



---

MSU Graduate Theses

---

Spring 2017

## The Effect of Wideband and Narrowband Noise on the Olivocochlear Bundle and the Cochlear Microphonic

Catherine Nicole Palmietto

As with any intellectual project, the content and views expressed in this thesis may be considered objectionable by some readers. However, this student-scholar's work has been judged to have academic value by the student's thesis committee members trained in the discipline. The content and views expressed in this thesis are those of the student-scholar and are not endorsed by Missouri State University, its Graduate College, or its employees.

---

Follow this and additional works at: <https://bearworks.missouristate.edu/theses>



Part of the [Speech Pathology and Audiology Commons](#)

### Recommended Citation

Palmietto, Catherine Nicole, "The Effect of Wideband and Narrowband Noise on the Olivocochlear Bundle and the Cochlear Microphonic" (2017). *MSU Graduate Theses*. 3180.

<https://bearworks.missouristate.edu/theses/3180>

This article or document was made available through BearWorks, the institutional repository of Missouri State University. The work contained in it may be protected by copyright and require permission of the copyright holder for reuse or redistribution.

For more information, please contact [bearworks@missouristate.edu](mailto:bearworks@missouristate.edu).

**THE EFFECT OF WIDEBAND AND NARROWBAND NOISE ON THE  
OLIVOCOCHLEAR BUNDLE AND THE COCHLEAR MICROPHONIC**

A Doctoral Thesis

Presented to

The Graduate College of  
Missouri State University

In Partial Fulfillment

Of the Requirements for the Degree

Doctor of Audiology

By

Katie Palmietto

May 2017

Copyright 2017 by Catherine Palmietto

# **THE EFFECT OF WIDEBAND AND NARROWBAND NOISE ON THE OLIVOCOCHLEAR BUNDLE AND THE COCHLEAR MICROPHONIC**

Communication Sciences and Disorders

Missouri State University, May 2017

Doctor of Audiology

Katie Palmietto

## **ABSTRACT**

In humans, activation of the olivocochlear bundle (OCB) can have a suppression or enhancement effect on cochlear processes. This phenomenon was studied via OCB activation effects on otoacoustic emissions (OAEs). However, it has been suggested that cochlear microphonics (CMs) can provide better, more detailed information regarding OCB function. In the present study, 22 normal hearing female subjects between the ages of 18-30 were recruited and the OCB was examined via the recording of CMs under changes in three conditions: OCB activating noise, stimulus polarity and stimulus frequency. Specifically, the present study examines the effects of activating wideband noise and narrowband noise centered at 1 and 0.5 kHz, presented contralaterally. CMs were elicited using 0.5 and 1 kHz tone bursts. Stimuli were presented using both condensation and rarefaction polarity. CM response amplitude for each condition was collected. Data analysis using repeated measures ANOVA revealed that OCB activation did not cause a significant change in the CM response. These results indicate that the recorded response may not have reflected activity from the apical end of the cochlea.

**KEYWORDS:** olivocochlear bundle, cochlear microphonics, outer hair cells, cochlear processes, wideband noise, narrowband noise

This abstract is approved as to form and content

---

Abdullah Jamos, Au.D.  
Chairperson, Advisory Committee  
Missouri State University

**THE EFFECT OF WIDEBAND AND NARROWBAND NOISE ON THE  
OLIVOCOCHLEAR BUNDLE AND THE COCHLEAR MICROPHONIC**

By

Katie Palmietto

A Doctoral Thesis  
Submitted to the Graduate College  
Of Missouri State University  
In Partial Fulfillment of the Requirements  
For the Degree of Doctor of Audiology

May 2017

Approved:

---

Abdullah Jamos, AuD.

---

Wafaa Kaf, MD, MSc, PhD

---

Mark Chertoff, PhD

---

Julie Masterson, PhD: Dean, Graduate College

## ACKNOWLEDGEMENTS

This study would not have been possible without the help of several individuals. Thank you to Dr. Abdullah Jamos, my research advisor, for your patience, guidance and support throughout this project. I would also like to thank the members of my thesis committee: Dr. Wafaa Kaf and Dr. Mark Chertoff and the CSD department head, Dr. Letitia White Minnis; I have learned so much from all of you and your guidance has been invaluable. I would also like to thank Dr. Todd Daniel for your help with data analysis. A special thank you to all of the participants in this study; thank you for “lending an ear!” Finally, I would like to thank my parents, Vito and Maureen, my step mother, Maggie, my brother, Vito Jr., my step-brother, Alex, and my step-sisters, Calie and Zoe. Words cannot express how much I appreciate all of you.

## TABLE OF CONTENTS

Introduction.....	1
Review of the Literature .....	4
Peripheral Auditory System Anatomy .....	4
Central Afferent Auditory System Anatomy .....	9
Physiology of the Ear.....	11
Physiology of the Central Auditory Pathway .....	14
Anatomy of the Efferent Auditory Pathway .....	15
Physiology of the Efferent Auditory Pathway .....	17
The Olivocochlear Bundle and Otoacoustic Emissions.....	19
The Medial Olivocochlear Bundle and Cochlear Microphonics .....	22
Frequency Specificity of the Medial Olivocochlear Bundle.....	27
Objectives .....	29
Methods.....	31
Participants.....	31
Instrumentation .....	32
Procedures.....	32
Measurement and Data Analysis .....	35
Results .....	37
Suppression and Enhancement Trends in One Participant .....	37
Suppression vs. Enhancement.....	38
Change in Cochlear Microphonic Response Amplitude.....	42
Discussion.....	47
Medial Olivocochlear Bundle Effects on Cochlear Microphonics .....	48
CM Generation and Recording from the Apical End of the Cochlea .....	50
Frequency Specific Effects of the MOCB in Relation to the Distribution of the MOCB Fibers in the Contralateral Cochlea.....	51
Use of CM for Determining MOCB Effects on the Apical Regions of the Cochlea .....	54
Suppression and Enhancement Effects of MOCB Activation in the CM Response .....	55
Study Limitations.....	59
Future Studies .....	60
References.....	61

## LIST OF TABLES

Table 1. Testing Conditions.....	34
Table 2. Suppression and Enhancement Trends for 0.5 kHz CMs.....	40
Table 3. Suppression and Enhancement Trends for 1 kHz CMs.....	41
Table 4. Paired sample <i>t</i> -test conducted for all conditions. ....	43



## LIST OF FIGURES

Figure 1. Waveform Markings.....	36
Figure 2. CM Response Suppression with 0.5 kHz tone burst in One Participant .....	37
Figure 3. CM Response Enhancement with 1 kHz tone burst in One Participant.....	38
Figure 4. Change in CM Amplitude with Noise Type and Stimulus Type.....	45
Figure 5. Change in CM amplitude with Noise Type and Stimulus Polarity .....	45
Figure 6. Change in CM Amplitude with Stimulus Type and Stimulus Polarity .....	46

## INTRODUCTION

Sensory systems are monitored and regulated by the central nervous system via efferent pathways. One such pathway is the auditory efferent system (Nolte, 2009). The human efferent auditory system has interested researchers for several decades (Guinan, 2006). First described in the early 1950s, effects of the auditory efferent system, specifically, the olivocochlear bundle (OCB), were studied with animal models. However, our understanding of the efferent auditory system in humans has increased significantly in recent years (Guinan, 2006). The OCB has been implicated in several auditory processes including protection from acoustic trauma, and aid in the detection of a signal in noise (Guinan, 2006). Traditionally, the effects of the efferent auditory system in humans have been measured indirectly by its impact on otoacoustic emissions because the OCB acts on cochlear outer hair cells (OHCs) (Guinan, 2014). These studies have shown that activation of the OCB will change otoacoustic emission (OAE) activity by suppressing or enhancing the OAE response (Cooper & Guinan, 2006; Guinan, 2006). Examination of the OCB via OAEs is considered the gold standard. However, this method of examination is problematic (Guinan, 2014). The already small OAE response shows relatively small changes when the OCB is activated. Additionally, neural responses are not reflected in the change in OAE amplitude with MOCB activation (Guinan, 2014). However, research with animal models has shown that the effects of the OCB on the auditory evoked potentials are far greater, including cochlear microphonic (CM) response (Puria, Guinan & Liberman, 1996). Therefore, studying the effects of the

OCB on CMs could allow researchers the opportunity to garner better, more detailed information about the mechanisms of the OCB.

Studies of the auditory efferent system use often wideband noise to activate the OCB (Maison, Micheyl, Andéol, Gallégo, Collet, 1999). However, some researchers have examined the effects of narrowband activating noise. In a study conducted by Maison, et al. (1999), efferent effects on DPOAEs were recorded in the presence of wideband noise and several types of narrowband noise. Researchers found that the suppression effects were greater with wider bandwidths. In another study, Chéry-Croze, Moulin and Collet (1996) found evidence of frequency specificity of the MOCB. Researchers recorded DPOAEs to several  $2f_1$ - $f_2$  values, including 1, 2, 3 and 5 kHz, while activating the MOCB using narrowband noise with varying center frequencies. Chéry-Croze et al. (1996) revealed that for  $2f_1$ - $f_2$  values of 1 kHz, suppression was greatest when narrowband noise was centered at 1 kHz. For  $2f_1$ - $f_2$  values of 2 kHz, suppression was greatest for narrowband activating noise centered at 1 and 2 kHz.

To the best of our knowledge, studies that examined the effects of the OCB via CMs have not used narrowband noise to evoke an OCB response. Prior research has determined a frequency effect of the medial OCB (MOCB) on the mechanical properties of the OHCs (Chéry-Croze et al., 1996). In the current study, we investigate the effects of the MOCB on CMs using narrowband noise. In doing so, we hope to evaluate the frequency characteristics of MOCB suppression effects on the electrical potentials of the OHCs. Data derived from the current study will hopefully provide more information about the intricate interplay between the OHCs and the MOCB. In this study, CMs will be recorded using condensation and rarefaction 0.5 and 1 kHz stimuli. Three types of

MOCB activating noise will be used: wideband noise, narrowband noise centered at 0.5 kHz and narrowband noise centered at 1 kHz. Additionally, CMs will be recorded without the use of MOCB activating noise to quantify changes in the CM response with MOCB activation.

## REVIEW OF THE LITERATURE

### Peripheral Auditory System Anatomy

**Outer and Middle Ear.** The peripheral auditory system consists of the outer, middle and inner ear and is housed in the temporal bone. Sound waves travel through the environment and are captured by the outer ear. The outer ear consists of the pinna and the external auditory meatus (EAM). The pinna protrudes from the head and is composed of cartilage and ligaments covered by skin (Gulya, 1997). It consists of grooves that help funnel sound waves into the EAM (Gulya, 1997; Musiek & Baran, 2007). The EAM is approximately 2.5 cm long and extends medially from the pinna to the tympanic membrane, forming a slight “s” shape (Lambert & Canalis, 2000). The tympanic membrane is a thin, concave membranous structure that marks the boundary between the outer and middle ear (Lambert & Canalis, 2000).

The middle ear is an air-filled space, approximately 2 cm<sup>3</sup> (Lambert & Canalis, 2000). The middle ear is bounded laterally by the tympanic membrane and medially by the petrous portion of the temporal bone (Lambert & Canalis, 2000). Pneumatized bone of the temporal bone forms the roof of the middle ear (Gulya, 1997). Several structures lie at the floor of the temporal bone, including the jugular bulb, the carotid artery and the eustacian tube, a muscular tube that leads from the middle ear space to the pharynx (Lambert & Canalis, 2000). The middle ear contains three small bones: the malleus, incus and stapes. Collectively, these bones are known as the ossicular chain (Lambert & Canalis, 2000; Gulya, 1997). The manubrium of the malleus is embedded in the medial layer of the tympanic membrane (Lambert & Canalis, 2000). The head of the malleus

then connects to the incus, which runs medially and articulates with the head of the stapes (Gulya, 1997). The footplate of the stapes connects to the oval window, one of two openings in the petrous portion of the temporal bone that marks the boundary between the middle and inner ear (Braun, Böhnke & Stark, 2012). The second opening in the temporal bone is inferior to the oval window and called the round window (Gulya, 1997).

**Inner Ear.** The inner ear is housed in the otic capsule of the temporal bone (Gulya, 1997, Raphael & Altschuler, 2003). The inner ear can be divided into the cochlea and the vestibular system (Lambert & Canalis, 2000; Gulya, 1997). Several channels and cavities run through the temporal bone; one of these cavities surrounds the cochlea (Gulya, 1997). The cochlea is a snail shell shaped structure; it winds around a bony core in two and a half turns and is approximately 10 mm in diameter at its base (Elliot & Shera, 2012). The cochlea is divided into the bony and membranous labyrinths (Gulya, 1997). The bony portion of the cochlea consists of the petrous portion of the temporal bone, the modiolus, and the osseous spiral lamina (Lambert & Canalis, 2000). The modiolus is the bony core at the center of the cochlea (Lambert & Canalis, 2000). The osseous spiral lamina, a shelf like structure that supports membranous cochlear structures, winds around the modiolus (Lambert & Canalis, 2000; Gulya, 1997). The modiolus contains the spiral ganglia, which leads to the cochlear nerve (Raphael & Altschuler, 2003). The medial end of the modiolus is continuous with the internal auditory meatus (IAM). The IAM is the channel through which the cochlear nerve, along with other neural structures, travels to the brainstem (Gulya, 1997).

The membranous labyrinth is a fluid filled sac that follows the shape of the bony labyrinth of the cochlea. It contains three ducts that wind around the modiolus: the scala

vestibuli, the scala media and the scala tympani (Lambert & Canalis, 2000). The scala vestibuli is the superior duct and is separated from the scala media by Reissner's membrane (Raphael & Altshuler, 2003). The oval window is located at the basal most end of the scala vestibuli. The scala media is separated from the inferior most duct, the scala tympani, by the basilar membrane. The round window lies at the basal most end of the scala tympani (Lambert & Canalis, 2000). The scala vestibuli and scala tympani are filled with perilymph and communicate at the apex of the cochlea via the helicotrema (Braun, et al., 2012; Raphael & Altshuler, 2003). Perilymph has the same chemical composition as cerebrospinal fluid and is high in sodium and low in potassium (Nodar, Sahley, Hughes & Musiek, 1997). The scala media does not communicate with the scala vestibuli or scala tympani. However, it is continuous with vestibular structures via the ductus reuniens (Musiek & Baran, 2007). The scala media contains endolymph and cortilymph (Raphael & Altshuler, 2003). Endolymph is produced by the stria vascularis, which is located at the end of the scala media opposite to the modiulus, and has high concentration of potassium and low concentration of sodium (Raphael & Altshuler, 2003).

