

STUDYING THE EFFECTS OF CHANGING EXPERIMENTAL PARAMETERS ON  
THE MEDIAL OLIVOCOCHLEAR EFFERENT FIBERS AND OUTER HAIR CELL  
ACTIVITY BY MEASUREMENT OF DISTORTION PRODUCT OTOACOUSTIC  
EMISSIONS

By

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by

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To my family and friends as well as the graduate students of the Behavioral Neuroscience  
Program at the University of Florida

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## TABLE OF CONTENTS

	<u>page</u>
ACKNOWLEDGMENTS .....	iv
LIST OF TABLES .....	vii
LIST OF FIGURES .....	viii
KEY TERMS .....	ix
ABSTRACT .....	x
CHAPTER	
1 GENERAL INTRODUCTION .....	1
2 GENERAL METHODS .....	10
Subjects.....	10
Instrumentation, Stimulus Parameters, and Testing Paradigms .....	10
Distortion Product Otoacoustic Emission Analysis.....	12
3 EXPERIMENT 1 .....	13
Introduction.....	13
Methods .....	16
Results.....	16
Discussion.....	18
4 EXPERIMENT 2 .....	25
Introduction.....	25
Methods .....	30
Results.....	32
Discussion.....	33
5 EXPERIMENT 3 .....	42
Introduction.....	42
Methods .....	43

Results.....	44
Discussion.....	45
6 GENERAL CONCLUSIONS.....	49
LIST OF REFERENCES .....	53
BIOGRAPHICAL SKETCH .....	60

## LIST OF TABLES

<u>Table</u>	<u>page</u>
3-1 Comparison of the minimum, maximum, and average rapid adaptation magnitude .....	22

## LIST OF FIGURES

<u>Figure</u>	<u>page</u>
3-1 Effects of primary stimulus levels on absolute DPOAE amplitudes .....	22
3-2 Relationship between rapid adaptation magnitude and the correlation of fit of the exponential to the DPOAE as a result of stimulus levels.....	23
3-3 Effects of stimulus levels on rapid adaptation magnitude and time constants.....	24
4-1 Effects of attention on absolute DPOAE amplitudes in Group 1.....	38
4-2 Effects of attention on rapid adaptation magnitudes and time constants in Group 1 .....	39
4-3 Effects of attention on absolute DPOAE amplitudes in Group 2.....	40
4-4 Effects of attention on rapid adaptation magnitudes and time constants in Group 2 .....	41
5-1 Effects of experience on DPOAE amplitudes .....	47
5-2 Effect of experience on rapid adaptation magnitude and time constants .....	48

## KEY TERMS

MOC – Medial Olivocochlear. Refers to any part of a system originating in the medial olivocochlear nucleus.

OAE – Otoacoustic emission. Sound that is emitted by the outer hair cells in response to stimulation from an auditory sound. OAEs can be measured in the ear canal and provide a general description of outer hair cells. OAEs are inversely related to the damage of the outer hair cells.

DPOAE – Distortion product otoacoustic emission. An OAE that is produced by presenting the ear with two primary tones that interact and create activity in the outer hair cells at other places on the basilar membrane.

TEOAE – Transient evoked otoacoustic emission. An OAE that is created by presenting the ear with a chirp, click, or tone burst. TEOAEs are created from activity over broad regions of the cochlea.

SOAE – Spontaneous otoacoustic emission. OAEs that occur without any stimulus.

L1 – Intensity level of the first stimulus used to produce a DPOAE.

L2 – Intensity level of the second stimulus used to produce a DPOAE.

F1 – Frequency of the first stimulus used to produce a DPOAE.

F2 – Frequency of the second stimulus used to produce a DPOAE.

2f1-f2 – The DPOAE studied most often because it produces the largest absolute DPOAE amplitude.

dB SPL – Decibel sound pressure level. Standard unit to measure sound.

DPGram – Distortion product otoacoustic emission gram. A graph displaying the absolute DPOAEs as a function of the stimulus frequencies.

