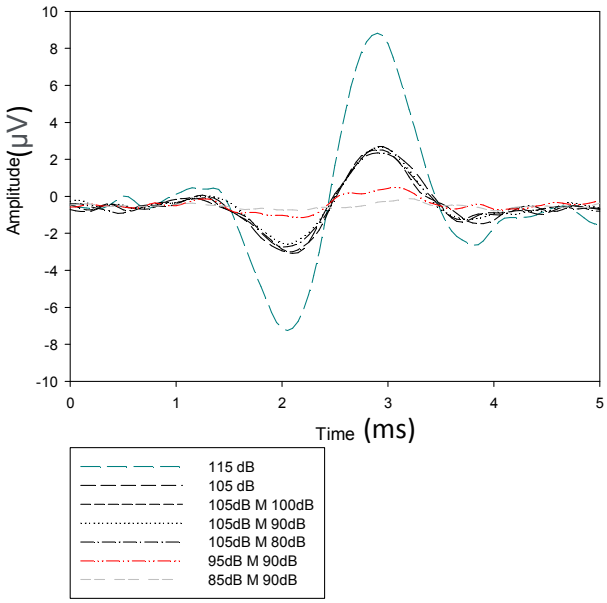


1k Hz:
Participant 2

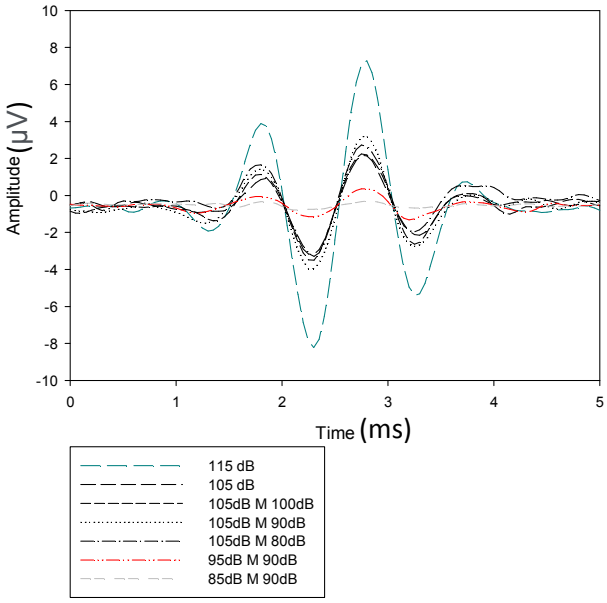


Appendix D3: Participant 3 all conditions

500 Hz:
Participant 3

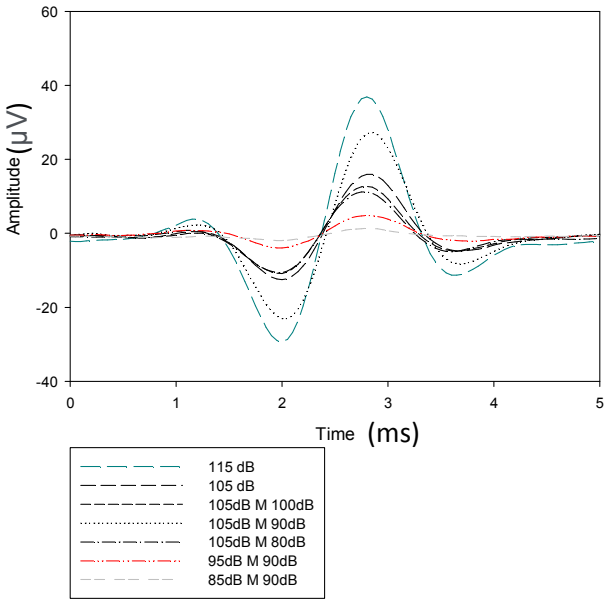


1k Hz:
Participant 3

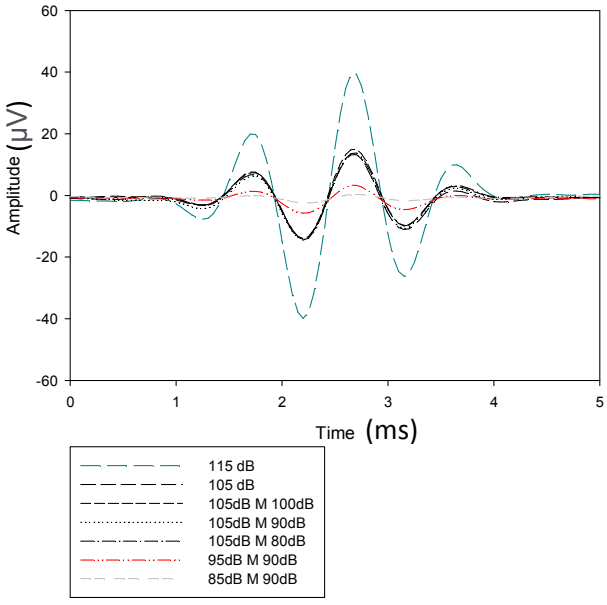


Appendix D4: Participant 4 all conditions

500 Hz:
Participant 4

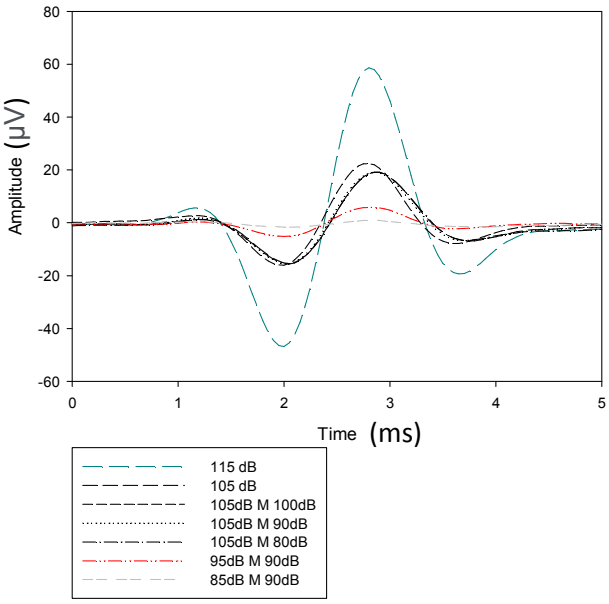


1k Hz:
Participant 4

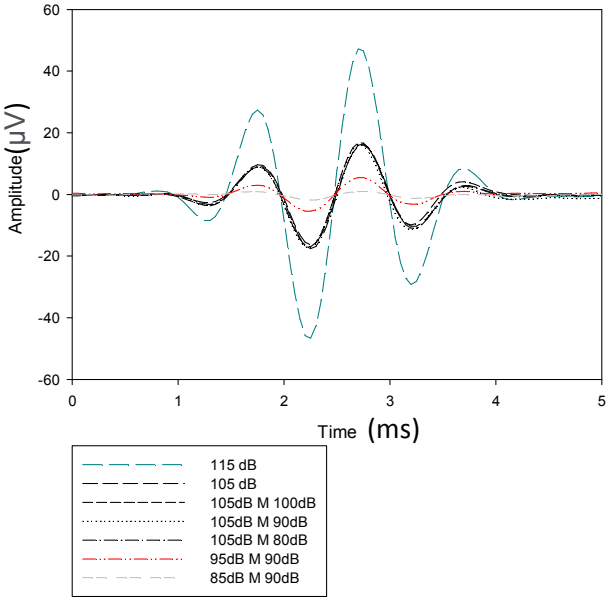


Appendix D5: Participant 5 all conditions

500 Hz:
Participant 5

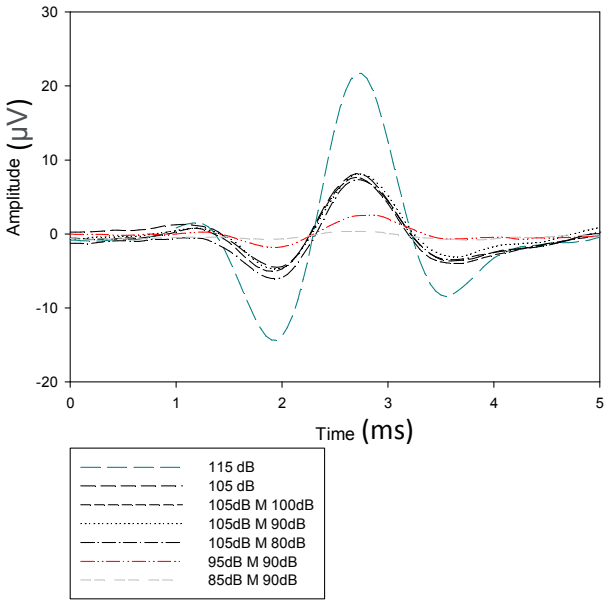


1k Hz:
Participant 5

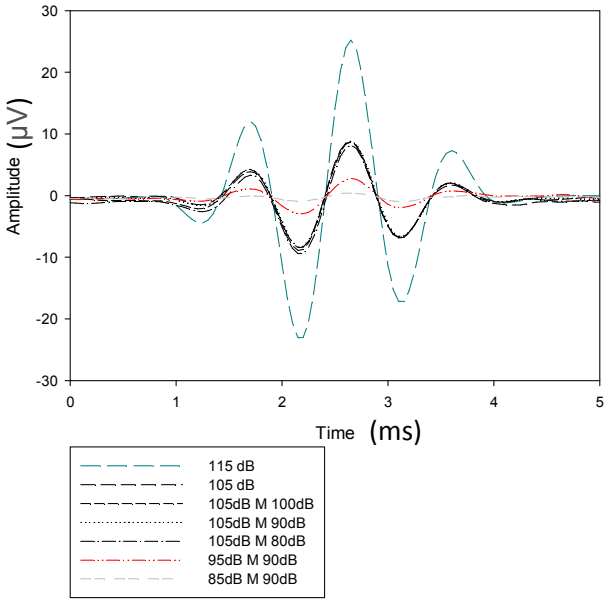


Appendix D6: Participant 6 all conditions

500 Hz:
Participant 6

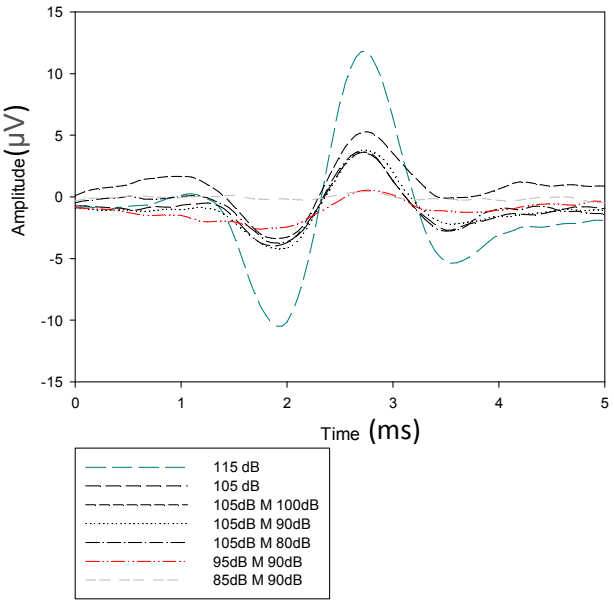


1k Hz:
Participant 6

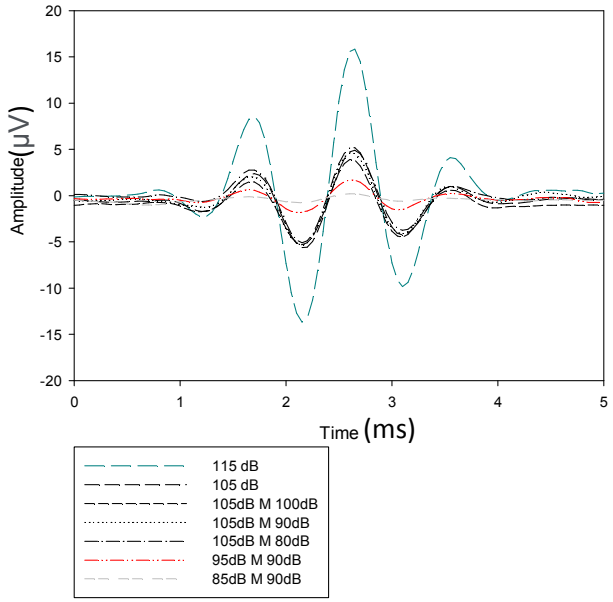


Appendix D7: Participant 7 all conditions

500 Hz:
Participant 7