The osseous spiral lamina winds around the modiulus from base to apex. It is widest at the base and gradually thins as it travels to the apex (Gulya, 1997). The osseous spiral lamina connects with the basilar membrane. Converse to the osseous spiral lamina, the basilar membrane is widest at the apex and gradually becomes narrower as it reaches the base (Raphael & Altshuler, 2003). The width of the basilar membrane plays a role in the tonotopic organization of the cochlea (Raphael & Altshuler, 2003). The outer edge of the basilar membrane is continuous with the spiral ligament (Lim, 1980). These

structures, the osseous spiral lamina, the basilar membrane and the spiral ligament form the floor and outermost wall of the basilar membrane. These structures also support the organ of Corti, the end organ of hearing (Braun, et al., 2012; Musiek & Baran, 2007).

The organ of Corti runs the entire length of the cochlea and contains several structures, including supporting structures, nerve fibers and sensory cells, specifically inner hair cells (IHCs) and OHCs (Raphael & Altshuler, 2003). Like the basilar membrane, the organ of Corti increases in mass from the base to the apex (Lim, 1980). The tectorial membrane lies at the top of the organ of Corti. This structure articulates with the stereocillia of the OHCs (Lim, 1980). The organ of Corti is filled with cortilymph and is separated from the endolymph by a structure called the reticular lamina, which forms the ceiling of the organ of Corti (Musiek & Baran, 2007; Raphael & Altshuler, 2003). Each structure of the organ of Corti is continuous throughout the entirety of the cochlea, including the inner and outer hair cells (Musiek & Baran, 2007; Raphael & Altshuler, 2003).

**Inner and Outer Hair Cells.** The inner and outer hair cells are arranged in rows on opposite sides of the tunnel of Corti, a support structure formed by pillar cells. IHCs form a single row and the outer hair cells (OHCs) are arranged in three rows (Nodar, et al., 1997). There are approximately 3,500 IHCs and 12,000 OHCs (Elliot & Shera, 2012). Structurally and functionally, the IHCs and OHCs are very different. The OHCs are cylindrical cells (Nodar, et al., 1997; Raphael & Altshuler, 2003). Their length changes as they are arranged throughout the cochlea (Raphael & Altshuler, 2003). OHCs at the base of the cochlea are shorter, approximately 0.20  $\mu\text{m}$ , whereas apical OHCs are longer, approximately 80  $\mu\text{m}$  (Nodar, et al., 1997). The OHCs contain several proteins, including



actin, prestin, and myosin (Elliot & Shera, 2012). These proteins play a role in contractile properties of the OHCs. Several stereocilia project from the top of the OHCs in three rows and are arranged to form a “W” shape (Lim, 1980). The stereocilia are more numerous at the basal end of the cochlea and are relatively stiff. They are embedded in the tectorial membrane (Nodar, et al., 1997; Raphael & Altshuler, 2003). When the outer hair cell contracts, the tectorial membrane is pulled down and shears the stereocilia of the IHCs (Elliot & Shera, 2012). The OHCs synapse with type II neurons; a single neuron projects to several OHCs, resulting in less innervation relative to the IHCs (Hamill & Price, 2014; Nodar, et al., 1997).

The IHCs are goblet shaped cells, approximately 35  $\mu\text{m}$  in length (Hamill & Price, 2014; Musiek & Baran, 2007). Approximately 50-70 stereocilia project from the top of each IHC and are arranged in three rows to form a “U” shaped pattern. Unlike the stereocilia of the OHCs, these do not project into the tectorial membrane (Lim, 1980). The stereocilia are varying lengths; stereocilia grow in length from the base to the apex (Nodar, et al., 1997). The length of the stereocilia also vary within a single IHC. The longest of these is referred to as the kinocillium (Musiek & Baran, 2007). The IHCs synapse with type I neurons, several of which synapse with a single IHC (Nodar, et al., 1997). These neurons fire when the kinocillium is sheared. IHCs play the primary role in sending signals to the brain in the presence of auditory stimuli (Musiek & Baran, 2007).

The stereocilia of the IHCs and OHCs are structured similarly. Stereocilia are connected to one another via filaments called cross-links (Nodar, et al., 1997). These structures allow the stereocilia to move in concert with one another. Each stereocilia contains several pores through which ions can enter and exit. Structures called tip links

aid in the opening of the stereocilia pores. When the pores open, depolarization occurs and the cell fires (Elliot & Shera, 2012). The electrical signal travels through the cochlear nerve to the central auditory system (Hughes & Nodar, 1985).

### **Central Afferent Auditory System Anatomy**

The central afferent auditory pathway begins at the auditory nerve. Specifically, the neuroglia-neurolemma junction of the cochlear nerve, where peripheral Schwann cell derived myelin is separated from glial cell derived myelin, marks the distal most part of the central auditory system (Luxon & Cohen, 1997). Following the auditory nerve, the afferent auditory pathway includes the cochlear nucleus, the superior olivary complex, the lateral lemniscus, inferior colliculus, the medial geniculate body and finally, the auditory cortex (Musiek & Baran, 2007). For the purposes of the current study, the auditory pathway to the level of the superior olivary complex will be discussed.

The cochlear nerve, like the cochlea, is tonotopically organized; those fibers most sensitive to low frequency sounds are located medially, whereas fibers sensitive to high frequency sounds are in the periphery (Luxon & Cohen, 1997). The cochlear nerve originates from the spiral ganglion and leads to the pons in the brainstem (Hamill & Price, 2014). The spiral ganglion is located within the modiolus of the cochlea, and it is composed of axons that receive information from the inner and outer hair cells (Swartz & Harnsberger, 1992). From the modiolus, the cochlear nerve travels through the inferior anterior portion of the fundus of the internal auditory canal (Swartz & Harnsberger, 1992). As the cochlear nerve moves more medially through the internal auditory meatus, it joins the inferior and superior branches of the vestibular nerve to become the

vestibulocochlear nerve (Swartz & Harnsberger, 1992). The vestibulocochlear nerve continues to traverse the inferior auditory canal and enters the brainstem between the medulla and the pons. Specifically, the vestibulocochlear nerve bifurcates into an ascending and descending branch and terminates at the anterior ventral cochlear nucleus and the dorsal and posterior ventral cochlear nuclei, respectively (Swartz & Harnsberger, 1992; Luxon & Cohen, 1997).

The cochlear nucleus (CN) is located at the restiform body, or the inferior cerebellar peduncle (Swartz & Harnsberger, 1992; Luxon & Cohen, 1997). It is divided into three parts: the dorsal CN, the anterior ventral CN and the posterior ventral CN. Output from the CN travels through three primary tracts: the ventral stria, which contains fibers from the anterior ventral cochlear nucleus; the dorsal stria, which contains fibers from the dorsal CN; and intermediate stria, which contains fibers from the posterior ventral CN (Musiek & Baran, 2007). Most the fibers from the CN project to the superior olivary complex, though some, specifically fibers from the dorsal stria, bypass the pons and synapse to the contralateral lateral lemniscus. In general, the ventral and intermediate stria travel to the contralateral superior olivary complex, although some fibers travel ipsilaterally (Luxon & Cohen, 1997; Musiek & Baran, 2007). Other fibers from the CN travel to the ipsilateral and contralateral inferior colliculus.

The superior olivary complex (SOC) is in the pons, but positioned more medially than the CN (Luxon & Cohen, 1997). The SOC is comprised of three regions: the medial and lateral superior olives and the nucleus of the trapezoid body. The medial superior olive and the lateral superior olive are connected by the acoustic chiasm. The crossed connections of the acoustic chiasm travel to and from the medial and lateral olivary

complex and the inferior colliculus. Fibers from the SOC project to the ipsilateral inferior colliculus and the lateral lemniscus (Wackym, et al., 2000). While the CN receives only ipsilateral input, the SOC receives input from the ipsilateral and contralateral CN and is the distal most region of the central auditory pathway to receive binaural input (Luxon & Cohen, 1997).

### **Physiology of the Ear**

**Outer and Middle Ear.** Sound energy undergoes several changes as it travels from the pinna to the brain. Sound waves enter the outer ear as acoustic energy (Hamill & Price, 2014; Nodar, et al., 1997). The sound waves travel from the pinna, through the EAM to the tympanic membrane. The tympanic membrane vibrates in the presence of sound waves and in turn vibrates the ossicular chain (Nodar, et al., 1997). These vibrations transform the acoustical energy to mechanical energy as sound enters the middle ear. The middle ear acts as an impedance matching system, allowing the mechanical energy of the middle ear to be efficiently transferred into the fluid filled cochlea (Hughes & Nodar, 1985). This is achieved in three ways: the ossicular chain acts as a lever, the large surface area of the tympanic membrane increases the force displaced on the relatively smaller surface area of the oval window, and the placement of the concave tympanic membrane relative to the manubrium of the malleus results in a bucking motion when the tympanic membrane vibrates (Nodar et al., 1997). Each of these mechanism increases the mechanical energy of stimulus before it reaches the cochlea (Hughes & Nodar, 1985; Nodar et al., 1997).

**Inner Ear.** The cochlea transduces mechanical energy from the middle ear into hydraulic energy (Nodar, et al., 1997). It then transforms the hydraulic energy into chemical, and later electrical energy that is ultimately transmitted to the brain. As the vibratile action of the ossicular chain pushes the footplate of the stapes into the oval window, the perilymph in the scala vestibuli is displaced (Elliot & Shera, 2012; Nodar, et al., 1997). The cochlea is filled with fluid, which is noncompressible (Hamill & Price, 2014). Consequently, the movement of the oval window creates a hydraulic disturbance that travels from the basal end to the apical end of the cochlea (Nodar, et al., 1997). As fluid travels, it displaces the basilar membrane (Nodar, et al., 1997). The basilar membrane is wide and floppy at the apex and narrow and stiff at the base (Lim, 1980). When the basilar membrane moves, it forms a wave that travels along the cochlea (Nodar, et al., 1997). This traveling wave is essential to the transduction of hydraulic energy into chemical and neural energy which is received by the brain (Musiek & Baran, 2007). The point of maximum displacement is determined by the characteristics of the stimulus. The basal end of the cochlea is most sensitive to high frequency signals, whereas the apical end of the cochlea is most sensitive to low frequency sounds (Lippe, 1986). Therefore, a high frequency stimulus will cause a wave that will peak in the base of the cochlea and vice versa (Musiek & Baran, 2007; Raphael & Altshuler, 2003). The speed of the traveling wave plays a large role in the tonotopic organization of the cochlea. The velocity of the traveling wave is determined by several factors, including the physical characteristics of the auditory stimulus, the basilar membrane, and the organ of Corti (Musiek & Baran, 2007). The stiffness of the basilar membrane ultimately affects

the speed of the traveling wave; as the traveling wave travels from the base to the apex the velocity decreases.

The scala media is filled with endolymph and cortilymph (Raphael & Altshuler, 2003). Endolymph has a positive electrical charge of 80 mV and is high in potassium and low in sodium. The chemical composition of cortilymph is like that of perilymph and it has a charge of 0 mV (Musiek & Baran, 2007). The fluids of the scala media do not mix with other cochlear fluids as the scala media is not continuous with the scala vestibuli nor the scala tympani. Therefore, the endolymph and cortilymph can maintain their charge when the cochlea is at rest. The cochlear hair cells have a negative charge; the IHC voltage is -40 mV and the outer hair cells voltage is -70 mV. The difference in voltage between the hair cells and the surrounding fluid create an electrical differential approximately 100 mV that is essential to cell depolarization and subsequent nerve firing (Elliot & Shera, 2012). When a mechanical stimulus disturbs the basilar membrane of the cochlea, the resulting wave travels the length of the cochlea. The OHCs contract and expand in response to the stimulus (Elliot & Shera, 2012). Because the stereocillia of the OHCs are embedded in the tectorial membrane, OHC movement causes the tectorial membrane to be pulled down and the stereocillia of the IHCs are sheared toward the stria vascularis. The resulting movement of the stereocillia cause pores within the stereocillia to open and  $K^+$  ions from the endolymph rush into the cell. This causes the cell to depolarize and release neurotransmitters in the presynaptic cleft, causing the auditory nerve to fire (Elliot & Shera, 2012; Hamill & Price, 2014).

**Outer Hair Cells.** OHCs are essential to the transduction of the cochlea. As mentioned previously, the contractile action of the OHCs causes the tectorial membrane to be pulled down, shearing the IHCs and allowing them to fire. The contractile motion is the result of proteins embedded in the surface of the OHCs. Of these proteins, prestin is responsible for the electromotile action of the OHCs (Elliot & Shera, 2012). Prestin is a motor protein that contains a “voltage sensor” that can detect a change in voltage of the cell and a molecule that reacts to that change, causing movement (Raphael & Altschuler, 2003). Specifically, Cl<sup>-</sup> in the OHC plasma membrane binds to prestin when the cell voltage changes during depolarization and hyperpolarization (Oliver, et al. 2000). During depolarization, the Cl<sup>-</sup> then moves to the cytoplasmic end of the cell membrane which causes the cell to contract. During hyperpolarization, Cl<sup>-</sup> moves to the extracellular side of the membrane, causing the cell to elongate (Oliver, et. al, 2000). When Cl<sup>-</sup> is removed from the cell, axial stiffness of the OHC decreases significantly (He, Jia, & Dallos, 2003). The OHCs are considered a cochlear amplifier; their movement causes greater movement of the basilar membrane, thereby increasing the motion of the traveling wave (Raphael & Altschuler, 2003). The CM is generated by the action of the OHCs (Santarelli, Scimemi, Dal Monte, & Arslan, 2006).

### **Physiology of the Central Auditory Pathway**

The CN is tonotopically organized in a manner similar to the auditory nerve. Low frequency auditory nerve fibers synapse on the lateral regions of the CN, whereas high frequency fibers project to the medial region of the CN where the dorsal, posterior ventral and anterior ventral CN regions reside. Firing pattern from the auditory nerve is either

modified or preserved by the CN (Musiek & Baran, 2007). In cats, it has been shown that sectioning of the ventral stria of the CN can diminish the ability to detect sound and to distinguish sound in noise whereas sectioning of the intermediate and dorsal stria has little to no effect on the ability to hear in noise (Musiek and Baran, 2007).

The SOC is also somewhat tonotopically organized; the medial nucleus is most sensitive to low frequency sounds. However, the lateral nucleus is responsive to sounds of all frequencies (Luxon & Cohen, 1997). The SOC is the distal most structure of the central auditory pathway to receive binaural input (Luxon & Cohen, 1997). Because of this binaural input, the SOC can compare input from the ipsilateral and contralateral ear, thereby playing an important role in detecting interaural timing and intensity differences (Luxon & Cohen, 1997; Wackym, Storper & Newman, 2000). Binaural input is coded with excitatory and inhibitory neurons. In general, stimuli from the ipsilateral ear cause a greater inhibitory response than stimuli from the contralateral ear and vice versa (Musiek & Baran, 2007).