Abstract of Thesis Presented to the Graduate School  
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The function of medial olivocochlear (MOC) efferent fibers has been extensively explored through several testing paradigms. Medial olivocochlear efferent fibers send impulses from the brainstem to the outer hair cells where they synapse to control outer hair cell activity. Outer hair cell activity amplifies the signals that are being conducted by inner hair cells and transmitted by the afferent fibers by amplifying the movement of the basilar membrane. Medial olivocochlear efferent fibers control outer hair cells by rapidly decreasing the activity of the outer hair cells within approximately 150ms of signal presentation. Current theories of MOC efferent function include: suppression as a protection mechanism, detection of signal in noise, and aid in selective auditory attention. The purpose of this Thesis was to explore changing experimental parameters and determining the effects on MOC efferent activity by measuring outer hair cell activity with distortion product otoacoustic emission (DPOAE) testing.

In Experiment 1, we studied the effects of changing the stimulus presentation levels on DPOAE amplitude and rapid adaptation magnitude. We found a general increase in rapid adaptation magnitude with an increase in stimulus intensity. We also noticed a greater signal to noise ratio when stimulus levels increased to a certain point. Our results suggest that L1=80 dB SPL, L2=75 dB SPL is the optimum stimulus combination to present to human subjects to measure the MOC efferent activity.

Experiment 2 focused on studying the role that MOC efferent fibers play in selective auditory attention. Our data show an increase in absolute DPOAE amplitude when subjects were asked to attend to a visual stimulus by reading DVD subtitles or a book compared to when subjects attended to the auditory stimulus by counting tones. However, there was no increase in absolute DPOAE amplitude when subjects increased their attentional load by attending to a visual stimulus and performed the physical task of playing a video game. We think that the physical movement occurring when subjects played a video game created an additional suppression from the MOC efferent fibers due to myogenic artifacts.

In Experiment 3, we had subjects who had exceptional signal-to-noise ratios return for 2 additional sessions to determine the effect of experience on DPOAE measurement. We compared DPOAEs across three sessions. We noticed a decrease in absolute DPOAE amplitude in session 2 and 3 but no additional decrease in absolute DPOAE amplitude from session 2 to session 3. This suggests that the activity of the outer hair cells change with familiarity of the same stimulus.

## CHAPTER 1

### GENERAL INTRODUCTION

Two types of hair cells are located in the cochlea. Inner hair cells are the sensory units that transduce fluctuations of the basilar membrane into the neural code of the auditory nerve (Hudspeth, 1997a). Outer hair cells amplify mechanical vibration in the cochlea by increasing the movement of the basilar membrane, which facilitates transduction of the mechanical energy, and aides in the sensation of hearing (Dallos and Harris, 1978; Ehret, 1979; Brownell et al., 1985; Smith et al., 1987; Morlet et al., 1996). The outer hair cell amplification modulates auditory sensitivity (Hudspeth, 1997b). When outer hair cells are damaged or destroyed, there is an increase of auditory detection thresholds of about 50–60 dB (Stebbins et al., 1979; Smith et al., 1987); suggesting that outer hair cells are necessary for detection of lower intensity sounds.

It has been suggested that outer hair cells and inner hair cells evolved and act independently of each other with no direct neural interaction between the systems (Spoendlin, 1975; Tumarkin, 1979). There are two different neural pathways that innervate the outer and inner hair cells in the cochlea. The different patterns of innervations suggest the two pathways have different functions. Afferent fibers relay signals from the hair cells to the brain; whereas, efferent tracts carry signals from the brainstem to the hair cells.

Two different afferent pathways emanate from the cochlea: Type-1 and Type-2 afferent fibers. Inner hair cells synapse with the myelinated Type-1 afferent fibers, which represent approximately 95% of all afferent fibers. Between 10 and 20 Type-1 afferent

fibers synapse with each inner hair cell. These fibers transmit neural impulses from inner hair cells to the cochlear nucleus and the auditory central nervous system. The remaining 5% of afferent fibers, Type-2 unmyelinated afferent fibers, synapse directly onto the outer hair cells. Type-2 afferent fiber synapses are rather sparse and several outer hair cells are innervated by each Type-2 fiber. The function of these fibers is unknown; however, they are thought to be excitatory and synapse over diverse regions of the cochlear nucleus (Leake-Jones and Synder, 1982; Berglund et al., 1996).