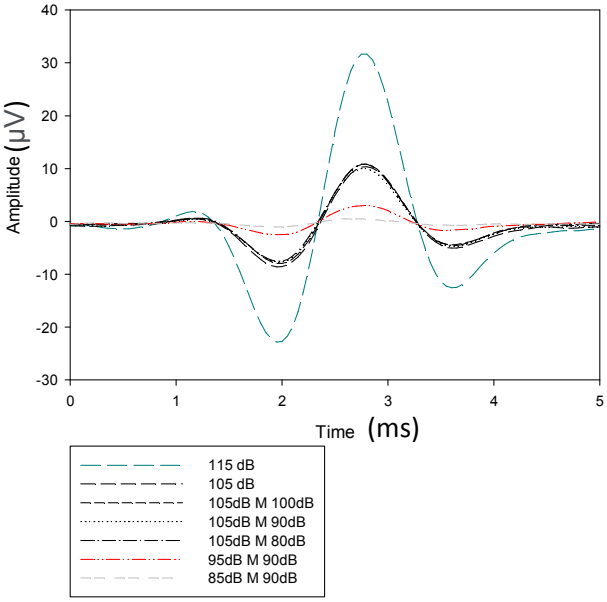


1k Hz:
Participant 7

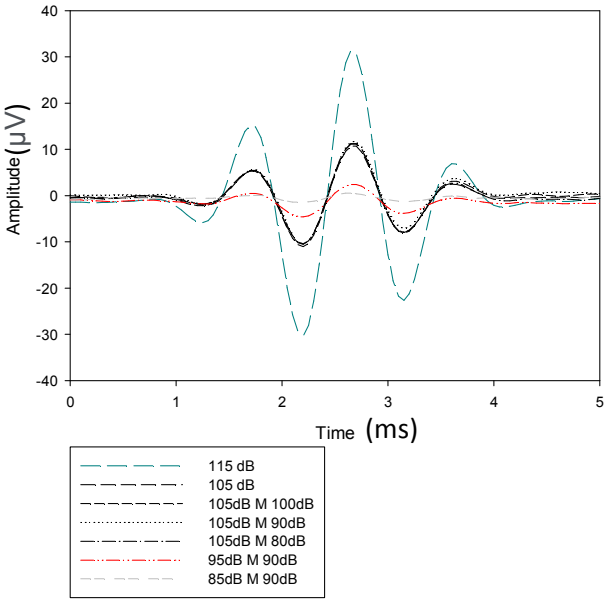


Appendix D8: Participant 8 all conditions

500 Hz:
Participant 8

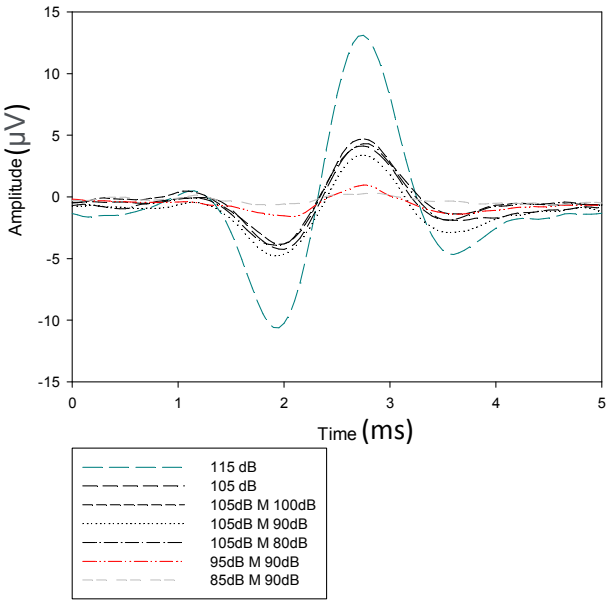


1k Hz:
Participant 8

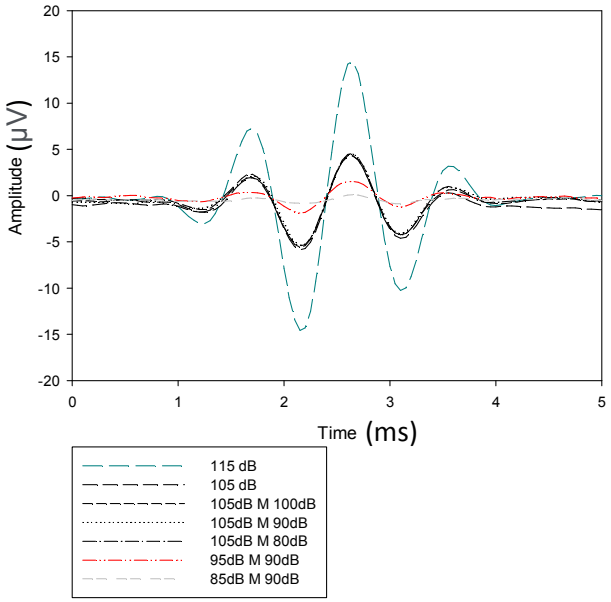


Appendix D9: Participant 9 all conditions

500 Hz:
Participant 9

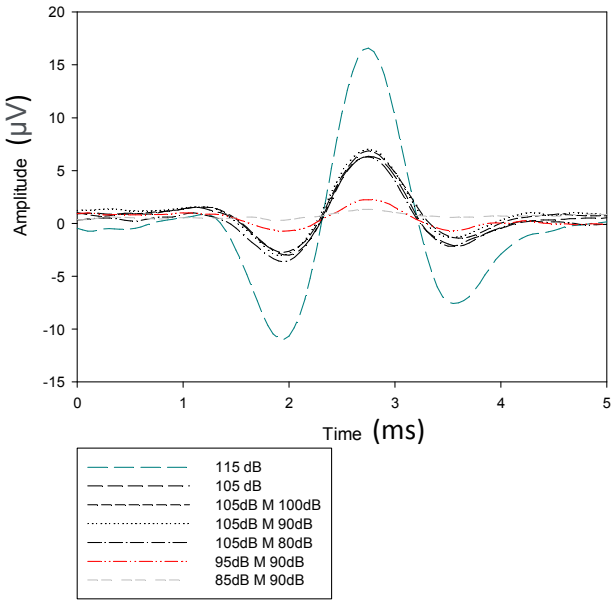


1k Hz:
Participant 9

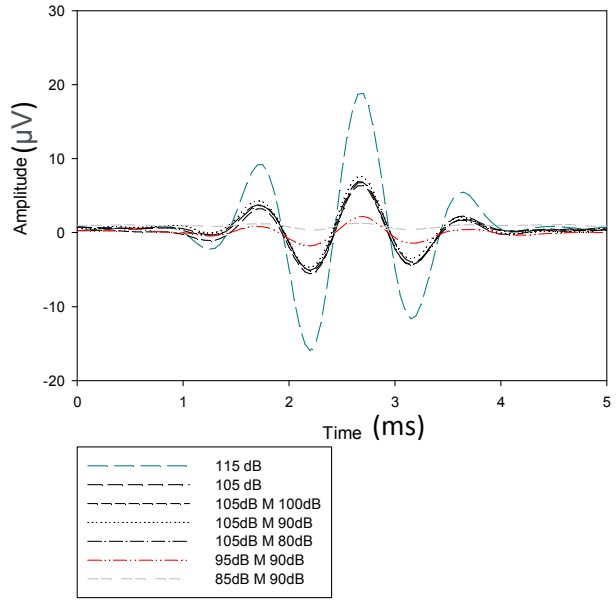


Appendix D10: Participant 10 all conditions

500 Hz:
Participant 10

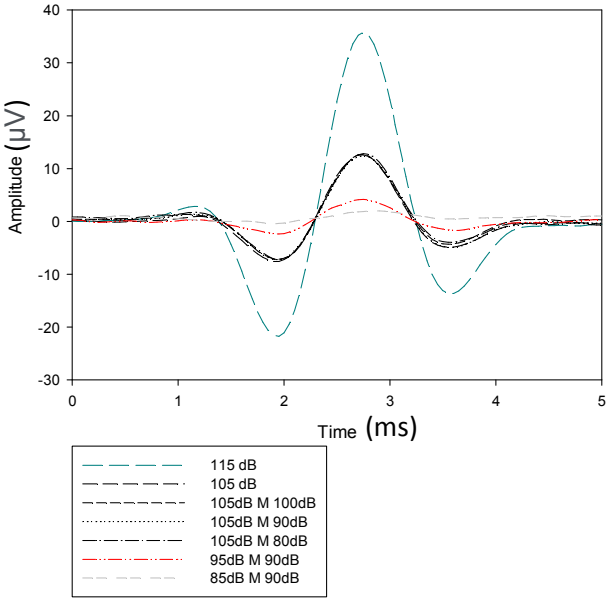


1k Hz:
Participant 10

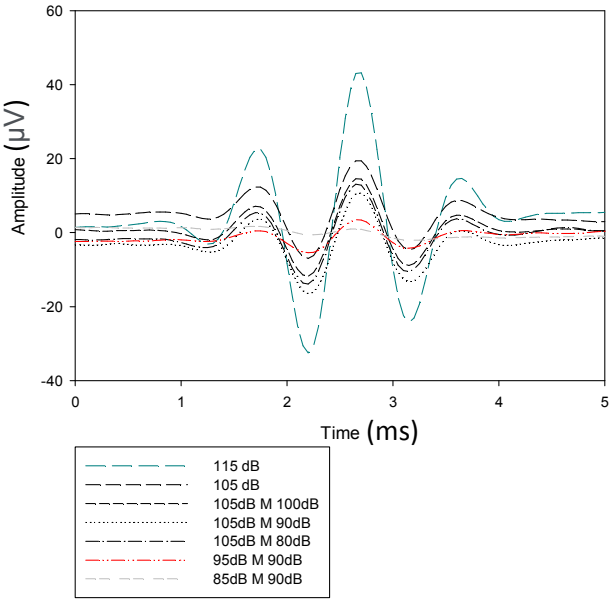


Appendix D11: Participant 11 all conditions

500 Hz:
Participant 11



1k Hz:
Participant 11



Appendix E: Analyses of Possible Interaction Effects of Main Effects

E1:105dB SPL monaural masking conditions (100dB, 90dB, & 80dB HL) at 1000 Hz: interaction of latency and amplitude