### **Anatomy of the Efferent Auditory Pathway**

The efferent auditory system works in conjunction with the afferent system, though there are some many differences in the structure of the pathways. Efferent neurons make up a small portion of the total number of neurons in the auditory system; of the 30,000 auditory neurons, only 500 run efferently (Hamill & Price, 2014). The efferent auditory system courses along the same pathway as the afferent system, but runs in the opposite direction. It originates at the auditory cortex and subcortex and terminates at the cochlea (Murdin & Davies, 2008; Musiek, 1986). It can be divided into two segments:



the rostral efferent system and the OCB. The rostral system courses caudally to the SOC, and the OCB courses caudally from the SOC (Musiek & Baran, 2007).

The rostral efferent system runs from the auditory cortex to the internal capsule, proceeding to the ipsilateral pulvinar and reticular nuclei of the thalamus (Musiek & Baran, 2007; Musiek, 1986). The fibers then run to the dorsal and ventral MGB and the IC, although it is important to note that some fibers project from the cortex directly to the IC. Some fibers also run from the cortex to the contralateral IC (Musiek, 1986). The pathway of the rostral efferent system contains several areas at which it merges with the afferent system, creating a complex network of feedback loops (Musiek & Baran, 2007).

More is known about the OCB than the rostral efferent system (Hamill & Price, 2014). Neurons from the SOC merge with the vestibular nerve (Nolte, 2009). These fibers then travel to the cochlear division of the vestibulocochlear nerve and project to the organ of Corti. Two types of fibers travel from the SOC and affect the activity of the cochlea (Musiek, 1986). The lateral olivocochlear (LOC) fibers originate from the lateral superior olive (Raphael & Altshuler, 2003). In humans, these fibers are thin, unmyelinated and the majority synapse with the dendrites of the type I afferent neurons on the ipsilateral side (Cuiman, 2010; Gifford & Guinan, 1987; Hill, Prasher & Luxon, 1997). LOC fibers exit the brainstem and join the auditory nerve at the anastomosis of Oort and enter the cochlea (Raphael & Altshuler, 2003). The lateral superior olive contains two types of neurons: small and large. Small neurons terminate in dense patches and synapse over approximately 10-20% of the length of the cochlea. Large neurons are more diffuse and run through the inner spiral bundle (Cuiman, 2010). These neurons

synapse over 80-95% of the length of the cochlea. Delay and chopper neurons are present in the LOC, which can be attributed to some of its characteristics (Cuiman, 2010).

The MOCB fibers on the other hand, originate from the periolivary portion of the medial superior olive (Cuiman, 2010; Hill et al., 1997). Medial fibers are thicker than LOC fibers. Most of these fibers run contralateral to the peripheral regions of the ventral cochlear nucleus (Cuiman, 2010). MOC fibers are myelinated throughout their course until they exit the modiolus through the habula perforata. After exiting, they continue to run in the spiral bundle and the tunnel of Corti (Cuiman, 2010). There the MOC fibers synapse at the base of the outer hair cells of the cochlea, rather than an afferent neuron like LOC fibers (Cuiman, 2010; Hill et al., 1997). While the LOC is the largest component of the auditory efferent system in mammals, particularly high frequency hearing animals, it is relatively small in humans. The size of the MOC component, on the other hand, increase with low frequency hearing capacity in mammals (Cuiman, 2010).

Within the cochlea, lateral efferents are distributed equally across the ipsilateral cochlea, whereas medial efferents are denser at the mid and basal regions (Cuiman, 2010). Moreover, efferent fibers are largest at the basal end of the cochlea. Most efferent fibers synapse with the first row of outer hair cells, however, at more basal regions of the cochlea, efferent fibers begin to synapse with other rows (Larsen & Liberman, 2009).

### **Physiology of the Efferent Auditory Pathway**

The OCB plays an important role in the auditory system function, though the nature of its role has been the subject of much debate (Elgueda, Delano, & Robles, 2011). It is a gain control system which allows it to protect the cochlea from excessive noise

exposure by reducing basilar membrane motion (Lieberman, et al., 2014). It has also been proposed that the efferent system plays a role in attention by modulating cochlear sensitivity and auditory discrimination by “unmasking” the signal from surrounding background noise (Dhar & Hall, 2012; Elgueda et al., 2011). Moreover, it has been suggested that the OCB is essential in localization abilities. Specifically, medial olivocochlear nucleus allows for the decoding of interaural time and phase differences (Cuiman, 2010). The OCB is activated by presenting noise to either ipsilateral test ear or the contralateral non-test ear. In animals, the OCB is often activated via electrical stimulation in the 4<sup>th</sup> ventricle.

Several years prior, it was proposed that OCB activation affected the outer hair cells of the cochlea. In a study conducted by Siegel and Kim (1981) the crossed OCB was activated using electrodes in the 4<sup>th</sup> ventricle in adult chinchillas. Compound action potential thresholds and distortion product otoacoustic emissions (DPOAEs) under multiple stimulus parameters were recorded. Tensor tympani and stapedial muscles were severed to prevent interference of the acoustic reflex in the recorded response. Siegel and Kim (1981) performed perfusions in the scala tympani using artificial perilymph and the procedure was repeated; the crossed OCB was activated, and CAP thresholds and DPOAEs were measured. The effects of the crossed OCB activation were negated when the scala tympani was perfused with artificial perilymph. Artificial perilymph contained curare which blocked the acetylcholine receptors in the post synaptic membrane of the outer hair cells. This suggests that the crossed OCB activation effects are post synaptically mediated by the outer hair cells (Siegel & Kim, 1981).

It has been verified that OCB activation affects the activity of the cochlea; specifically, MOCB activation reduces cochlear sensitivity by attenuating the action of the outer hair cells (Elgueda et al., 2011). MOCB fibers directly innervate the outer hair cells. When activated, it changes the impedance and the membrane potential of the outer hair cells, thereby reducing outer hair cell motility and subsequent basilar membrane motion (Elgueda et al., 2011). Additionally, the MOCB plays a role in the tuning of the auditory nerve by modulation of the outer hair cells (Zheng, McFadden, Henderson, Ding & Burkard, 2000).

A study conducted by Liberman, Liberman & Maison in 2014 examined the role of the LOCB in protecting the cochlea against the effects of noise exposure in aging mammals. Young mice were divided into three groups: a control group, a group in which the crossed OCB was severed and a group in which the LOCB was destroyed. Hearing sensitivity in mice was then assessed several times over the course of 45 weeks using auditory brainstem response and DPOAEs. LOCB function was also assessed. The LOCB was activated with electrical shocks applied to the 4<sup>th</sup> ventricle and effects on DPOAEs were monitored. Then, cochleae were removed and analyzed histologically to evaluate the extent of the lesion and to evaluate the integrity of the neural connections. Researchers found that lesioned mice were more susceptible to age related reduction in cochlear neural responses, which suggests that the LOCB works to prevent age related, noise induced hearing loss.

### **The Olivocochlear Bundle and Otoacoustic Emissions**

OAEs were first described by Kemp in 1978. When a suprathreshold auditory stimulus is presented in ears with normal middle ear status and normal hair cell function,

the cochlea produces a measurable signal. Kemp attributed this to the nonlinearity mechanisms and transduction processes of the cochlea. However, new mechanisms for OAE generation have come to light in recent years. A study conducted by Shera and Guinan (1999) revealed that there are two main mechanisms in play in the generation of OAEs: nonlinear distortion and reflection. Nonlinear distortion, or wave fixed OAEs, are the result of the stimulus itself and are attributed to the action of the outer hair cells in response to sound. Reflection, or place fixed OAEs, are the product of the stimuli reflecting from protuberances along the basilar membrane (Shera and Guinan, 1999).

OAEs can also be classified by stimulus. There are two main types of stimulus based OAEs, spontaneous (SOAEs) and evoked (EOAEs). Spontaneous OAEs are produced without external stimulation. Evoked OAEs, on the other hand, are produced in response to stimuli and include transient evoked OAEs (TEOAEs) and distortion product OAEs (DPOAEs) (Keefe, Feeney, Hunter, Fitzpatrick, 2016). TEOAEs are produced in response to short duration clicks, which reflect off the area of the cochlea, create distortions and produce a measurable response (Keefe, et al., 2016; Shera & Guinan, 1998). DPOAEs occur when two tones, F1 and F2, are presented to the test ear simultaneously to stimulate the cochlea. The interaction of the two tones with the basilar membrane causes the cochlea to produce a tone that is arithmetically related to the F1 and F2 frequencies that can be measured by a probe microphone (Shera & Guinan, 1998).

Measurement of the efferent system can be performed indirectly by observing its effect on OAEs (Mountain, 1980). This is the primary method of examining the effects of OCB mediated cochlear suppression in humans and is considered the gold standard. This was first observed by Mountain (1980) who found that the activation of the OCB caused

DPOAE magnitude, specifically  $2f_1-f_2$ , to decrease. This led Mountain (1980) to postulate that the OCB acted upon some mechanism within the cochlea. Siegel and Kim (1981) confirmed these results and found that the activation of the contralateral OCB also affected the magnitude of DPOAEs in chinchillas when the distortion product was  $2f_1-f_2$ . However, Siegel and Kim also found that the  $2f_1-f_2$  response either decreased or increased depending on the stimulus frequency, which suggests that the mechanisms of the OCB are more complex than Mountain's study originally suggested.

Examination of the effects of OCB activation in humans is traditionally examined by monitoring its effects on OAEs. OAEs are quick and non-invasive and offer a convenient method by which to examine the effects of the MOCB (Zhao, Dewey, Boothalingham, Dhar, 2015). However, this method is problematic. In a review of the literature, Guinan (2014) notes that changes in the cochlear neural response is the most important change mediated by the activation of the MOCB. However, these changes are not necessarily apparent when MOCB effects are monitored with OAEs (Guinan, 2014). Additionally, MOCB activation tends to produce only small changes in the already small OAE response (Guinan, 2014). Therefore, it is difficult to find statistical significance in the effects of activation. However, research has shown that OCB activation has a far greater effect on the CM response. In a study conducted by Puria, Guinan and Liberman (1995), MOCB effects on DPOAEs and compound action potentials (CAPs) were compared in cats. Researchers found that the suppression effects were greater in CAPs, which suggests that it is advantageous to use evoked potentials to obtain better, more detailed information about the effects of the MOCB.

## **The Medial Olivocochlear Bundle and Cochlear Microphonics**

The CM is an evoked potential that is recorded in response to a stimulus. Specifically, the CM indirectly reflects the alternating current of the transduction processes of the OHCs and directly reflects the oscillation of the OHCs in response to a stimulus (Santarelli, et al., 2006; Withnell, 2001). The CM is a preneural response. Unlike most auditory evoked potentials, it is generated at the level of the OHCs rather than the auditory neural pathway (Santarelli, et. al., 2006). The CM can be recorded extratympanically at the external auditory canal, or at the tympanic membrane, or transtympanically at the round window (Santarelli, et al., 2006). The CM can be generated using clicks or tone bursts. Given that the CM is a measure of the OHC response, it is very sensitive to OHC dysfunction. The CM is difficult to record in the presence of cochlear hearing loss (Santarelli, et al., 2006).

Electrocochleography (ECoChG) is used to record the summing potential and the compound action potential of the cochlea. The summing potential reflects the direct current of the basilar membrane, specifically reflecting the nonlinear transduction processes of the IHCs (Schoonhoven, 2006). Like the CM, it is a presynaptic response. The compound action potential is a post synaptic response and reflects the synchronous firing of the auditory nerve (Schoonhoven, 2006). The compound action potential is also used to indirectly examine the effects of the MOCB. Like the CM, the summing potential and the compound action potential can be elicited by clicks or tone bursts. They can also be recorded extratympanically or transtympanically.

It is well known that activation of the OCB in animals inhibits the action of the auditory nerve and increases the magnitude of the CM (Elgueda et al., 2011; Fex, 1959;

Siegel & Kim, 1981). However, to the best of our knowledge, this mechanism has only been studied in humans until recently. Therefore, little is known regarding the effects of MOCB activation on neural and preneural responses in humans.

Fex (1959) was among the first to describe the effects of OCB activation on the CM. CMs were recorded via an electrode on the round window in 11 cats under anesthesia. Electrodes were placed in the 4<sup>th</sup> ventricle to activate the OCB. Stimuli was presented to the cats via speakers. Fex (1959) found that the magnitude of the CM increased and the magnitude of the CAP decreased with electrical stimulation of the OCB in all cases. To determine if the effect resulted from the auditory reflex, the stapedial and tensor tympani muscles were severed in one animal, but the modifications on the CM and CAP remained the same. The effect also increased with increasing electrical stimulation to the OCB (Fex, 1959).

MOCB research tends to focus on MOCB effects rather than the method of activation. However, the literature suggests that different methods of stimulation will cause different effects. More importantly, the MOCB must be activated to a certain degree before effects can be seen (Maison et al., 1999). A study conducted by Maison et al., (1999) sought to examine the relationship between the physical characteristics of the MOCB activating stimulus and the effect on the cochlea. EOAEs were recorded in 155 normal hearing human subjects with and without application of contralateral noise. Subjects were divided into groups, each participating in one of four experiments. The first experiment compared contralateral EOAE suppression effects using a tone, wideband noise, and narrowband noise as the suppression stimulus. The narrowband noise used in this experiment was centered at 1 kHz, with a bandwidth of  $\pm 1/6$  octave



and a slope of 24 dB/octave. The second group examined EOAE suppression as a function of contralateral noise bandwidth. Several types of noise were used for this group. Contralateral noise was centered at 1 or 2 kHz and had a bandwidth of  $\pm 1/16 - 1$  octave. Contralateral noise centered at 1 kHz was also presented separately with a smaller bandwidth of 0.025 – 0.4 kHz. In the third group, the effect of increasing of contralateral noise bandwidth and the effect of sub-bands were examined. Contralateral noise was centered at 1 or 2 kHz with a bandwidth of  $\pm, +$  or  $- 1/16 - 1$  octave. In the final group, a spectral analysis of the EOAE amplitude effects was performed. Narrowband noise was centered at 1 kHz with a bandwidth of  $\pm 1/16 - 1$  octave.

Ultimately, it was found that efferent suppression of EOAEs was greatest as a function of widening bandwidth, until approximately 2 octaves. It can be assumed that a greater MOCB activation with wider bandwidth results from a summation of inputs in the afferent auditory pathway. Maison et al. (1999) noted that the suppression effect increased with increasing bandwidth regardless of the consistency of the energy level across the spectrum. Additionally, researchers found that bandwidth on the higher end of the spectrum had a greater effect on suppression.