The second neural system, descending or efferent fibers, originate in the brainstem and extend to the outer hair cells in the cochlea via the medial olivocochlear bundle, and synapse on the afferent fibers innervating the inner hair cells via the lateral olivocochlear bundle. Studies have shown that stimulation of the medial olivocochlear (MOC) efferent tracts decreases cochlear and outer hair cell activity by reducing the active mechanical responses of the outer hair cells (Siegel and Kim, 1982; Liberman et al., 1996; Kujawa and Liberman, 2001). The suppression is due to the release of acetylcholine into the synapse from the MOC efferent fibers. These fibers suppress the electromotility of the outer hair cells by altering conductance due to stimulation of the cochlea from an auditory stimulus (Warren and Liberman, 1989; Kujawa and Liberman, 2001; Bassim et al., 2003; Halsey et al., 2005; Meinke et al., 2005).

The exact function of the MOC efferent fibers is still under review; however, there are three theories. It has been suggested that the MOC efferent fibers, by suppressing outer hair cell activity, act to protect the hair cells from acoustic over-stimulation and noise-induced hearing loss (Handcock and Zeisberg, 1982; Maison and Liberman, 2000; Rajan, 2001; Vazquez et al., 2001; Le Prell et al., 2003). Maison and

Liberman (2000) showed that the magnitude of the MOC reflex was inversely related to the amount of hearing loss resulting from intense noise exposure. Their results showed that animals with strong MOC reflexes had a greater magnitude of suppression of outer hair cell activity and, therefore, suffered less noise induced hearing loss than those that had weak MOC reflexes. They concluded that suppression from the MOC system protects the ear from acoustic injury. Using a more direct approach, Handrock and Zeisberg (1982) cut the MOC efferent fibers in guinea pigs and presented high intensity stimuli. Compared with control animals, de-efferented animals had greater temporary and permanent threshold shifts implying the ear suffered more trauma. They concluded that, under normal conditions, MOC efferent fibers protect animals from such trauma and thus serve as a protective mechanism.

Several authors have argued against the protection hypothesis (Kirk and Smith, 2003; Smith et al., submitted). Since nearly all mammalian species have MOC efferent fibers, loud noise would have to be a common feature of natural acoustic environments if MOC efferent fibers evolved for acoustic protection. Traumatic level acoustic stimuli are very rare in natural environments; sounds capable of producing noise-induced hearing loss are generally manmade (e.g., music, power tools, and vehicles). Therefore, it is unlikely that the MOC efferent fibers evolved for this function and other hypotheses need to be explored.

Improving the coding of auditory signals in background noise is another suggested function of the MOC efferent fibers (Winslow and Sachs, 1988; Morlet et al., 1999; Shera et al., 2002; Brown et al., 2003; May et al., 2004). Winslow and Sachs (1988) demonstrated that background noise enables the auditory nerve fibers to signal intensity

changes in noise backgrounds that would normally cause saturation. They reported that subjects had an enhanced ability to detect intensity changes when presented with noise compared to silence. They concluded the MOC efferent fibers increase detecting intensity changes within background noise. Detection of a signal in noise also allows animals to detect biologically relevant stimuli in constant noise such as wind and water (Kirk and Smith, 2003). This increases the detection of the transient sound of an oncoming predator while in constant natural background noise, which is important for survival. In humans, detecting signals in noise is important for speech detection and discrimination.