Wilks lambda=.98534, F(4, 22)=.04075, p=.99660

Conditions	mean latency Mean	mean latency Std.Err.	mean latency -Std.Err	mean latency +Std.Err	mean amplitude Mean	mean amplitude Std.Err.	mean amplitude -Std.Err	mean amplitude +Std.Err	N
1	2.227	0.342	1.885	2.569	10.857	2.012	8.845	12.869	5
2	2.229	0.342	1.887	2.571	11.919	2.012	9.907	13.931	5
3	2.226	0.342	1.884	2.568	11.839	2.012	9.827	13.851	5

E2: 105dB SPL monaural masking conditions (100dB, 90dB, & 80dB HL) at 500 Hz: interaction of latency and amplitude
Wilks lambda=.93282, F(4, 10)=.08846, p=.98402

Conditions	mean latency Mean	mean latency Std.Err.	mean latency -Std.Err	mean latency +Std.Err	mean amplitude Mean	mean amplitude Std.Err.	mean amplitude -Std.Err	mean amplitude +Std.Err	N
1	2.002	0.461	1.541	2.463	11.530	2.398	9.132	13.928	3
2	2.015	0.461	1.554	2.476	12.827	2.398	10.429	15.225	3
3	2.011	0.461	1.550	2.472	11.001	2.398	8.603	13.398	3

E3: Latencies b/w 1000 and 500 Hz at 105dB SPL monaural masking conditions (100dB, 90dB, & 80dB HL): interaction of latency and frequency
Wilks lambda=.99388, F(4, 16)=.01230, p=.99967

Conditions	mean 1000 Hz latencies Mean	mean 1000 Hz latencies Std.Err.	mean 1000 Hz latencies -Std.Err	mean 1000 Hz latencies +Std.Err	mean 500 Hz latencies Mean	mean 500 Hz latencies Std.Err.	mean 500 Hz latencies -Std.Err	mean 500 Hz latencies +Std.Err	N
1	1.988	0.312	1.676	2.299	2.429	0.530	1.898	2.959	4
2	1.988	0.312	1.676	2.300	2.431	0.530	1.900	2.961	4
3	1.981	0.312	1.669	2.293	2.423	0.530	1.893	2.954	4

E4: Amplitudes b/w 1000 and 500 Hz at 105dB SPL monaural masking conditions (100dB, 90dB, & 80dB HL): interaction of amplitude and frequency
Wilks lambda=.90968, F(4, 10)=.12117, p=.97170