To the best of our knowledge, more is known about MOCB effects on the CM response in the animal model. Many of these studies suggest that MOCB activation will influence the electrical response of the OHCs. In a study conducted by Zheng et al. (2000), 6 chinchillas were chronically de-efferented on one side via sectioning of the OCB and the inferior vestibular nerve. The other ear was used as a control. Electrodes were implanted on the round window and the IC of the test ear. Evoked potentials were elicited using tone bursts at 0.5-16 kHz via the sound field. Stimulus intensity started

below threshold and was increased in 5 dB steps until it reached 80 dB SPL. 100 sweeps were performed. DPOAEs were measured; the f1 and f2 ratio was held constant at 1.2, and L1 was equal to L2. Intensity was increased in 5 dB steps from 0-80 dB SPL. CMs were measured using continuous tones at octave intervals through 1-8 kHz. Tones were presented at an intensity level of 10 dB SPL and increased to 80 dB SPL in 5 dB steps. After the experiments were completed, the chinchillas were euthanized and cochleae were removed and examined via light microscopy and acetylcholinesterase (AChE) staining to determine whether de-efferentation was successful.

Evoked potential thresholds appeared to be higher for de-efferented ears; the difference was significant for tone bursts at 1 kHz, but not at other frequencies. DPOAE testing with stimulus levels below 50 dB SPL did not reveal any significant differences between de-efferented ears and ears with an intact OCB. However, DPOAE amplitudes were enhanced in de-efferented ears with stimulus frequencies between 1-2 kHz at higher intensity levels. Finally, CM testing revealed depressed amplitudes for de-efferented ears for most stimulus frequencies. For low frequencies presented at a low intensity level, CM magnitude was similar between efferented and de-efferented ears. However, as stimulus level increased, CM magnitude decreased in de-efferented ears. CM amplitude was consistently depressed for high frequency stimuli in de-efferented ears.

These results contradict previous studies concerning the effects of the OCB on evoked potentials. However, this study is unique in that the chinchilla were de-efferented and evoked potentials were obtained when the animals were awake, thereby eliminating the influence of sedatives. Additionally, Zheng et al. (2000) noted that CMs were also obtained via the round window. Results obtained in this study suggest that the OCB

exhibits tonic influence over OHC electrical properties (Zheng et al., 2000). Because of this tonic influence, Zheng et al., suggest that MOCB activation will enhance the CM response in chinchillas. Finally, this study indicates that MOCB activation will affect the CM response for CM elicited with 1-8 kHz stimuli and that MOCB activation will have a different frequency effect for CMs than for DPOAEs.

The MOCB affects the electromechanical properties of the cochlea in several ways (Cuiman, 2010). The MOCB may release neurotransmitters that affect the OHCs. It has also been argued that the MOCB exhibits a tonic influence on the basilar membrane. The MOCB modifies the mechanical characteristics of the basilar membrane and OHCs via acetylcholine (Cuiman, 2010). These mechanisms directly affect the CM response (Zheng et al., 2000). When acetylcholine is administered and the MOCB is stimulated, calcium-dependent potassium channels are activated, which ultimately increase the magnitude of the CM response (Elgoyhen, Johnson, Boulter, Vetter, Heinemann, 1994; Zheng et al., 2000).

Effects of MOCB frequency specificity on the CM response is largely unknown. However, several studies have examined MOCB frequency specificity via OAEs. While it appears that the MOCB itself is frequency specific, suppression effects on OAEs are not tuned. Velenovsky and Glatke (2002) examined MOCB suppression effects on TEOAEs using wideband and narrowband activating noise at varying intensity levels. Velenovsky and Glatke wanted to determine if the suppression effects of narrowband noise could match the suppression effects of wideband noise if the narrowband noise was equal in loudness or intensity to the wideband noise. In the first experiment, wideband noise and narrowband noise were presented contralaterally at 60 dB SPL and TEOAEs

were measured. In the second experiment, wideband noise and narrowband noise with equivalent loudness were presented contralaterally and TEOAEs were recorded. Wideband noise was the most effective in suppressing TEOAEs. However, narrowband noise at the same intensity level as the wideband noise did not significantly suppress the TEOAEs. The spectral spread of energy in wideband noise is less dense than the spectral energy of narrowband noise. This research indicated that the spectral spread of noise was not a significant factor in MOCB activation. Velenovsky and Glatke (2002) postulated that wideband noise was a more effective suppressor because it affected a larger portion of the basilar membrane relative to narrowband noise. When the narrowband noise intensity was increased so it was perceived to be as loud as the narrowband noise, suppression effects increased, but were still smaller than the wideband suppression effects. Although there was an increase in spectral energy, the limited bandwidth of the narrowband stimulus caused a smaller effect on the basilar membrane. This indicates that neither intensity nor loudness influence the MOCB effects on TEOAEs; rather it is the bandwidth of the suppression stimulus that causes the suppression effects.

### **Frequency Specificity of the Medial Olivocochlear Bundle**

DPOAEs have also been used to examine the frequency specificity of the MOCB. In contrast to the results obtained by Velenovsky and Glatke in 2002, researchers have found that the MOCB can exhibit some frequency specificity. In a study conducted by Chéry-Croze, Moulin, and Collet (1993) suppression effects of narrowband noise centered at various frequencies in 39 subjects via DPOAEs were evaluated. DPOAEs with  $f_2$  frequencies of 1, 2, 3 or 5 kHz were recorded in subjects in the presence of

contralateral narrowband noise with center frequencies between 0.25-8 kHz. The center frequency of the narrowband noise was varied randomly between subjects and the degree of suppression was recorded. Researchers found that DPOAEs with a  $f_2$  of 1 kHz exhibited suppression when contralateral noise centering at or near 1 kHz was presented. Researchers also found that DPOAEs with a  $f_2$  of 2 kHz was significantly suppressed when contralateral noise centered at or around 2 kHz. However, it was also found that narrowband center frequencies below 2 kHz could also significantly suppress DPOAEs with a  $f_2$  of 2 kHz. This could be attributed to the interaction of distortion products along the basilar membrane. Researchers attribute these suppression effects to a frequency specificity of the MOCB, stating that MOCB tuning is like the tuning of the afferent auditory pathway. They reported that fibers of the MOCB are more sensitively tuned to the frequencies corresponding to the tuning of the OHCs to which they synapse. Therefore, it can be inferred that narrowband noise will most effectively suppress OAEs at frequencies corresponding to the center frequency of the narrowband noise (Chéry-Croze, Moulin & Collet, 1993).

## OBJECTIVES

The examination of the MOCB is traditionally conducted via its effects on OAEs. Though this methodology is considered the gold standard, it is problematic. To avoid these issues, the effects of the MOCB can be studied using an electrophysiologic response, specifically CMs. The effects of the MOCB on CMs are well understood in animal models; their effects in humans have not been studied until recently. To the best of our knowledge, this is one of the few studies that have examined the function of the MOCB in humans using the CM response. One of the first studies using this paradigm was conducted as an AuD doctoral thesis at Missouri State University for the Communication Sciences and Disorders department in the same laboratory (Jamos, Kaf, Ferraro, Chertoff, DiSarno, & Franklin, 2012). In this study, Jamos et al. (2012), observed the effects of the MOCB on the CM response while varying several conditions, including stimulus intensity level, stimulus frequency, and ear in which noise was presented. Results from this study suggested that 0.5 kHz tone burst stimuli presented at 50 dB nHL with contralateral noise caused the greatest change in the CM response (Jamos et al., 2012). Several parameters from the current study are adapted from this study.

The proposed study seeks to investigate the effects of MOCB stimulation on CMs under changes in three conditions: MOCB activating noise, stimulus phase, and stimulus frequency. Specifically, the current study examines the effects of activating wideband noise, and narrowband noise centered around 1 kHz and 0.5 kHz, presented contralaterally. 0.5 and 1 kHz tone bursts were used to elicit CMs. Finally, stimuli were

presented using both condensation and rarefaction polarity. The present study seeks to examine the relationship between frequency and MOCB activation. The null hypothesis has several parts, which includes: noise bandwidth will not influence the degree of MOCB effect on the CM response, stimulus polarity will not influence the degree of MOCB effect on the CM response, and stimulus type will not have influence the degree of MOCB effect on the CM response.

## METHODS

### Participants

Prior approval for the procedures of the current study were obtained from the Missouri State University Institutional Review Board (IRB) (number: IRB-FY2016-122, approval date: March 12, 2016). Twenty-two female subjects, aged 18-30 years old were recruited for the current study. Male subjects were excluded, because females have been found to have a stronger efferent auditory system (Robinette & Glatke, 2007). Subjects were recruited from the Missouri State University campus. The majority of these subjects were recruited from the Department of Communication Sciences and Disorders. To be eligible for the study, participants needed to meet several criteria, including:

1. Clear ear canals and intact tympanic membrane, as determined by otoscopy.
2. Normal hearing sensitivity, with thresholds at or below 25 dB HL for pure tones between 0.25-8 kHz (Schlauch & Nelson, 2009).
3. Normal middle ear status, as confirmed by 0.226 kHz tympanometry. Tympanograms must be consistent with Jerger type A tympanograms and have admittance values between 0.3 and 1.5 mmho. Middle ear pressure must be less than or equal to  $\pm 50$  daPa (Shanks & Shohet, 2009).
4. Present CM response without stimulus artifact.
5. An acoustic reflex threshold in the contralateral ear of greater than 60 dB SPL for wideband noise and narrowband noise at 0.5 and 1 kHz.

Subjects were screened to determine if they meet these criteria before participating in the study.



## **Instrumentation**

Several materials were necessary to conduct this study. Otoscopy was performed using a handheld Welch-Allyn otoscope. Hearing thresholds were obtained using a Grason-Stadler Audiostar audiometer. The audiometer was calibrated to ANSI Standard S3.6 1996 and the sound booth in which hearing thresholds are obtained met ANSI Standard S3.1 1991. The audiometer was calibrated on July 17, 2015. Tympanograms and acoustic reflexes were obtained using a Grason-Stadler middle ear analyzer. CM potentials were measured with the Intelligent Hearing Systems (IHS) Smart-Evoked Potential (SmartEP), version 5.1. CMs were obtained in a sound booth. Two types of electrodes were used to record CMs: disposable electrodes and homemade, tympanic membrane electrodes. Tympanic membrane electrodes were made using silver wire threaded through a plastic tube and tied with a piece of cotton at one end, as described by Ferraro and Durrant in 2006. The cotton was soaked with electro-conducting gel using a 1 ml syringe and placed against the tympanic membrane. The wire at the other end of the electrode was attached to an alligator clip, which was then soldered to an electrode cable. Noise used to activate the MOCB was presented to the contralateral ear with a foam insert ER-3A earphone. Activating noise was produced by the Grason Stadler Audiostar system. Stimuli was presented to the test ear with a foam insert ER-3A.

## **Procedure**

Otoscopy was performed on each subject to ensure that ear canals were clear of any occlusive material, and that tympanic membranes appear healthy and normal. Then,

behavioral hearing thresholds at 0.25-8 kHz, tympanograms and acoustic reflexes were obtained. Finally, ECoChG was performed to ensure that a true CM response was present.

For the ECoChG recording, subjects were seated in a reclining armchair, and were instructed to relax while staying awake and to move as little as possible. CMs were measured in the right ear because research has shown that MOCB effects are greater in the right ear (Brashears, Morlet, Berlin & Hood, 2003). A horizontal montage was used. Forehead and left mastoid were gently scrubbed using NuPrep and the ground electrode was placed at Fpz and the noninverting (+) electrode was placed on the left mastoid. The inverting (-), TM electrode was soaked with electroconducting gel for several minutes to ensure good conductivity. The TM electrode was then placed inside the right ear canal, resting directly on the tympanic membrane. Participants were asked to inform the researcher when they felt the TM electrode rest against their tympanic membrane, at which point insertion was completed. Electrode impedances were monitored; impedances were at a level of 5 k $\Omega$  or below before testing began. ER 3A insert earphones were placed in left and right ear canal for the presentation of noise and ECoChG stimuli, respectively. A control recording for each participant was taken with the right insert earphone pinched, while presenting 0.5 and 1 kHz. This measure was used to ensure that the recorded CM responses were not a result of stimulus artifact.

For all conditions, stimuli were presented at an intensity level of 85 dB nHL and at a rate of 27.1/second. The amplifier was set to 100,000 and 1,000 sweeps were used. For all conditions a 0.1-3 kHz filter was used. Activating noise was presented at 50 dB HL. A trapezoidal envelope was used with a 2-10-2 rise/fall time. Four baseline recordings were taken using 0.5 and 1 kHz tone burst with condensation and rarefaction

stimuli (Table 1). These recordings did not include contralateral noise. To determine the level of change in the CM response, baseline responses were subtracted from experimental responses recorded in the presence of noise.

Table 1. Testing conditions. Table 1 describes the parameters of each of the testing conditions. These conditions were used for each subject in the study. Recording of all conditions lasted approximately one hour. Baseline and experimental conditions are included.

Type of condition	Stimulus Frequency	Stimulus Phase	Contralateral noise
Baseline	0.5 kHz tone burst	Rarefaction	None
Baseline	1 kHz tone burst	Rarefaction	None
Baseline	0.5 kHz tone burst	Condensation	None
Baseline	1 kHz tone burst	Condensation	None
Experimental	0.5 kHz tone burst	Rarefaction	Wideband noise
Experimental	0.5 kHz tone burst	Rarefaction	Narrowband noise at 0.5 kHz
Experimental	0.5 kHz tone burst	Rarefaction	Narrowband noise at 1 kHz
Experimental	0.5 kHz tone burst	Condensation	Wideband noise
Experimental	0.5 kHz tone burst	Condensation	Narrowband noise at 0.5 kHz
Experimental	0.5 kHz tone burst	Condensation	Narrowband noise at 1 kHz
Experimental	1 kHz tone burst	Rarefaction	Wideband noise
Experimental	1 kHz tone burst	Rarefaction	Narrowband noise at 0.5 kHz
Experimental	1 kHz tone burst	Rarefaction	Narrowband noise at 1 kHz
Experimental	1 kHz tone burst	Condensation	Wideband noise
Experimental	1 kHz tone burst	Condensation	Narrowband noise at 0.5 kHz
Experimental	1 kHz tone burst	Condensation	Narrowband noise at 1 kHz

The order of presented conditions were randomized for each subject. Subjects were randomly divided into two groups; group A was tested using 0.5 kHz TB stimuli first and group B was tested using 1 kHz TB stimuli first. Additional conditions (e.g. type

of contralateral noise, and phase of stimuli) were then randomized within groups. After testing was completed with a specific tone burst frequency, the subject was tested with the remaining tone burst frequency. For example, if a subject was put into group A, all conditions were recorded using 0.5 kHz tone burst stimuli, then, the same procedures were repeated using 1 kHz stimuli. Contralateral noise was presented at a level of 50 dB HL. There were twelve total conditions not including baseline conditions (Table 1).