Giraud et al. (1997) studied the extent to which the MOC efferent fibers aid in detecting speech phonemes in noise by comparing patients that had undergone a vestibular neurotomy, in which efferent fibers are cut, with normal patients. Normal patients showed an increase in word discrimination when presented with contralateral noise versus a silent environment, while vestibular neurotomy patients did not show the same improvement in word discrimination. Giraud et al. (1997) concluded that the cut MOC efferent fibers failed to improve the detection of a transient signal because the MOC reflex did not occur to suppress the noise. Likewise, Kumar and Vanaja (2004) presented contralateral noise and measured speech identification. Speech identification was significantly improved with the presence of contralateral noise. They also concluded the MOC efferent system may have a role in increasing the detection and discrimination of signals in noise by suppressing background noise.

A more recent theory suggests the MOC efferent fibers may also play a role in selective auditory attention. The theory of selective attention suggests that we can

change the sensation of a stimulus and adapt our behavior by using top-down processing to focus on a specific stimulus (Meric and Collet, 1994a). Selective auditory attention suggests that focusing attention on an auditory stimulus changes the sensation of that stimulus. Therefore, selective auditory attention allows for controlling what is heard and what is tuned out with top-down mechanisms.

Michie et al. (1996) suggested that we use the MOC efferent system to aid in selectively attending to a particular auditory stimulus. Linked to the MOC efferent activity, outer hair cell activity has been shown to change with changes in attentional conditions (Puel et al., 1988; Froehlich et al., 1990; Froehlich et al., 1993; Giard et al., 1994; Meric and Collet, 1994b; Michie et al., 1996; Maison et al., 2001; Smith et al., submitted). Studies have shown variable results, however, when measuring the effect of selective attention on outer hair cell activity. When subjects were asked to attend to a visual stimulus, several studies have shown a significant decrease in activity of the outer hair cells (Puel et al., 1988; Meric and Collet, 1994b), while a significant increase in outer hair cell activity has been shown when subjects were asked to attend to the auditory stimulus (Giard et al., 1994). In contrast, some studies saw a significant increase in outer hair cell activity when attending to a visual stimulus (Froehlich et al., 1990), while a significant decrease in outer hair cell activity has been found when subjects were asked to attend to an auditory stimulus (Michie et al., 1996; Maison et al., 2001). Avan and Bonfils (1992) found no difference in outer hair cell activity when subjects were asked to attend to different stimuli; however, variability in activity increased when subjects were attending to a visual stimulus. Recently, work in our laboratory resulted in a significant increase in outer hair cell activity when the subject was asked to attend to a visual

stimulus by either reading a book or DVD subtitles compared to when subjects were attending to an auditory stimulus by counting tones (Smith et al., submitted). Smith et al. (submitted) concluded that the MOC efferent fibers increased the activity of the outer hair cells when subjects were attending to a visual stimulus relative to attending to an auditory stimulus. Although the exact relationship is unclear, MOC efferent fibers seem to play a role in changing the activity of outer hair cells during selective auditory attention. Further investigations need to focus on creating standard attentional conditions to draw definitive conclusions across studies.

Measuring otoacoustic emissions (OAEs) has served as a non-invasive technique to evaluate the MOC efferent system by relating to outer hair cell activity (Froehlich et al., 1990; Avan and Bonfils, 1992; Harris et al., 1992; Giard et al., 1994; Liberman et al., 1996; Michie et al., 1996; Abdala, 1998; Sun and Kim, 1999; McGee et al., 2000; Kim et al., 2001; Kujawa and Liberman, 2001; Luebke et al., 2002; Guinan et al., 2003; Lonsbury-Martin and Martin, 2003; Martin et al., 2003; Smith et al., submitted).

Otoacoustic emissions were first reported by Kemp (1978), who suggested that one of the functions of the outer hair cells is to generate mechanical energy. Again, the mechanical energy facilitates the transduction process, but also travels in a “reverse” direction where it can be measured as sound, called an OAE, in the ear canal (Flock, 1980; Brownell, 1984). Because outer hair cell activity is controlled by the MOC efferent fibers, OAE recordings should serve as effective measures of MOC efferent activity.