Conditions	mean 1000 Hz amplitude Mean	mean 1000 Hz amplitude Std.Err.	mean 1000 Hz amplitude -Std.Err	mean 1000 Hz amplitude +Std.Err	mean 500 Hz amplitude Mean	mean 500 Hz amplitude Std.Err.	mean 500 Hz amplitude -Std.Err	mean 500 Hz amplitude +Std.Err	N
1	11.121	3.127	7.995	14.248	11.530	2.398	9.132	13.928	3
2	12.248	3.127	9.122	15.375	12.827	2.398	10.429	15.225	3
3	12.178	3.127	9.052	15.305	11.001	2.398	8.603	13.398	3

E5: 105dB SPL binaural masking conditions (100dB, 90dB, & 80dB HL) at 1000 Hz: interaction of latency and amplitude
Wilks lambda=.99937, F(4, 22)=.00172, p=.99999

Conditions	mean latency Mean	mean latency Std.Err.	mean latency -Std.Err	mean latency +Std.Err	mean amplitude Mean	mean amplitude Std.Err.	mean amplitude -Std.Err	mean amplitude +Std.Err	N
1	2.218	0.337	1.881	2.555	12.636	2.305	10.331	14.941	5
2	2.228	0.337	1.891	2.565	12.575	2.305	10.270	14.880	5
3	2.220	0.337	1.883	2.557	12.817	2.305	10.512	15.122	5

E6: 105dB SPL binaural masking conditions (100dB, 90dB, & 80dB HL) at 500 Hz: interaction of latency and amplitude
Wilks lambda=.99015, F(4, 10)=.01240, p=.99964

Conditions	mean latency Mean	mean latency Std.Err.	mean latency -Std.Err	mean latency +Std.Err	mean amplitude Mean	mean amplitude Std.Err.	mean amplitude -Std.Err	mean amplitude +Std.Err	N
1	1.963	0.449	1.514	2.413	10.709	2.280	8.429	12.989	3
2	1.972	0.449	1.522	2.421	10.570	2.280	8.291	12.850	3
3	1.998	0.449	1.549	2.448	10.307	2.280	8.027	12.586	3

E7: Latencies b/w 1000 and 500 Hz at 105dB SPL binaural masking conditions (100dB, 90dB, & 80dB HL): interaction of latency and frequency
Wilks lambda=.89609, F(4, 16)=.22556, p=.92011

Conditions	mean 1000 Hz latencies Mean	mean 1000 Hz latencies Std.Err.	mean 1000 Hz latencies -Std.Err	mean 1000 Hz latencies +Std.Err	mean 500 Hz latencies Mean	mean 500 Hz latencies Std.Err.	mean 500 Hz latencies -Std.Err	mean 500 Hz latencies +Std.Err	N
1	1.983	0.306	1.677	2.288	2.379	0.519	1.860	2.898	4
2	1.984	0.306	1.678	2.289	2.379	0.519	1.860	2.898	4
3	1.983	0.306	1.677	2.288	2.406	0.519	1.887	2.925	4

E8: Amplitudes b/w 1000 and 500 Hz at 105dB SPL binaural masking conditions (100dB, 90dB, & 80dB HL): interaction of amplitude and frequency
Wilks lambda=.98734, F(4, 10)=.01598, p=.99941

Conditions	mean 1000 Hz amplitudes Mean	mean 1000 Hz amplitudes Std.Err.	mean 1000 Hz amplitudes -Std.Err	mean 1000 Hz amplitudes +Std.Err	mean 500 Hz amplitudes Mean	mean 500 Hz amplitudes Std.Err.	mean 500 Hz amplitudes -Std.Err	mean 500 Hz amplitudes +Std.Err	N
1	12.550	3.679	8.871	16.229	10.709	2.280	8.429	12.989	3
2	12.667	3.679	8.987	16.346	10.570	2.280	8.291	12.850	3
3	12.770	3.679	9.090	16.449	10.307	2.280	8.027	12.586	3

E9: Varying intensity conditions (105dB, 95dB, & 85dB SPL) with 90dB HL masker at 1000 Hz: interaction of latency and amplitude
Wilks lambda=.23025, F(4, 22)=5.9621, p=.00209

Conditions	mean latency Mean	mean latency Std.Err.	mean latency -Std.Err	mean latency +Std.Err	mean amplitude Mean	mean amplitude Std.Err.	mean amplitude -Std.Err	mean amplitude +Std.Err	N
1	2.229	0.339	1.890	2.568	11.919	1.279	10.639	13.198	5
2	2.220	0.339	1.881	2.559	3.589	1.279	2.309	4.868	5
3	2.152	0.339	1.813	2.491	1.060	1.279	-0.220	2.339	5

E10: Varying intensity conditions (105dB, 95dB, & 85dB SPL) with 90dB HL masker at 500 Hz: interaction of latency and amplitude
Wilks lambda=.13996, F(4, 10)=4.1825, p=.03026

Conditions	mean latency Mean	mean latency Std.Err.	mean latency -Std.Err	mean latency +Std.Err	mean amplitude Mean	mean amplitude Std.Err.	mean amplitude -Std.Err	mean amplitude +Std.Err	N
1	2.015	0.462	1.553	2.477	12.827	1.538	11.289	14.365	3
2	2.036	0.462	1.574	2.498	3.890	1.538	2.352	5.428	3
3	2.042	0.462	1.580	2.503	1.173	1.538	-0.365	2.711	3

E11: Latencies b/w 1000 and 500 Hz at varying intensity conditions (105dB, 95dB, & 85dB SPL) with 90dB HL masker: interaction of latency and frequency
Wilks lambda=.16882, F(4, 16)=5.7351, p=.00464

Conditions	mean 1000 Hz latencies Mean	mean 1000 Hz latencies Std.Err.	mean 1000 Hz latencies -Std.Err	mean 1000 Hz latencies +Std.Err	mean 500 Hz latencies Mean	mean 500 Hz latencies Std.Err.	mean 500 Hz latencies -Std.Err	mean 500 Hz latencies +Std.Err	N
1	1.988	0.312	1.676	2.300	2.431	0.532	1.899	2.963	4
2	1.983	0.312	1.671	2.295	2.445	0.532	1.913	2.977	4
3	1.916	0.312	1.604	2.228	2.477	0.532	1.944	3.009	4

E12: Amplitudes b/w 1000 and 500 Hz at varying intensity conditions (105dB, 95dB, & 85dB SPL) with 90dB HL masker: interaction of amplitude and frequency
Wilks lambda=.15724, F(4, 10)=3.8046, p=.03939