To ensure repeatability, each recording was taken twice. Therefore, there were a minimum of thirty-two recordings, including eight baseline recordings and twenty-four experimental recordings. Testing lasted approximately two hours. Twenty-two subjects were tested, however, only eighteen subjects produced usable results. Subject data was excluded from the study if CMs could not be recorded, or if repeatable waveforms could not be produced.

### **Measurement and Data Analysis**

After data was collected, the amplitude of each CM recording was obtained. The three largest, consecutive waves from each baseline recording were marked at the peak and trough and amplitude was recorded and averaged. Then, using the latency range established by the marked baseline waves, three waves from the experimental tracing were marked at the peak and trough and the amplitude was recorded and averaged (Fig. 1). These averages were input into an Excel spreadsheet and were used in the final data analysis. Experimental waveforms were compared only to baseline waveforms from the same subject, as norms for CMs have not been established (Santarelli, et al., 2006). Each experimental waveform was compared only to the baseline tracing matching its eliciting

tone burst and polarity. A difference score between the baseline and experimental conditions was calculated by subtracting the experimental amplitude average from the baseline average for the corresponding condition. For some experimental conditions, amplitude either increased or decreased from the baseline amplitude; a negative difference score indicated that suppression of the response occurred and a positive score indicated that enhancement of the response occurred. However, only the magnitude of change was used in the descriptive statistics of this study to meet the conditions of the null hypothesis. To determine the magnitude of change, the difference score was converted to its absolute value.

Statistical analysis was carried out with SPSS. The absolute values representing the magnitude of change in the waveform from the baseline to the experimental condition were compared using a repeated measures ANOVA and post hoc analysis for the following variables: stimulus frequency 2(0.5 kHz vs. 1 kHz) x 3 MOCB activating noise (BBN vs. NBN at 0.5 kHz vs. NBN at 1 kHz) x 2 stimulus polarity (condensation vs. rarefaction).

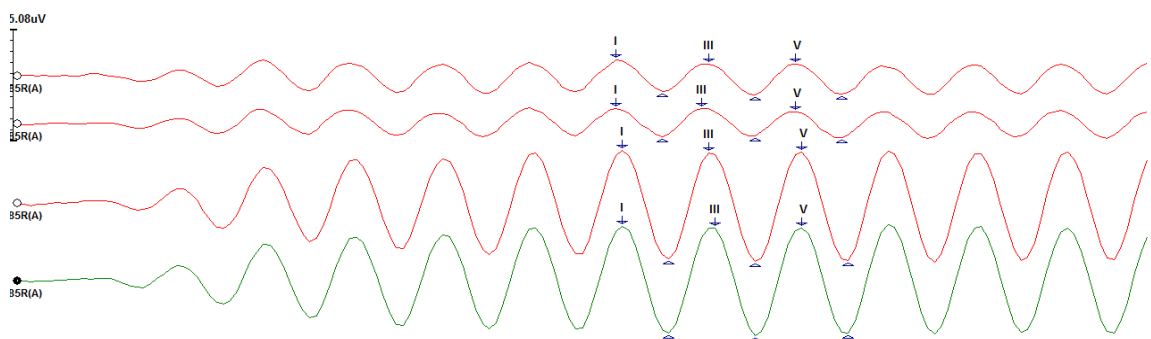


Figure 1. Waveform Markings. This figure shows the method by which waveforms were marked. The top two traces are baseline waveforms. The bottom two traces are experimental waveforms.

## RESULTS

### Suppression and Enhancement Trends in One Participant

Initial analysis of the data showed that the amplitude for all CM waveforms changed in the experimental conditions, either via suppression or enhancement. Fig. 2 & 3 below show that, for one participant, enhancement and suppression of the CM response was relatively consistent, regardless of the polarity used for the CM eliciting stimulus.

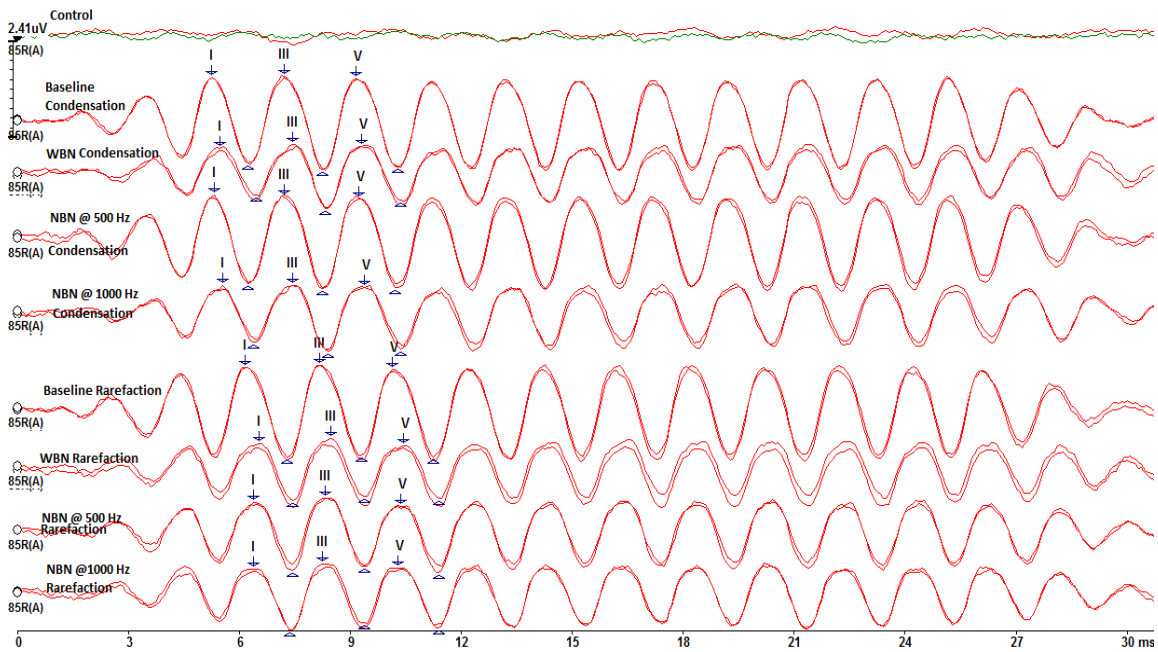


Figure 2. CM Response Suppression with 0.5 kHz tone burst in One Participant. The top four traces were elicited using condensation stimuli and the bottom four waveforms were elicited using rarefaction stimuli. The very top trace represents a control run to confirm the presence of a response, then waveforms are placed in the following order: baseline, WBN condition, NBN at 0.5 kHz condition and NBN at 1 kHz condition. In general, 0.5 kHz waveforms were suppressed with the application of noise.

For the participant in Figure 2, application of noise had a suppression effect for all CM waveforms eliciting using 0.5 kHz tone burst stimuli. Conversely, for CM

waveforms elicited using 1 kHz tone burst stimuli, the noise condition caused an enhancement effect (Fig. 3). The magnitude of change was not as great for waves elicited using rarefaction stimuli regardless of tone burst frequency. However, due to the variability across participants, these specific conclusions cannot be applied to all participants. Instead, MOCB activation noise caused some change in the magnitude of the response for all participants.

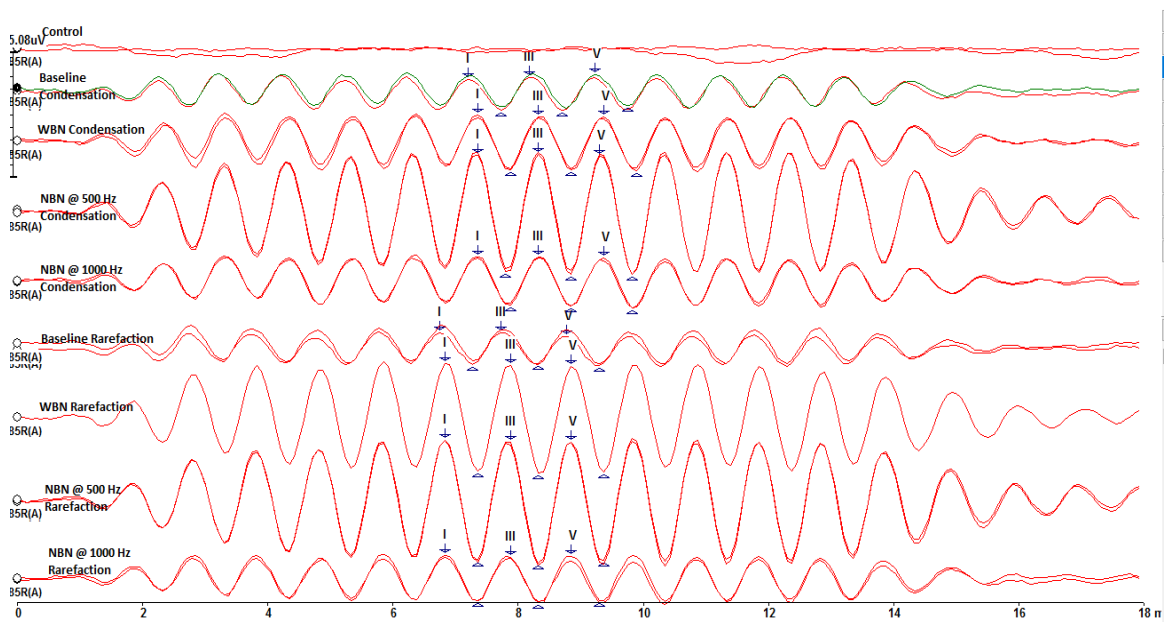


Figure 3. CM Response Suppression with 1 kHz tone burst in One Participant. The top four waveforms were elicited using condensation stimuli and the bottom four waveforms were elicited using rarefaction stimuli. The very top trace represents a control run to confirm the presence of a response, then waveforms are placed in the following order: baseline, WBN condition, NBN at 0.5 kHz condition and NBN at 1 kHz condition. It indicates that waveforms tended to be enhanced with the application of noise.

### Suppression vs. Enhancement

CM data showed suppression and/or enhancement across participants. Table 2 & 3 below summarize general trends in suppression and enhancement for all experimental

conditions. For most participants, application of wideband noise and narrowband noise centered at 0.5 kHz had a suppression effect, regardless of the polarity or stimulus type. Application of narrowband noise centered at 1 kHz did not show a clear suppression or enhancement trend.

Stimulus polarity did not influence the direction of change in the waveform amplitude. Condensation and rarefaction waves under the same stimulus frequency and activating noise tended to be either suppressed or enhanced at the same rate. It is interesting to note that for 0.5 kHz tone burst waveforms, there was a greater change in waveform amplitude for waves that were enhanced than for waveforms that were suppressed (Table 2). For 1 kHz tone burst waveforms, the opposite effect occurred (Table 3). There was a greater change in waves that were suppressed than for waveforms that were enhanced in all experimental conditions.

**Suppression and Enhancement Trends for Wideband Noise.** Wideband noise caused suppression effects for most participants (Table 2). However, it should be noted that the magnitude of change was greater for those waveforms that were enhanced. For 0.5 kHz tone burst CM waveforms presented with condensation stimuli, wideband noise caused suppression in 67% of participants and enhancement in 33% of participants (Table 2). The same effect was seen when rarefaction stimuli was used. For 1 kHz tone burst CM waveforms presented with condensation stimuli, wideband noise caused suppression in 67% of participants and enhancement in 33% of participants (Table 3). When CMs were elicited with rarefaction stimuli, wideband noise caused suppression in 56% of participants and enhancement in 44% of participants.



Table 2. Suppression and Enhancement Trends for 0.5 kHz CMs. The mean and standard deviation of change in amplitude for each condition are shown. Additionally, the percentage subjects who demonstrated either suppression or enhancement are indicated.

Condition	Suppression			Enhancement		
	N (%)	Change in Amplitude ( $\mu\text{V}$ )	$\Sigma$	N (%)	Change in Amplitude ( $\mu\text{V}$ )	$\sigma$
WBN Condensation	12 (67%)	-0.088	0.064	6 (33%)	0.187	0.298
WBN Rarefaction	12 (67%)	-0.107	0.071	6 (33%)	0.183	0.292
NBN @ 0.5 kHz Condensation	9 (50%)	-0.035	0.26	9 (50%)	0.055	0.054
NBN @ 0.5 kHz Rarefaction	12 (67%)	-0.084	0.055	6 (33%)	0.171	0.213
NBN @ 1 kHz Condensation	9 (50%)	-0.058	0.031	9 (50%)	0.115	0.220
NBN @ 1 kHz Rarefaction	8 (44%)	-0.103	0.072	10 (56%)	0.120	0.225

### Suppression and Enhancement Trends for Narrowband Noise at 0.5 kHz.

When narrowband noise centered at 0.5 kHz was used to activate the MOCB, suppression effects were seen for the majority of participants. For CMs elicited using 0.5 kHz tone bursts with condensation stimuli, narrowband noise centered at 0.5 kHz caused suppression in 50% of participants and enhancement in 50% of participants. For rarefaction waves under the same conditions, 67% of waves were suppressed and 33% of

waves were enhanced (Table 2). When 1 kHz tone bursts with condensation polarity were used to elicit CMs, suppression occurred in 72% of participants and enhancement occurred in 28% of participants. For rarefaction stimuli, suppression occurred for 67% of participants and enhancement occurred in 33% of participants (Table 3).

Table 3. Suppression and Enhancement Trends for 1 kHz CMs. The mean and standard deviation of change in amplitude for each condition are shown.