Distortion product otoacoustic emissions (DPOAEs) and transient evoked otoacoustic emissions (TEOAEs) have been used to study MOC efferent function. Distortion product otoacoustic emissions are generated by stimulating the ear with two

primary tones, which interact in a non-linear manner to create mechanical activity at a third, unique place on the basilar membrane. The frequencies of the DPOAEs are determined by the relationship of the two primary tones that stimulate the ear. Transient evoked otoacoustic emissions differ in that they can be generated with a broadband click, chirp, or tone burst and reflect the outer hair cell activity over broad regions of the basilar membrane. Distortion product otoacoustic emissions are used more often than TEOAEs because they provide more reliable responses than TEOAEs and are, therefore, used in clinical applications (Lonsbury-Martin et al., 1995; Silva and Ysunza, 1998). Secondly, tone pips and clicks have not produced the MOC efferent suppression effects in TEOAE studies as the stimulus is too short for the MOC reflex to occur (Avan and Bonfils, 1992; Guinan et al., 2003). Studies using the DPOAE paradigm primarily use the cubic,  $2f_1-f_2$ , DPOAE to study the MOC efferent fibers as it results in the highest absolute DPOAE amplitude, providing the best signal to noise ratio.

The suppression activity of the MOC efferent reflex is measured with DPOAE rapid adaptation. Adaptation is a characteristic of all sensory systems. In the peripheral auditory system, rapid adaptation is characterized as a decrease in outer hair cell activity after stimulus presentation; and is measured as a decrease in DPOAE amplitude. Adaptation occurs with two time constants, rapid and slow. A time constant describes the time it takes for the DPOAE to decrease in level by 63.2%. Rapid adaptation has a time constant of 60–100ms and slow adaptation has a time constant of approximately 1000ms. Brown et al. (2003) reported that a form of short-term adaptation, with a time constant of 125ms, occurs in the MOC efferent fibers themselves. This form of adaptation, likely carried by the MOC efferent fibers to the outer hair cells, mimics the adaptation effect

measured by the DPOAE, but is significantly smaller in magnitude. Many authors have shown that the MOC efferent fibers control rapid adaptation in the outer hair cells and, therefore, we can measure the suppression of the outer hair cell activity with rapid adaptation of DPOAEs (Liberman et al., 1996; Yoshida et al., 1999; Kim et al., 2001, Brown et al., 2003).

Rapid adaptation in DPOAEs was first related to MOC function in cats by Liberman et al. (1996) and has since been shown in mice (Sun and Kim, 1999), gerbils (McGee et al., 2000) guinea pigs (Kujawa and Liberman, 2001), rabbits (Luebke et al., 2002), and humans (Kim et al., 2001). Kim et al. (2001) showed that adaptation in humans, like other species, was characterized by two distinct time constants. However, DPOAE rapid adaptation recorded in human subjects appears smaller than those measured in laboratory animals (Liberman et al., 1996; Kim et al., 2001; Kujawa and Liberman, 2001; Guinan et al., 2003; Martin et al., 2003). Bassim et al. (2003) also recorded DPOAE adaptation in humans and characterized the effects of ipsilateral, contralateral, and bilateral stimulation on rapid adaptation magnitude. They concluded that the rapid adaptation process in humans is similar to that in non-human animals, showing greater adaptation when stimulated binaurally versus monaurally and additional adaptation when stimulated contralaterally several seconds after the onset of the ipsilateral stimulation. This suggests that humans and non-human animals display the same effects of adaptation on outer hair cell activity.

Lesioning MOC efferent fibers abolish the rapid adaptation of outer hair cells. Liberman et al. (1996) lesioned MOC efferent fibers in cats and reported a complete lack of rapid adaptation following the lesioning; however, the slow component was

unaffected. Brown et al. (2003) confirmed these results with MOC efferent lesions in guinea pigs. This suggests that the two time constants are produced by separate systems, with rapid adaptation controlled by MOC efferent fibers and slow adaptation resulting from other mechanisms. The aminoglycoside antibiotic Gentamicin has potent anti-cholinergic properties which block MOC efferent influence over the outer hair cells by blocking the binding of acetylcholine (Smith et al., 1994). Yoshida et al. (1999) administered Gentamicin to guinea pigs and studied the effects on adaptation of the outer hair cells. When Gentamicin was given, there was a loss of rapid but not slow adaptation. These studies confirmed that the MOC efferent fibers are responsible for the rapid adaptation effect of the outer hair cells.