Conditions	mean 1000 Hz amplitudes Mean	mean 1000 Hz amplitudes Std.Err.	mean 1000 Hz amplitudes -Std.Err	mean 1000 Hz amplitudes +Std.Err	mean 500 Hz amplitudes Mean	mean 500 Hz amplitudes Std.Err.	mean 500 Hz amplitudes -Std.Err	mean 500 Hz amplitudes +Std.Err	N
1	12.248	1.971	10.278	14.219	12.827	1.538	11.289	14.365	3
2	3.646	1.971	1.675	5.616	3.890	1.538	2.352	5.428	3
3	1.057	1.971	-0.913	3.028	1.173	1.538	-0.365	2.711	3

E13: Unmasked conditions (115dB and 105dB SPL) at 1000 Hz: interaction of latency and amplitude
Wilks lambda=.39282, F(2, 7)=5.4099, p=.03799

Conditions	mean latency Mean	mean latency Std.Err.	mean latency -Std.Err	mean latency +Std.Err	mean amplitude Mean	mean amplitude Std.Err.	mean amplitude -Std.Err	mean amplitude +Std.Err	N
1	2.238	0.343	1.895	2.582	32.915	4.342	28.572	37.257	5
2	2.232	0.343	1.888	2.575	11.522	4.342	7.180	15.864	5

E14: Unmasked conditions (115dB and 105dB SPL) at 500 Hz: interaction of latency and amplitude
Wilks lambda=.27826, F(2, 3)=3.8907, p=.14678

Conditions	mean latency Mean	mean latency Std.Err.	mean latency -Std.Err	mean latency +Std.Err	mean amplitude Mean	mean amplitude Std.Err.	mean amplitude -Std.Err	mean amplitude +Std.Err	N
1	2.005	0.462	1.543	2.467	29.906	4.652	25.254	34.559	3
2	2.019	0.462	1.557	2.481	11.495	4.652	6.843	16.147	3

E15: Latencies b/w 1000 and 500 Hz at unmasked conditions (115dB and 105dB SPL): interaction of latency and frequency
Wilks lambda=.97172, F(2, 5)=.07276, p=.93079

Conditions	mean 1000 Hz latencies Mean	mean 1000 Hz latencies Std.Err.	mean 1000 Hz latencies -Std.Err	mean 1000 Hz latencies +Std.Err	mean 500 Hz latencies Mean	mean 500 Hz latencies Std.Err.	mean 500 Hz latencies -Std.Err	mean 500 Hz latencies +Std.Err	N
1	1.994	0.312	1.682	2.306	2.427	0.528	1.898	2.955	4
2	1.988	0.312	1.676	2.300	2.428	0.528	1.899	2.956	4

E16: Amplitudes b/w 1000 and 500 Hz at unmasked conditions (115dB and 105dB SPL): interaction of amplitude and frequency
Wilks lambda=.32602, F(2, 3)=3.1010, p=.18615

Conditions	mean 1000 Hz amplitudes Mean	mean 1000 Hz amplitudes Std.Err.	mean 1000 Hz amplitudes -Std.Err	mean 1000 Hz amplitudes +Std.Err	mean 500 Hz amplitudes Mean	mean 500 Hz amplitudes Std.Err.	mean 500 Hz amplitudes -Std.Err	mean 500 Hz amplitudes +Std.Err	N
1	34.038	6.676	27.362	40.714	29.906	4.652	25.254	34.559	3
2	11.821	6.676	5.145	18.497	11.495	4.652	6.843	16.147	3

REFERENCES

Black, F. O., & Pesznecker, S. C. (2003). Vestibular adaptation and rehabilitation. *Current opinion in otolaryngology & head and neck surgery*, *11*(5), 355–360. Doi: 10.1097/00020840-200310000-00008

Bleeker, J. D., & De Vries, H. (1949). The microphonic activity of the labyrinth of the pigeon; the cochlea. *Acta oto-laryngologica*, *37*(4), 289–297. Doi: 10.3109/00016484909120248

Böhmer, A., Hoffman, L. F., & Honrubia, V. (1995). Characterization of vestibular potentials evoked by linear acceleration pulses in the chinchilla. The American journal of otology, 16(4), 498–504.

Brown, D. J., Pastras, C. J., & Curthoys, I. S. (2017). Electrophysiological Measurements of Peripheral Vestibular Function-A Review of Electrovestibulography. Frontiers in systems neuroscience, 11, 34. doi: 10.3389/fnsys.2017.00034

Burkard RF, Secor C. (2002). Overview of auditory evoked potentials. In: Katz J. ed. Handbook of Clinical Audiology (pp. 233–248). New York: Lippincott; Williams and Wilkins.

Burke, L.A., & Naylor, G. (2020). Daily-Life Fatigue in Mild to Moderate Hearing Impairment: An Ecological Momentary Assessment Study. Ear and Hearing, doi: 10.1097/aud.0000000000000888

Casale, J., Browne, T., Murray, I., & Gupta, G. (2020). Physiology, Vestibular System.

[Updated 2020 May 24]. In StatPearls [Internet]. Treasure Island, FL: StatPearls Publishing. https://www.ncbi.nlm.nih.gov/books/NBK532978/#_NBK532978_pubdet_

Chihara, Y., Wang, V., & Brown, D. J. (2013). Evidence for the utricular origin of the vestibular short-latency-evoked potential (VsEP) to bone-conducted vibration in guinea pig. Experimental brain research, 229(2), 157–170. doi: 10.1007/s00221-013-3602-5

Cullen, K. E. (2019). Vestibular processing during natural self-motion: implications for perception and action. Nature reviews. Neuroscience, 20(6), 346–363. doi: 10.1038/s41583-019-0153-1

Curthoys, I. S. (2010). A critical review of the neurophysiological evidence underlying clinical vestibular testing using sound, vibration and galvanic stimuli. Clinical neurophysiology : official journal of the International Federation of Clinical Neurophysiology, 121(2), 132–144. doi 10.1016/j.clinph.2009.09.027

Dimiccoli, M., Girard, B., Berthoz, A., & Bennequin, D. (2013). Striola magica. A functional explanation of otolith geometry. *Journal of computational neuroscience*, *35*(2), 125–154. Doi: 10.1007/s10827-013-0444-x

Dobbels, B., Peetermans, O., Boon, B., Mertens, G., Van de Heyning, P., & Van Rompaey, V. (2019). Impact of Bilateral Vestibulopathy on Spatial and Nonspatial Cognition: A Systematic Review. Ear and Hearing, 40(4), 757–765. doi: 10.1097/AUD.0000000000000679

Duncan, J. S., Stoller, M. L., Francl, A. F., Tissir, F., Devenport, D., & Deans, M. R.