Condition	Suppression			Enhancement		
	N (%)	Change in Amplitude ( $\mu\text{V}$ )	$\sigma$	N (%)	Change in Amplitude ( $\mu\text{V}$ )	$\sigma$
WBN Condensation	12 (67%)	-0.153	0.208	6 (33%)	0.071	0.064
WBN Rarefaction	10 (56%)	-0.292	0.625	8 (44%)	0.058	0.081
NBN @ 0.5 kHz Condensation	13 (72%)	-0.331	0.890	5 (28%)	0.077	0.052
NBN @ 0.5 kHz Rarefaction	12 (67%)	-0.400	0.966	6 (33%)	0.097	0.044
NBN@1 kHz Condensation	11 (61%)	-0.153	0.219	7 (39%)	0.068	0.058
NBN@1000 kHz Rarefaction	8 (44%)	-0.201	0.251	10 (56%)	0.081	0.057

### Suppression and Enhancement Trends for Narrowband Noise at 1 kHz.

Trends for suppression and enhancement were less clear when the MOCB was activated

with narrowband noise centered at 1 kHz. When CMs were elicited with 0.5 kHz tone bursts with condensation stimuli, suppression effects were seen in 50% of participants and enhancement effects were seen in 50% of participants. When rarefaction stimuli was used, suppression effects occurred in 44% of participants and enhancement effects occurred in 56% of participants. When CMs were elicited with 1 kHz tone bursts with condensation stimuli, suppression effects were seen with 61% of participants and enhancement effects were seen with 39% of participants. With rarefaction stimuli, suppression effects occurred in 44% of participants and enhancement effects occurred in 56% of participants. suppression in 67% of participants and enhancement in 33% of participants.

### **Change in Cochlear Microphonic Response Amplitude**

For data analysis, CM amplitude was collected for each waveform. Three consecutive, robust waveforms were chosen from the baseline tracings and marked at the peak and trough. Then, experimental waveforms were marked at the same latency range as the marked baseline waves. Amplitudes of the marked waves were recorded and averaged for each waveform. As two tracings were taken for each condition, this provided six data points for each condition. Amplitudes for each experimental condition were subtracted from their corresponding baseline condition which were matched for tone burst stimulus frequency and polarity. Then, differences were converted to their absolute value to determine the magnitude of change and to remove any influence of direction of change; i.e. if the waveform was suppressed or enhanced in the experimental condition.

Absolute amplitude was used to compare the experimental conditions to the baseline recording. A paired sample *t*-test was used to evaluate the amplitude data (Table 4). The *t*-test value did not show any significant comparisons between any of the experimental conditions to the baseline.

Table 4. Paired sample *t*-test conducted for all conditions. The *p*-value and Cohen's *d* are included.

Condition			<i>t</i> (17)	<i>p</i> -value	Cohen's <i>d</i>
<b>0.5 kHz</b>	Rarefaction	WB	-0.19	0.85	-0.02
		NB 500	0.03	0.98	0.00
		NB 1000	0.41	0.69	0.04
	Condensation	WB	0.08	0.94	0.01
		NB 500	0.65	0.52	0.02
		NB 1000	0.66	0.52	0.06
<b>1 kHz</b>	Rarefaction	WB	-1.13	0.28	-0.21
		NB 500	-1.16	0.26	-0.27
		NB 1000	-1.11	0.28	-0.11
	Condensation	WB	-1.59	0.13	-0.15
		NB 500	-1.15	0.26	-0.27
		NB 1000	-1.34	0.20	-0.13

Values were entered into SPSS and a 2 x 2 x 3 repeated measures analysis of variance (ANOVA) was conducted to determine the effects of noise and stimulus polarity on CM amplitude to 0.5 kHz and 1 kHz tone burst stimuli. The ANOVA results revealed no significant main effect of stimulus type [ $F(1, 17) = 1.416, p = 0.25, \eta^2 = 0.077$ ] no

significant main effect of stimulus polarity [ $F(1, 17) = 2.794, p = 0.113, \eta^2 = 0.141$ ] and no significant main effect of noise type [ $F(2, 34) = 0.883, p = 0.423, \eta^2 = 0.049$ ]. Also, the ANOVA results did not show significant two-way interaction between noise type and stimulus type [ $F(2, 34) = 1.023, p = 0.370, \eta^2 = 0.057$ ], stimulus type and stimulus polarity [ $F(1, 17) = 0.006, p = 0.938, \eta^2 = 0$ ], stimulus polarity and noise type [ $F(2, 34) = 0.728, p = 0.490, \eta^2 = 0.041$ ], nor three-way interaction between noise type, stimulus type and stimulus polarity [ $F(2, 34) = 0.604, p = 0.553, \eta^2 = 0.034$ ].

Overall, the greatest change in amplitude occurred with narrowband noise centered at 0.5 kHz as shown in Figures 4 and 5. When data was divided by stimulus frequency, wideband noise caused the greatest change for 0.5 kHz CM waves, while NBN at 0.5 kHz caused the greatest change for 1 kHz CM waves (Figure 4). When CM waves are grouped by polarity, NBN at 0.5 kHz again showed the greatest change in amplitude for both condensation and rarefaction (Figure 5). When CMs were grouped by stimulus type and polarity, CMs elicited with 1 kHz tone burst and rarefaction polarity showed the greatest change in amplitude with MOCB activation (Figure 6). Ultimately, these figures show that NBN at 0.5 kHz was caused the greatest magnitude of change for most conditions, regardless of which elements were compared. Additionally, CMs elicited using rarefaction polarity and 1 kHz tone burst also caused the greatest magnitude of change for most conditions. These trends were consistent throughout the data. However, as stated previously, none of these changes were statistically significant.

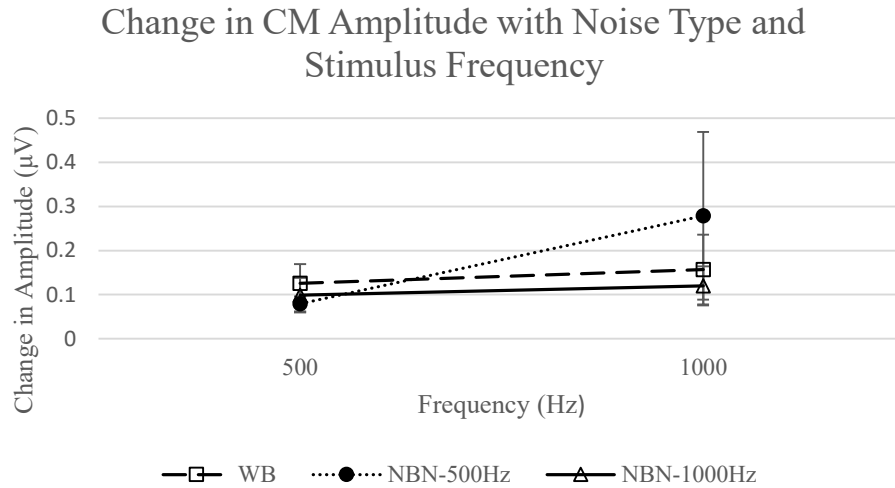


Figure 4. The magnitude of change of the CM amplitude with MOCB activating noise for 500 and 1 kHz tone burst waveforms. For 0.5 kHz tone burst CM waveforms, WBN (dashed line) caused the greatest change in amplitude. For 1 kHz tone burst CM waveforms, NBN centered at 0.5 kHz (dotted line) caused the greatest change.

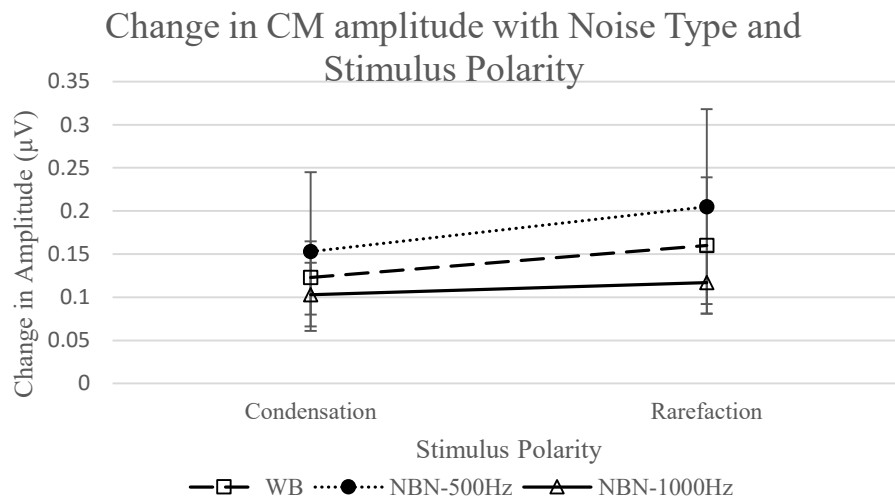


Figure 5. The magnitude of change for CMs elicited with condensation stimuli and CMs elicited with rarefaction stimuli. This graph shows that NBN at 0.5 kHz (dotted line) caused the greatest change in amplitude for both condensation and rarefaction waveform.

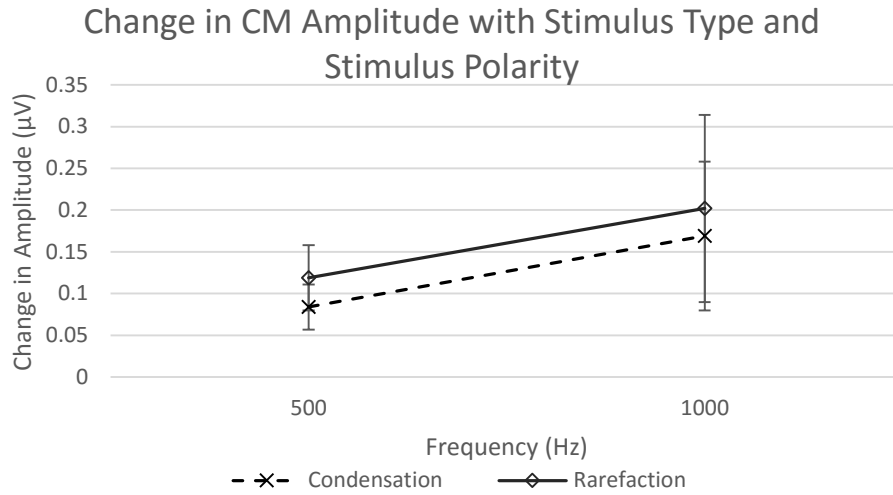


Figure 6. A comparison of the magnitude of change in CM amplitude for stimulus type and stimulus polarity. This figure demonstrates that the magnitude of change was greatest for CMs elicited with 1 kHz tone burst with a rarefaction polarity (solid line).

## DISCUSSION

The OCB is an important part of the cochlea and of cochlear function. The OCB has been implicated in several cochlear processes including localization and protection from acoustic trauma (Cuiman, 2010; Liberman, et al., 2014). Understanding the function of the OCB has important implications for the hearing sciences, including the expansion of clinical diagnostic procedures and a better understanding of cochlear pathophysiology. The OCB is the distal arm of the auditory efferent pathway. The auditory efferent pathway originates in the brain and terminates at the cochlea. The OCB originates from the superior olivary complex and can be divided into the lateral (LOCB) and medial (MOCB) (Liberman and Brown, 1986). More is known about the MOCB than the LOCB; for the purposes of the current study, only the MOCB was examined. The MOCB acts primarily on OHCs. Specifically, the MOCB increases the stiffness of the OHCs and reduces their electromotility (Cuiman, 2010; Guinan, 2006). For many years, MOCB function was measured via change in the OAE response, which is a response generated by the OHCs. This is considered the gold standard methodology for MOCB investigation. However, the current study investigates the usage of CMs for measuring the frequency specificity of the MOCB. Few studies have measured MOCB effects on human cochlea via CMs; to the best of our knowledge, this is the first study to investigate the effects of stimulus bandwidth on the human efferent system using the CM response.

For the current study, CMs were generated using 0.5 kHz and 1 kHz tone bursts using both condensation and rarefaction polarity. The MOCB was activated using either wideband noise (WB), narrowband noise centered at 0.5 kHz (NBN) and NBN centered at 1 kHz. Data analysis revealed that neither stimulus polarity nor noise type caused a



significant effect on CM amplitude. Therefore, we are unable to reject the null hypothesis. While the primary goal of this study was to investigate the effects of bandwidth on the MOCB response, this study also provides some important information on the utility of CMs for the investigation of MOCB effects on the lower frequencies. Data for the current study indicates that stimulus polarity and noise type did not have a significant effect on MOCB function. However, data gathered from studies that examine the MOCB via change in OAEs show that noise bandwidth does have a significant effect. This suggests that, while the MOCB response to a change in activating noise bandwidth may have been significant, CM recordings in the current protocol may not have been successful in recording that change.

### **Medial Olivocochlear Bundle Effect in Cochlear Microphonics**

It has been well established that activation of the MOCB will cause significant change in OAEs (Guinan, 2006). Interestingly, the current study did not reveal a significant change in CM amplitude with MOCB activation. To the best of our knowledge, MOCB effects on the CM response in the human model have only been examined in two studies. The first was conducted in the same laboratory as the current study. Najem, Kaf, Ferraro, DiSarno, and Mitchell (2011), compared the effects of MOCB activation on DPOAEs and CMs. CMs and DPOAEs were recorded from 16 female subjects with and without MOCB activating noise. DPOAEs were recorded using an  $f_2/f_1$  ratio of 1.22 and had an L1 of 65 dB SPL and an L2 of 50 dB SPL. CMs were recorded using clicks, 0.5 kHz and 2 kHz tone bursts, presented at 90 dB SPL. Stimuli was presented using a condensation and rarefaction polarity. The contralateral wideband

noise was presented at 60 dB SPL. Logarithmic ratios were applied to the CM and DPOAE responses to facilitate comparisons. Najem et al. (2011) found that, while MOCB activation suppressed or enhanced the DPOAE and CM responses, MOCB activation did not have a significant effect overall. This is in agreement with the current study. Najem et al. (2011) argued that using low frequency tone bursts to elicit CMs may have prevented a significant finding.

However, a study conducted by Jamos et al. (2012) in the same laboratory revealed a significant change in the CM response with MOCB activation. Jamos et al. (2012) measured change in CM amplitude with MOCB activation under three conditions. The MOCB was activated using wideband noise presented ipsilaterally and contralaterally. Activating noise was presented at 3 levels: 40 dB SPL, 50 dB SPL and 60 dB SPL. Finally, CMs were elicited using tone bursts at 0.5 and 2 kHz. CMs recorded without wideband noise were used as a baseline. Amplitude of the baseline tracings were compared to the amplitude of CMs recorded with wideband activating noise. Data analysis revealed a significant change in CM amplitude. Specifically, magnitude of change was greatest when MOCB activating noise was presented at 50 dB SPL, when activating noise was presented contralaterally and when CMs were elicited with 0.5 kHz tone bursts. Again, these results are not in agreement with the current study, nor are they in agreement with the study conducted by Najem, et al. (2011). The current study used 0.5 kHz tone bursts to elicit CMs and MOCB activating noise was presented contralaterally at 50 dB SPL, similar to the recommendation of Jamos et al. (2012). The difference between the results of the current study and the study conducted by Jamos et al. (2012) may be due to the differences in recording parameters. Specifically, Jamos et

al. (2012) elicited CMs with stimuli at 80 dB nHL. The current study elicited CMs using stimuli at 85 dB nHL, which is a much higher intensity and may have saturated the outer hair cells. These conflicting results indicates that additional research is necessary in this area.