The experiments in this master's thesis were conducted to study the MOC efferent fibers and function. In Experiment 1, we examined the proposal that rapid adaptation is affected by the level of the stimulus primaries. We manipulated primary tone stimulus levels and measured the effects on DPOAEs. In Experiment 2, we examined the role MOC efferent fibers play in selective auditory attention by asking subjects to perform different attentional tasks and comparing DPOAEs across conditions. In Experiment 3, we investigated the role of experience and familiarity on DPOAE measurement. We asked subjects to return for multiple sessions and compared DPOAEs across sessions.

## CHAPTER 2 GENERAL METHODS

### **Subjects**

The majority of our participants were students enrolled at the University of Florida. Some of the student participants received partial course credit while other participants received compensation of \$10 per hour for their time spent in our studies. Seventy-three percent of our subjects were females. Eighty-four percent were between the ages of 18–22 years old. Each subject was asked to provide a brief medical history describing ear-related infections, surgery, history of noise exposure, as well as any medications taken in the previous 24 hours. All experiments were approved by the Internal Review Board of the University of Florida.

### **Instrumentation, Stimulus Parameters, and Testing Paradigms**

The two primary tones were generated digitally (Tucker-Davis Technologies, Gainesville, FL; AP2, DA3-3, PA4) and individually presented to each ear through separate transducers (Etymotic Research, Elk Grove Village, IL; ER-1), for a total of four transducers. Primary-tone levels, as well as the distortion product otoacoustic emissions (DPOAEs), were measured continuously in the ear canal with a low-noise microphone (Etymotic Research; ER10B+). The DPOAEs were amplified 40 dB, digitized (Tucker-Davis Technologies; DA2), and stored to the hard drive. At the end of each session, the DPOAEs were analyzed using a heterodyne method described by Kim et al. (2001), which consisted of heterodyning a band of spectral components around the DPOAE.

The acoustic system was calibrated in the ear canal individually for each transducer at the beginning of every test session. Calibration tests were also repeated several times during the session to determine if any small changes in ear probe placement or orientation had occurred, which would result in unwanted variations in DPOAE measurements during trials. The system also monitored the primary tone levels on a trial-by-trial basis. Any changes in DPOAE or primary levels resulted in stopping the session to reinsert or replace the ear probe and recalibrate before the session was resumed.

At the beginning of each session, a distortion product otoacoustic emission gram (DPgram) was measured to characterize the sensitivity of the ear. Distortion product otoacoustic emission grams are used clinically to assess the quality of the outer hair cells, determine the extent as well as predict hearing loss, and test the hearing of uncooperative patients by providing a graph of DPOAEs as a function of the stimulus frequencies, which relate to outer hair cell activity (Harris et al., 1992; Arnold et al., 1999; Di Girolamo et al., 2001; Lonsbury-Martin and Martin, 2003; Shaffer et al., 2003). We use the DPgram to determine which frequency combination will give us the greatest absolute DPOAE amplitude. To create the DPgram, the primary tone parameters used were frequencies at  $F_2/F_1=1.21$ , and stimulus levels of  $L_1=70$  dB SPL and  $L_2=65$  dB SPL. The DPOAEs were measured as  $F_2$  was systematically increased from 1.5 to 8 kHz. A graph displaying the DPOAEs for each frequency combination was created and the  $F_1$  and  $F_2$  combination that produced the largest absolute DPOAE was chosen for the remainder of the session. The best frequency varied across subjects as well as between sessions. If a subject participated in several sessions, a DPgram was conducted at the beginning of each new session and a best frequency was chosen for that session.

Following the DPgram, we began testing each condition with 128 3-second long stimulus presentations with primary tone parameters of F2/F1=1.21.