(2017). Celsr1 coordinates the planar polarity of vestibular hair cells during inner ear development. Developmental biology, 423(2), 126–137. doi: 10.1016/j.ydbio.2017.01.020

Eatock, R. A., & Songer, J. E. (2011). Vestibular hair cells and afferents: two channels for head motion signals. Annual review of neuroscience, 34, 501–534. doi: 10.1146/annurev-neuro-061010-113710

El-Kashlan, H.K. & Handelsman, J.A. (2008). Computerized Vestibular Testing. In P.C. Weber, Vertigo & Disequilibrium (pp. 4-14). New York, NY: Thieme.

Fattal, D., Hansen, M. & Fritzsch, B. (2018). Aging-Related Balance Impairment and Hearing Loss. In M. Rizzo, S. Anderson, & B. Fritzsch, The Wiley Handbook on the Aging Mind and Brain (pp. 315-336). Hoboken, NJ: Wiley-Blackwell. Doi: 10.1002/9781118772034.CH16

Fujimoto, C., Suzuki, S., Kinoshita, M., Egami, N., Sugasawa, K., & Iwasaki, S. (2018). Clinical features of otolith organ-specific vestibular dysfunction. Clinical neurophysiology : official journal of the International Federation of Clinical Neurophysiology, 129(1), 238–245. doi: 10.1016/j.clinph.2017.11.006

Goldberg J. M. (2000). Afferent diversity and the organization of central vestibular pathways. Experimental brain research, 130(3), 277–297. doi: 10.1007/s002210050033

Greenwalt, N. L., Patterson, J. N., Rodriguez, A. I., Fitzpatrick, D., Gordon, K. R., & Janky, K. L. (2020). Bone Conduction Vibration Vestibular Evoked Myogenic Potential (VEMP) Testing: Reliability in Children, Adolescents, and Young

Adults. Ear and hearing, 10.1097/AUD.0000000000000925. Advance online publication. https://doi.org/10.1097/AUD.0000000000000925

Hall III, J.W. (2007). Introduction to auditory evoked response measurement. In J.W. Hall III, New Handbook of Auditory Evoked Responses (pp. 58-108). Boston, MA: Pearson Education Inc.

Han, P., Zhang, R., Chen, Z., Gao, Y., Cheng, Y., Zhang, Q., & Xu, M. (2016). Evaluation of ocular and cervical vestibular evoked myogenic potentials in a conductive hearing loss model. Journal of otology, 11(4), 192–197. doi: 10.1016/j.joto.2016.12.002

Harsha, W.J., Phillips, J.O., & Backous, D.D. (2008). Clinical Anatomy and Physiology. In P.C. Weber, Vertigo & Disequilibrium (pp. 41-52). New York, NY: Thieme.

Jones TA, Jones SM. (2007). Vestibular evoked potentials. In: Auditory Evoked Potentials: Basic Principles and Clinical Application, edited by Burkard RF, Eggermont JJ, Don M. Philadelphia, PA: Lippincott Williams & Wilkins.

Jones, SM. (2008). Vestibular sensory evoked potentials. In G.P. Jacobson & N.T. Shepard, Balance Function Assessment and Management (pp.379–404). San Diego, CA: Plural Publishing.

Kim, H.H., Wilson, D.F., Wiet, R.J. (2008). Aging and Balance. In P.C. Weber, Vertigo & Disequilibrium (pp. 113-118). New York, NY: Thieme.

Mattingly, J. K., Portnuff, C. D., Hondorp, B. M., & Cass, S. P. (2015). Sudden Bilateral Hearing Loss After Cervical and Ocular Vestibular Evoked Myogenic Potentials. Otology & neurotology : official publication of the American Otological Society,

American Neurotology Society [and] European Academy of Otology and Neurotology, 36(6), 961–964. doi 10.1097/MAO.0000000000000764

Phillips, A. J., & Marchbanks, R. J. (1989). Effects of posture and age on tympanic membrane displacement measurements. British journal of audiology, 23(4), 279–284. doi: 10.3109/03005368909076515

Pyykkö, I., Aalto, H., Grönfors, T., Starck, J., and Ishizaki, H. (1995). Vestibular evoked responses in man: methodological aspects. Acta Otolaryngol. Suppl. 520, 117–119. doi: 10.3109/00016489509125205

Renga V. (2019). Clinical Evaluation of Patients with Vestibular Dysfunction. Neurology research international, 2019, 3931548. doi: 10.1155/2019/3931548

Rine, R. M., & Wiener-Vacher, S. (2013). Evaluation and treatment of vestibular dysfunction in children. NeuroRehabilitation, 32(3), 507–518. doi: 10.3233/NRE-130873

Rosengren, S. M., & Colebatch, J. G. (2006). Vestibular evoked potentials (VsEPs) in patients with severe to profound bilateral hearing loss. Clinical neurophysiology : official journal of the International Federation of Clinical Neurophysiology, 117(5), 1145–1153. doi: 10.1016/j.clinph.2005.12.026

Shin, R.K. & Jensen, J.M. (2010) Dizziness and Vertigo. In W.J. Weiner, C.G. Goetz, R.K. Shin & S.L. Lewis (6th Ed), Neurology for the Non-Neurologist (pp. 412-426). Philadelphia, PA: Lippincott Williams & Wilkins.

Simo, H., Yang, S., Qu, W., Preis, M., Nazzal, M., & Baugh, R. (2015). Meniere's disease: importance of socioeconomic and environmental factors. *American journal of otolaryngology*, *36*(3), 393–398. doi: 10.1016/j.amjoto.2015.01.009

Smith, K. J., McCaslin, D. L., Jacobson, G. P., & Burkard, R. (2019). The Effect of Recording Montage and Tone Burst Duration on Cervical and Ocular Vestibular Evoked Myogenic Potential Latency and Amplitude. American journal of audiology, 28(2), 300–307. doi: 10.1044/2018_AJA-17-0055

Smith, P.F. (2019). The Growing Evidence for the Importance of the Otoliths in Spatial Memory. Frontiers in neural circuits, 13, 66. doi: 10.3389/fncir.2019.00066

Stewart, C. E., Altschuler, R. A., Cacace, A. T., Hall, C., Holt, A. G., Murnane, O., King, W. M., Akin, F. W. Effects of noise exposure on the vestibular system: A systematic review. Frontiers in Neurology 11:593919 doi: 10.3389/fneur. (in press).