### **CM Generation and Recording from the Apical End of the Cochlea**

Not all OHCs contribute equally to the generation of the CM response. Animal studies have demonstrated that CMs recorded at the promontory are generated primarily by the basal end of the cochlea (Dallos, 1971; Patuzzi, Yates, & Johnstone, 1989; Withnell, 2001). Patuzzi, Yates and Johnstone (1989), demonstrated that, for guinea pigs, CMs generated via low frequency stimuli (0.1-2 kHz) could be recorded even after the ablation of the apical turn of the cochlea, indicating that the measured CM recorded activity at the basal end of the cochlea. They suggest that, in some cases, ablation of the apical regions of the cochlea has the potential to enhance CMs generated with low frequency stimuli as they prevent the phase cancellation of CMs generated by the basal end (Patuzzi, et al., 1989). They developed a model of guinea pig cochlear contribution of CMs generated with 0.2 kHz stimuli that showed that less than 2% of the response was generated by regions more apical than the 8-kHz place-frequency region of the cochlea.

Moreover, the electrical potential that generates the CM decays as the signal travels toward the basal end of the cochlea (Patuzzi, et al., 1989; Withnell, 2001). Indeed, the recorded low frequency CM may only reflect passive activity from the cochlea, as the cochlear amplifier has the greatest effect on the region of the cochlea that corresponds to the characteristic frequency and the region one half octave of the characteristic frequency

(Withnell, 2001). These factors have a much greater influence on CMs generated with low frequency stimuli than those generated with high frequency stimuli. It would stand to reason that CMs recorded extratympanically, a more far-field approach, would also reflect electrical potentials at the basal, rather than the apical end of the cochlea.

The current study examined CMs generated using 0.5 kHz and 1 kHz tone bursts. In humans, 0.5 kHz and 1 kHz place frequencies are located in the more apical end of the cochlea. Animal studies have revealed that the CM reflects activity from only the first few millimeters of the cochlea (Withnell, 2001). Therefore, the measured response in the current study only reflected activity from the basal end of the cochlea, even though the basal end of the cochlea was not being stimulated directly. While change in the MOCB response might have occurred with the differences in stimulus type, and activating noise, the change in CM response did not reflect that. Moreover, it was not able to reflect that change.

### **Frequency Specific Effects of the MOCB in Relation to the Distribution of MOCB Fibers in the Contralateral Cochlea**

One objective of the current study was to examine the frequency specificity of MOCB activation for the more apical end of the cochlea. In doing so, it is important to examine the anatomical and physiological frequency characteristics of the MOCB. MOCB fibers run from the internal auditory canal to the basal end of the cochlea. Like afferent fibers, efferent fibers have characteristic frequencies and terminate at roughly the same frequency place as their afferent counterparts (Lieberman & Brown, 1986; Robertson, 1984). There are distinct differences between MOCB fibers that correspond to

the basal end of the cochlea and those that correspond to the apical end of the cochlea. Animal studies have revealed that the MOCB is sharply tuned; the tuning curve of the MOCB for high characteristic frequencies is relatively like that of afferent cochlear nerve fibers (Lilaonitkul & Guinan, 2009). The tip of efferent tuning curve is not as sharp as that of an afferent fiber (Liberman & Brown, 1987). Interestingly, the same study by Liberman and Brown (1987) showed that the efferent tuning curves for low characteristic frequencies were broader than those for efferent fibers with high characteristic frequencies. Moreover, the discharge rates for fibers with low characteristic frequencies tended to saturate at a much greater rate than fibers with high characteristic frequencies. Finally, distribution of efferent fibers is more concentrated in the basal end relative to the apical end of the cochlea (Cuiman, 2010; Lilaonitkul & Guinan, 2009).

Lilaonitkul and Guinan, (2009) explored whether MOCB effects were frequency specific in humans via change in stimulus frequency OAEs (SFOAEs). This study outlined several interesting findings, including: MOCB activation affects the entire cochlea, suppression effects occurred when suppression stimuli were two octaves below probe frequency, and the increasing MOCB effects with increasing bandwidth saturated at around four octaves. SFOAEs are generated near the place of the probe tone and areas toward the basal end of the cochlea; the suppression effects of dissimilar noise suggest that the MOCB effects are not limited to the place frequency of the suppression stimuli. Instead, these effects spread along the length of the cochlea and affect probe-tone place, which is located closer to the basal end of the cochlea.

The current study examined if the bandwidth of the MOCB activating noise had a significant effect on MOCB activation. The results of the current study showed that noise

bandwidth did not cause any significant change in MOCB activation. Lilaonitkul and Guinan (2009) found that the measured effects of MOCB activation reflected a global cochlear response. The researchers used change in SFOAEs to determine MOCB effects, which is a measure that also reflects a more global cochlear response, relative to CMs which only demonstrate activity from first few millimeters of the basal end of the cochlea. The current study, on the other hand, measured effects of MOCB activation via change in CM amplitude. The CM measurement only reflects those effects that happen at the basal end of the cochlea. Therefore, while the change in activating noise bandwidth may have caused significant changes in MOCB activation, this change may not have been adequately reflected in the CM response. Finally, Lilaonitkul and Guinan (2009) used noise with a very wide bandwidth, 6.7 octaves. The researchers reported that effects of noise bandwidth greater than 2 octaves on the MOCB effects is unknown (Lilaonitkul & Guinan, 2009).

To the best of our knowledge, Lilaonitkul and Guinan (2009) are the only researchers to a global cochlear efferent effect. Other investigations have demonstrated a far more limited MOCB effect, especially for the apical end of the cochlea. Aedo, et al. (2015) demonstrated that, for chinchillas, MOCB activating tones caused the greatest effect on the CAP amplitude when the activating tone was equal to or close to the probe tone frequency. Moreover, this study demonstrated that MOCB activation did not have a significant effect on CM amplitude. Other studies have indicated that MOCB activation is strongest at areas corresponding to speech frequencies in the cochlea or at regions of the cochlea where MOCB fibers are densest (Larsen & Liberman, 2009).

## **Use of CM for Determining MOCB Effects on the Apical Regions of the Cochlea**

The current study strives to obtain a greater understanding of the utility of the CM response for the examination of MOCB effects in the apical region of the cochlea. Data analysis from the current study revealed that MOCB activation did not have a significant effect on CMs generated with low and mid frequency tone burst stimuli. Wiederhold and Peak (1966) investigated MOCB effects in anesthetized cats. The MOCB was activated using a series of electrical shocks at the area of decussation of the crossed MOCB and CMs were recorded via a wire electrode placed near the round window. Wiederhold and Peake compared the effects of MOCB activation on CMs generated with a high frequency acoustic transient with a spectral maxima of 1 kHz and a low frequency acoustic transient with a spectral maxima of 0.4 kHz. They found that MOCB effects were far less for CMs generated using the low frequency acoustic transient. These results agree with the current study.

Probe ear frequency dependence for slow efferent response were determined by Sridhar, Liberman, Brown, and Sewell (1995). Researchers found that for CAP suppression was only significant for CAPs generated using high frequency stimuli of > 10 kHz in anesthetized guinea pigs. They also found that fast efferent response was most significant for CAPs generated using 8 kHz stimuli. MOCB activation was caused by electrical shocks, which has a different generator and effect than the noise evoked slow efferent responses (Larsen and Liberman, 2009; Sridhar, et al., 2009). Larsen and Liberman (2009) used tone pips at 4, 5.6, 8, 11.3, 16, 22.6 or 32 kHz to elicit the CAP response with MOCB activation and found that CAP suppression appeared to be relatively insensitive to probe frequency. However, when CAP suppression was divided

into “onset” and “build-up” effects, a frequency dependency was seen. Onset responses were most sensitive to 9-16 kHz probe tone, whereas build-up responses were most responsive to probe tones of 7-9 kHz and 10-14 kHz. Again, this indicates that efferent effects, both fast and slow, have the greatest effect on the basal end of the cochlea.

### **Suppression and Enhancement Effects of MOCB Activation in the CM Response**

The current study revealed that activation of the MOCB caused either a suppression or an enhancement effect in recorded CMs. In general, most waveforms were suppressed with MOCB activation. Specifically, for 0.5 kHz tone burst CM waves, WBN caused suppression effects in most participants (67% of condensation and rarefaction waves). NBN centered at 0.5 kHz for the same stimulus type caused suppression in 67% of rarefaction waves and 50% of condensation waves. NBN centered at 1 kHz for the same stimulus type caused suppression in 50% of condensation waves and 44% of rarefaction waves. Overall, suppression effects occurred in 57% of 0.5 kHz tone burst CM waveforms. For 1 kHz tone burst CM waves, WBN caused suppression in 67% of condensation waves and 56% of rarefaction waves. For NBN at 0.5 kHz, MOCB activation caused suppression in 72% of condensation waves and 67% of rarefaction waves. With NBN at 1 kHz, waveforms were suppressed in 61% of condensation waves and 44% of rarefaction waves. Overall, suppression occurred in 61% of 1 kHz tone burst CM waveforms.

The literature has also found similar suppression and enhancement effects. The data presented in the current study agree with Fex (1959) in one of the earliest experiments examining the effect of efferent stimulation on the CM response. Fex (1959)



found that electrical activation of the MOCB caused an enhancement effect and increased the amplitude of the CM response, and when electrical stimuli used to activate the MOCB was increased from 2 V to 3.2 V, a suppression effect was seen. According to Fex (1959), the level of MOCB activation had caused the change from enhancement to suppression. Fex (1959) used shock trains to activate the MOCB, which is not possible in research with human subjects. Furthermore, other studies have shown a similar trend of suppression and enhancement with MOCB activation. Santarelli et al. (2006) argue that enhancement effects on the CM may take place due to dysfunction of the efferent system, secondary to central nervous system disorder. They state that as the efferent system suppresses the auditory nerve response indirectly by suppressing the activity of the OHCs, it can be inferred that an increase in this response may be due to a malfunctioning efferent system. Indeed, in the investigation performed by Santarelli, et al. (2006), CM responses were recorded in individuals with central nervous system dysfunction and an enhancement of the response was found with efferent activation. Abdala, Mishra and Williams (2009) argues that the direction of change with MOCB activation is attributable to the phase relationship between frequencies when DPOAEs are used to measure the MOCB response. When DPOAE fine structure was considered and MOCB responses was only measured at the maxima of the DPOAE, suppression occurred 97% of the time. However, when MOCB effects were measured at every point along the DPOAE fine structure, suppression only occurred for 68% of the data points, which is generally in agreement with the current study. The maxima of the DPOAE fine structure represented the point at which the DP components were in phase with one another, exhibiting a summation effect. Abdala et al. (2009) argue that MOCB effects do not affect each

component of the response equally; the phase of the signal has a significant effect on the suppression or enhancement of the recorded response. When DP components were in phase with one another, i.e. at the maxima of the fine structure, the MOCB tended to have a suppression effect because the DP components were affected equally. At the minima of the fine structure, DP components were out of phase with one another; if the MOCB activation only affected one of those components, it would effectively limit the phase cancellation that would typically take place at the fine structure minima and falsely create an enhancement effect. Abdala et al. (2009) also suggest that concurrently reported suppression and enhancement effects on DPOAEs may be indicative of the phase relationship of the DP components rather than an effect facilitated by MOCB activation.

As the recorded CM response in the current study was produced using a single tone burst frequency, phase interactions between multiple frequencies is not a factor in the obtained results. However, the phase of the stimuli itself has been shown to influence the direction of change for the CM response with MOCB activation. Two studies prior to the current study investigated the effects of the MOCB in humans using the CM response. Najem, et al. (2011), in the same laboratory as the current study, compared the effects of the MOCB on DPOAEs and CMs. This study revealed that, for six participants, the use of a condensation stimulus polarity would cause suppression of the CM response and the use of a rarefaction stimulus polarity would cause enhancement of the CM response. These results are not in agreement with the current study, which showed that the direction of change was not affected by polarity when wideband noise was used. This may be due, in part to the differences in the stimuli used to evoke both the CM response and the MOCB effect. Najem et al. (2011) only found the above mentioned phase effects

when the CM response was elicited using 2 kHz tone burst. Moreover, these effects were only found with WBN. Data from the current study revealed that suppression and enhancement effects were reversed for a few participants when wideband noise was used. However, these trends were not consistent; for 0.5 kHz tone burst CM waves, two participants experienced suppression effects with condensation and enhancement effects with rarefaction, while two participants had the opposite effect. For 1 kHz tone burst CM waveforms, four participants experienced suppression effects with condensation and enhancement effects with rarefaction and two participants experienced the opposite. From this data, a conclusion cannot be drawn regarding variation in the direction of change with changing stimulus polarity.

Jamos et al. (2012), suggested that the phase of the signal as it reaches the TM plays a role in determining the direction of change in CM amplitude with MOCB activation. In research conducted in the same laboratory, researchers argued that when a condensation stimulus is presented to the ear canal, the OHCs hyperpolarize, and Prestin embedded in the OHCs cause the OHCs to elongate. The inhibitory neurotransmitter released by the activation of the MOCB causes the OHC to maintain its hyperpolarity, and causing an enhancement of the response with MOCB activation. When a rarefaction stimulus is used, the opposite occurs; the OHC is depolarized, Prestin contracts and the OHC is shortened. MOCB activation causes a release of inhibitory neurotransmitters that further decreases current flow through the OHC, resulting in a reduction of electromotility of the OHC and a subsequent decrease in CM amplitude. The results of the current study do not support this hypothesis, as there was no trend in suppression nor enhancement with changing stimulus.

## **Study Limitations**

The primary limitation of the current study was the use of a constant decibel level for contralateral eliciting noise, regardless of bandwidth. Wideband and narrowband noise were both presented at 50 dB HL. While the constant noise level allowed for an easier comparison between different noise types, it also allowed for inconsistent spreads of energy across the frequency spectrum. This is to say that the energy in wideband noise was more diffuse than the energy of the narrowband noise. Data analysis revealed that wideband noise did not have a significant effect on the CM response. This may have been due in part to the fact that the spectral spread of the wideband noise was not comparable to the spectral spread of the narrowband noise. The spectral spread of wideband noise is less dense than narrowband noise. This may have prevented a significant effect in the current study.

Activating the MOCB can have a different effect over time; therefore, CMs generated early in the study may have been impacted differently than those CMs generated later in the study (Larsen & Liberman, 2009). The effects of the slow efferent response would be easily detectable by changes in OAEs, an indicator of the mechanotransduction processes of the OHCs. However, the slow efferent response may not be easily detectable via CMs (Larsen & Liberman, 2009). Also, Larsen and Liberman (2009) showed that MOCB effects demonstrated a gradual increase, plateau, and then decay as activating noise persisted. Therefore, in the current study, those CMs recorded as noise was first presented would have not been subjected to as strong an MOCB response as those CMs recorded in later experimental trials. However, experimental conditions were randomized to minimize the effects of time on MOCB effects.

Furthermore, the recording of CM was conducted at a louder level (i.e. 85 dB nHL), which has the potential of saturating the OHCs. This could be a limiting factor to seeing the effect of MOCB on the OHCs, as their range of change will be limited during saturation.

### **Future Studies**

In the future, it would be advantageous to examine the effects of differing noise bandwidths on CM amplitude for higher frequency tone bursts. The current study used CMs to examine the MOCB effect on the apical end of the cochlea and found that MOCB activation did not cause a significant change. As the CM response is recorded from the basal end of the cochlea, a significant response might be found for CMs elicited with tone bursts at a higher frequency. Additionally, it would be useful to integrate MOCB effects on OAEs along with CMs to better understand if an effect was taking place with MOCB activation, particularly an OAE type that reflects a global change in the cochlea, such as SFOAEs. As MOCB effects on OAEs are better understood, the integration of OAEs in CM research on the MOCB would allow easier conclusions to be drawn from the MOCB effects on CMs. The effect on CMs and OAEs could be compared under standardized conditions and more could be understood about the effects on the differing mechanisms that generate both the CM and the OAE response.

## REFERENCES

- Abdala, C. Mishra, S. K., Williams, T. (2009). Considering distortion product optoacoustic emission fine structure in measurements of the medial olivocochlear reflex. *Acoustical Society of America* 125(3), 1584-1594.
- Aedo, C., Tapia, E., Pavez, E., Elgueda, D., Delano, P. H., Robles, L. (2015). Stronger efferent suppression of cochlear neural potentials by contralateral acoustic stimulation in awake than in anesthetized chinchilla. In Delano, P. H., & Elgoyhen, A. B. (Eds.), *Auditory Efferent System: New Insights from Cortex to Cochlea* (31-42). Frontiers in Systems Neuroscience.
- Brashears, S., Morlet, T., Berlin, C., & Hood, L. (2003). Olivocochlear Efferent Suppression in Classical Musicians. *Journal of the American Academy of Audiology* 14(6), 314-324.
- Braun, K., Böhnke, F., & Stark, T. (2012). Three-dimensional representation of the human cochlea using micro-computed tomography data: Presenting an anatomical model for further numerical calculations. *Acta Oto-Laryngologica*, 132(6), 603-613 11p. doi:10.3109/00016489.2011.653670
- Chéry-Croze, S., Moulin, A. & Collet, L. (1993). Effect of contralateral sound stimulation on the distortion product 2f1-f2 in humans: Evidence of a frequency specificity. *Hearing Research* 68, 53-58.
- Cooper, N. P. & Guinan, J. J. (2006). Efferent-mediated control of basilar membrane motion. *Journal of Physiology* 576(Pt 1) 49-54.
- Cuiman, R. R. (2010). The Efferent System or Olivocochlear Function Bundle – Fine Regulator and Protector of Hearing Perception. *International Journal of Biomedical Science* 6(4), 276-288.
- Dallos, P., He, D. Z. Z., Lin, X., Sziklai, I., Mehta, S., Evans, B. N. (1997). Acetylcholine, Outer Hair Cell Electromotility, and the Cochlear Amplifier. *Journal of Neuroscience* 17(6), 2212-2226.

- Dhar, S., & Hall, J. (2012). *Otoacoustic emissions: Principles, procedures, and protocols*. San Diego, CA: Plural Publishing.
- Elgueda, D., Delano, P. H., Robles, L. (2011). Effects of Electrical Stimulation of Olivocochlear Fibers in Cochlear Potentials in the Chinchilla. *Journal of the Association for Research in Otolaryngology* 12(3), 317-27.
- Elgoyhen, A. B., Johnson, D. S., Boulter, J., Vetter, D.E., Heinemann, S. (1994). Alpha 9: an acetylcholine receptor with novel pharmacological properties expressed in rat cochlear hair cells. *Cell* 79, 705-715.
- Elliot, S. J. & Shera, C. A. (2012). The cochlea as a smart structure. *Smart Materials and Structures* 21(6), 1-11.
- Ferraro, J. A. & Durrant, J. D. (2006). Electrocochleography in the evaluation of patients with Meniere's disease/endolymphatic hydrops. *American Journal of Audiology* 17(1), 45-68.
- Fex, J. (1959). Augmentation of Cochlear Microphonic by Stimulation of Efferent Fibres to the Cochlea. *Acta Otolaryngologica* 50, 540-1.
- Gifford, M.L., Guinan, J.J. (1987). Effects of cross-olivocochlear bundle stimulation on cat auditory nerve fiber responses to tones. *Journal of the Acoustical Society of America* 74, 115-123.
- Guinan, J. J. (2014). Olivocochlear efferent function: issues regarding methods and the interpretations of results. *Frontiers in Systems Neuroscience* 12, 1-5.
- Guinan J. J. (2006). Olivocochlear Efferents: Anatomy, Physiology, Function and the Measurement of Efferent Effects in Humans. *Ear and Hearing* 27(6), 589-607.
- Gulya, A. J. (1997) Anatomy and Embryology of the Ear. In G. B. Hughes, & M. L. Pensak (Eds.) *Clinical Otology*. New York: Thieme.
- Hamill, T. A. & Price, L. L. (2014). *The Hearing Sciences*. San Diego, CA: Plural Publishing.

- He, D. Z. Z., Jia, S., Dallos, P. (2003). Prestin and the Dynamic Stiffness of the Cochlear Outer Hair Cells. *Journal of Neuroscience* 23(27), 9089-9096.
- Hill, J.C., Prasher, D.K., Luxon, L.M. (1997). Latency of contralateral sound-evoked auditory efferent suppression of otoacoustic emissions. *Acta Otolaryngologica* 117, 343-351.
- Hughes, G. B., & Nodar, R. H. (1985). In G. B. Hughes (Ed.) *Textbook of Clinical Otology* (pp. 71-77). New York: Thieme.
- Jamos, A., Kaf, W., Chertoff, M., Ferraro, J., Franklin, C., & DiSarno, N. (2012). The effect of activating the olivocochlear bundle ipsilaterally and contralaterally on cochlear microphonic in humans. (Doctoral Thesis). Missouri State University, Springfield, MO.
- Keefe, D.H., Feeney, M.P., Hunter, L.L., Fitzpatrick, D.F. (2016). Comparisons of transient evoked otoacoustic emissions using chirp and click stimuli. *Journal of the Acoustical Society of America* 140.
- Kemp, D. T. (1978). Stimulated acoustic emission from within the human auditory system. *Journal of the Acoustic Society of America* 64 (5), 1386-1391.
- Lambert, P. R., Canalis, R. F. (2000). In Canalis, R. F. & Lambert, P. R. (Eds.), *The Ear: Comprehensive Otology* (pp. 571-586). Philadelphia, PA: Lippincott, Williams & Wilkins.
- Larsen, E., Liberman, M.C. (2009). Slow build-up of cochlear suppression during sustained contralateral noise: central modulation of olivocochlear efferents? *Hearing Research* 256 (1-2), 1-10.
- Liberman, M.C., & Brown, M.C. (1986). Physiology and anatomy of single olivocochlear neurons in the cat. *Hearing Research* 24, 17-36.
- Liberman, M. C., Liberman, L. D., Maison, S. F. (2014). Efferent Feedback Slows Cochlear Aging. *The Journal of Neuroscience* 34 (13), 4599-4607.



- Lilaonitkul, W., Guinan, J. J. (2009). Human Medial Olivocochlear Bundle Reflex: Effects as Functions of Contralateral, Ipsilateral, and Bilateral Elicitor Bandwidths. *Journal for the Association for Research in Otolaryngology* 10 (3), 459-470.
- Lim, D. J. (1980). Cochlear anatomy related to cochlear micromechanics. A review. *Journal of the Acoustical Society of America* 67 (5), 1686-1695.
- Lippe, W. R. (1986). Recent Developments in Cochlear Physiology. *Ear and Hearing* 7 (4), 233-239.
- Luxon, L. M., & Cohen, M. (1997). Central Auditory Dysfunction. In A. G. Kerr (Ed.) *Scott-Brown's Otolaryngology* (pp.1-32). Oxford: Reed Educational and Professional Publishing Ltd.
- Maison, S., Micheyl, C., Andéol, G., Gallégo, S., Collet, L. (1999). Activation of medial olivocochlear efferent system in humans: influence of stimulus bandwidth. *Hearing Research* 140, 111-125.
- Murdin, L., & Davies, R. (2008). Otoacoustic emission suppression testing: a clinician's window onto the auditory efferent pathway. *Audiological Medicine*, 6(4), 238-248.
- Musiek, F. E. (1986). Neuroanatomy, Neurophysiology, and Central Auditory Assessment. Part III: Corpus Callosum and Efferent Pathways. *Ear and Hearing* 7(6), 349-359.
- Musiek, F. E. & Baran, J. A. (2007). *The Auditory System: Anatomy, Physiology and Clinical Correlates*. Boston, MA: Pearson Education, Inc.
- Najem, F., Kaf, W., Ferraro, J., DiSarno, N., & Mitchell, W. (completed 2011). A comparison between contralateral suppression in cochlear microphonics and distortion product otoacoustic emissions. Doctoral Thesis, Missouri State University

- Nodar, R. H., Sahley, T. L., Hughes, G. B. & Musiek, F. E. (1997). Principles of Audiology and Auditory Physiology. In G. B. Hughes, & M. L. Pensak (Eds.) *Clinical Otology*. New York: Thieme.
- Nolte, J. (2009). *The Human Brain: An Introduction to its Functional Anatomy*. Philadelphia, PA: Mosby Elsevier.
- Oliver, D., He, D. Z. Z., Klöcker, N, Ludwig, J., Schulte, U., Waldegger, S., Ruppertsberg, J. P, Dallos, P., Fakler, B. (2000). Intracellular Anions as the Voltage Sensor of Prestin, the Outer Hair Cell Motor Protein. *Science* 292(5525) 2340-2343.
- Puria, S., Guinan, J. J., & Liberman, M. C. (1996). Olivocochlear reflex assays: Effects of contralateral sound on compound action potentials versus ear-canal distortion products. *Journal of the Acoustical Society of America*, 99(1), 500-507.
- Patuzzi, R.B., Yates, G.K., Johnstone, B.M. (1989). Changes in cochlear microphonic and neural sensitivity produced by acoustic trauma. *Hearing Research*, 39 (1-2), 189-202.
- Raphael, Y., & Altschuler, R. A. (2003). Structure and innervation of the cochlea. *Brain Research Bulletin*, 60, 397-422.
- Robinette, M. S. & Glatcke, T. J. (2007). *Otoacoustic Emissions: Clinical applications*. New York: Thieme
- Robertson, D. (1984). Horseradish peroxidase injection of physiologically characterized afferent and efferent neurones in the guinea pig spiral ganglion. *Hearing Research*, 15, 113-121.
- Santarelli, R., Scimemi, P., Dal Monte, E., Arslan, E. (2006). Cochlear microphonic potential recorded by transdympnic electrocochleography in normally hearing and hearing impaired ears. *Acta Otorhinolaryngologica Italica*, 26(2), 78-95.
- Schoonhoven, R. (2006). Responses from the cochlea: Cochlear Microphonic, Summating Potential, and Compound Action Potential. In Burkard, R. F., Don, M., Eggermont, J. J. (Eds.), *Auditory Evoked Potentials: Basic Principles and*

*Clinical Application* (pp. 180-195). Philadelphia, PA: Lippincott, Williams & Wilkins.

Schlauch, R. S., & Nelson, P. (2009). Pure tone evaluation. In J. Katz, L. Medwetsky, R. Burkhard, & L. Hood (Eds.), *Handbook of Clinical Audiology*. Philadelphia: Lippincott, Williams and Wilkins.

Schwartz, J. D. & Harnsberger, H.R. (1992). *Imaging of the Temporal Bone*. New York, NY: Thieme Medical Publishers.

Shanks, J. and Shohet, J. (2009) Tympanometry in Clinical Practice. In J. Katz, L. Medwetsky, R. Burkhard, & L. Hood, (Eds.), *Handbook of Clinical Audiology*. Philadelphia: Lippincott, Williams and Wilkins.

Shera, C. A. & Guinan, J. J. (1998). Evoked otoacoustic emissions arise by two fundamentally different mechanisms: A taxonomy for mammalian OAEs. *Journal of the Acoustical Society of America*, 105 (2), 782-98.

Siegel, J. H. & Kim, D. O. (1981). Efferent neural control of cochlear mechanics? Olivocochlear bundle stimulation affects cochlear biomechanical nonlinearity. *Hearing Research*, 6 (2), 171-182.

Sridhar, T.S., Liberman, M.C., Brown, M.C., Sewell, W.F. (1995). A novel cholinergic “slow effect” of efferent stimulation on cochlear potentials in the guinea pig. *Journal of Neuroscience*, 15 (5) 3667-78.

Velenovsky, D.S. & Glatcke, T.J. (2002). The effect of noise bandwidth on the contralateral suppression of transient evoked otoacoustic emissions. *Hearing Research*, 164, 39-48.

Wackym, P. A., Storper, I. S., & Newman, A. N. (2000). Cochlear and Vestibular Ototoxicity. In Canalis, R. F. & Lambert, P. R. (Eds.), *The Ear: Comprehensive Otolaryngology* (pp. 571-586). Philadelphia, PA: Lippincott, Williams & Wilkins.

Wiederhold, M. L., & Peake, W. T. (1966). Efferent inhibition of auditory-nerve responses: Dependence of acoustic stimulus parameters. *The Journal of the Acoustical Society of America*, 40(6), 1427-1430.

Withnell, R. H. (2001). Brief Report: The Cochlear Microphonic as an Indication of Outer Hair Cell Function. *Ear and Hearing*, 22, 75-77.

Zhao, W., Dewey, J. B., Boothalingam, S., Dhar, S. (2015). Efferent Modulation of Stimulus Frequency Otoacoustic Emission Fine Structure. *Frontiers in Systems Neuroscience*.

Zheng, X., McFadden, S. L., Henderson, D., Ding, D. Burkard, R. (2000). Cochlear microphonics and otoacoustic emissions in chronically de-efferented chinchilla. *Hearing Research*, 143, 14-22.