Stewart, C. E., Bauer, D. S., Kanicki, A. C., Altschuler, R. A., & King, W. M. (2020). Intense noise exposure alters peripheral vestibular structures and physiology. Journal of neurophysiology, 123(2), 658–669. doi: 10.1152/jn.00642.2019

Stewart, C. E., Kanicki, A. C., Altschuler, R. A., & King, W. M. (2018). Vestibular short-latency evoked potential abolished by low-frequency noise exposure in rats. Journal of neurophysiology, 119(2), 662–667. doi: 10.1152/jn.00668.2017

Stewart, C. E., Kanicki, A. C., Bauer, D. S., Altschuler, R. A., & King, W. M. (2020). Exposure to Intense Noise Causes Vestibular Loss. Military medicine, 185(Suppl 1), 454–461. doi: 10.1093/milmed/usz206

Sugita-Kitajima, A., & Koizuka, I. (2014). Evaluation of the vestibulo-ocular reflex using sinusoidal off-vertical axis rotation in patients with canal paresis. Auris, nasus, larynx, 41(1), 22–26. doi: 10.1016/j.anl.2013.04.014

Todd, N. P., McLean, A., Paillard, A., Kluk, K., & Colebatch, J. G. (2014). Vestibular evoked potentials (VsEPs) of cortical origin produced by impulsive acceleration applied at the nasion. Experimental brain research, 232(12), 3771–3784. doi: 10.1007/s00221-014-4067-x

Wiener-Vacher, S. (2001). Clinical Application of the Off Vertical Axis Rotation Test (OVAR). Otolith Functions and Disorders- Adv Otorhinolaryngol, 58, 88-97. Doi: 10.1159/ 000059114

Wiener-Vacher, S. R., Quarez, J., & Priol, A. L. (2018). Epidemiology of Vestibular Impairments in a Pediatric Population. Seminars in hearing, 39(3), 229–242. doi: 10.1055/s-0038-1666815

Wilson-Pauwels, L., Akesson, E.J., Stewart, P.A., & Spacey, S.D. (2002). Vestibulocochlear Nerve. In L. Wilson-Pauwels, E.J. Akesson, P.A. Stewart, & S.D. Spacey (2nd Ed.), Cranial Nerves in health and disease (pp.141-162). Hamilton, Ontario: BC Decker Inc.

Yagi, T. (2003). Vertigo caused by Semicircular Canal and Otolith Lesions. Journal of the Japan Medical Association-JMAJ, 46(7), 291-295.

ABSTRACT

PARAMETRIC STUDY OF SHORT LATENCY VESTIBULAR EVOKED POTENTIALS IN HEALTHY YOUNG ADULTS

by

SABAHET F. RIZVI

DECEMBER 2020

Advisor: Dr. Anthony T. Cacace

Major: Communication Sciences and Disorders

Degree: Doctor of Philosophy

The purpose of this study was to evaluate the feasibility of developing a novel approach of otolith assessment in humans. This approach used vestibular short-latency evoked potentials (VsEP) to evaluate some fundamental characteristics of VsEP responses in healthy young adults. Currently, measures for direct assessment of the otoliths are non-existent, as vestibular evoked myogenic potentials (VEMPs) rely on neck muscle contraction for cVEMPs or are a reflection of the vestibulo-ocular reflex (VOR) for oVEMPs, rather than the otoliths themselves (Fujimoto, Suzuki, Kinoshita, Egami, Sugasawa, & Iwasaki, 2018).

Stimuli consisted of bone-conducted vibrations elicited by a specialized vibrator (Bruel & Kjaer, model 4810; B&K mini-shaker) attached to a power amplifier (B&K, model 2718) that causes linear acceleration movements of the skull. Standard reusable surface electrodes with the reference electrode placed on the forehead (Fpz), ground placed on the mastoid process of left ear (M2), and a (Lilly or Sanabel) wick electrode (placed as on the left tympanic membrane) were used to record early electrical activity

(4ms). Data was collected and analyzed from 11 healthy young adults (6 males and 5 females) ranging in age from 19-39 years (mean: 23.1 years; SD: 6.9 years) who met the inclusion criteria for testing. Audiometric thresholds were tested to ensure normal hearing sensitivity (0.25-8 kHz; <25 dB HL, bilaterally).

A general analysis of the VsEPs was conducted through visual inspection of the waveforms and statistical analyses of the VsEP responses. The statistical analyses consisted of a series of one-way ANOVAs with repeated measures which included stimulus frequency (500 and 1000 Hz), intensity (115, 105, 95, & 85 dB SPL), along with masked (100, 90, & 80 dB HL) and unmasked conditions.

VsEPs appear to be promising due to the simplicity of the test and ease of analysis - looking at waveforms without requiring active participation from participants. It would be necessary to complete testing on additional healthy participants to ensure that there continues to remain a consistency across all VsEP conditions regardless of participant; as this study showed, no large outliers were found across results for any of the participants tested in this study. It would also be beneficial to assess additional VsEP parameters (e.g., contralateral masking, additional stimulus and masking levels, varying durations, etc) in known individuals with specific otolith dysfunction to see if able to find such consistency across disordered group in the future before this assessment will be translatable into a clinical setting.

Results of this study indicate that the amplitudes of the VsEPs are significantly impacted ($p<.05$) by the intensity of the stimulus, regardless of the frequency tested, with the higher intensity having higher mean amplitudes than the lower intensities tested. On

the other hand, the VsEP latencies remained consistent, regardless of the different frequencies, stimulus intensity, and masker levels assessed.

AUTOBIOGRAPHICAL STATEMENT

SABAHET FATIMA RIZVI

Sabahet F. Rizvi received both her Bachelor of Arts in Communication Sciences and Disorders and her clinical Doctor of Audiology degrees from Wayne State University in Detroit, Michigan. She is a member of both ASHA (CCC-A) and AAA (FAAA) and holds licensure to practice clinical audiology in Michigan. Her main research interest focuses on audiological issues secondary to chronic diseases. Her childhood hearing loss led her to audiology, and she truly believes that the best patient advocate is through self-advocacy and acquiring knowledge. She hopes to pass on her passion for learning to her students as she begins teaching in the near future.