### **Distortion Product Otoacoustic Emission Analysis**

Distortion produce otoacoustic emission rapid adaptation was measured as a change in the amplitude as a function of time following the onset of the stimulus. Graphs were created for each subject by averaging the DPOAE response to 128 stimulus presentations. Based on previous studies in both humans and in animals, a two-component exponential was fit to each curve using the Matlab curve fitting tool (Bassim et al., 2003; Kim et al., 2001). One exponential was fit to the rapid adaptation while another fit the slow adaptation. Matlab generated several measurements that were used for comparisons across study conditions, including: rapid adaptation magnitude, rapid adaptation time constant, slow adaptation magnitude, slow adaptation time constant, absolute level of the emission, and a correlation of the fit of the exponential to the DPOAE. The rapid adaptation magnitude was created by calculating the magnitude of change during the rapid time constant. The rapid adaptation time constant was the time it took for the DPOAE to drop 63.2% from the start of the first exponential decay. The slow adaptation magnitude was calculated as the magnitude of change during the slow adaptation time constant. The slow adaptation time constant was the time it took for the DPOAE to drop 63.2% for the second exponential decay. The absolute level was computed by averaging the level at the last 15% of the data points of each DPOAE for an average end level. The correlation of the fit of the exponential calculated how well the two-component exponential fit to the averaged DPOAE including both rapid and slow adaptation. All five factors were compared in a within subjects design.

## CHAPTER 3 EXPERIMENT 1

### Introduction

Distortion product otoacoustic emission (DPOAE) rapid adaptation is a reliable measure of medial olivocochlear (MOC) efferent activity (Halsey et al., 2005). Several authors have reported that adjusting the eliciting stimulus levels can affect the activity of the outer hair cells and, therefore, change several DPOAE measurements (Kujawa and Liberman, 2001; Halsey et al., 2005; Meinke et al., 2005). The tonotopic location where the primary stimulus frequencies, F1 and F2, overlap has been suggested as the region where DPOAEs are generated (Whitehead et al., 1995). Here, a portion of the F1 excitation pattern crosses into the region of excitation of F2. If the F1 level is increased, the tonotopic region of overlap is increased with a resulting increase of DPOAE absolute amplitude. Distortion product otoacoustic emission absolute amplitude has been shown by Whitehead et al. (1995) to be largest when the two primary tone levels, L1 and L2, are equal and at high stimulus levels. However, when primary tone levels are decreased, DPOAE amplitude is greatest when  $L1 > L2$ . This suggests that the relationship of the stimulus levels change when the stimulus levels are varied in intensity.

Although it has been suggested that the highest L1 and L2 levels will produce the largest DPOAE amplitude, it is unclear whether using higher primary tone levels to produce the largest DPOAE amplitude will result in increases in rapid adaptation magnitude. Guinan et al. (2003) reported larger otoacoustic emission (OAE) amplitudes when higher intensity stimulus levels were presented. Several studies suggest that larger

OAE amplitudes produce more MOC efferent activity, resulting in larger magnitudes of rapid adaptation (Whitehead et al., 1995; Guinan et al., 2003). Kujawa and Liberman (2001) studied the effects of the L1 and L2 manipulations on rapid adaptation magnitude in guinea pigs. When L1 was held constant at 70 dB SPL, 75 dB SPL, or 80 dB SPL, they recorded a larger rapid adaptation magnitude at L1=75 dB SPL compared with to the other L1 levels. When L1 was fixed at 75 dB SPL, L2 values of 68 dB SPL and 70 dB SPL produced the greatest magnitude of rapid adaptation. If highest primary levels produce the largest rapid adaptation magnitude, Kujawa and Liberman (2001) would have reported the greatest magnitude of rapid adaptation with stimulus levels of L1=80 dB SPL and a similar L2 level. Therefore, simulating with the highest intensity levels may not always produce the largest magnitude of rapid adaptation.

Rapid adaptation can also be measured as a positive change in outer hair cell activity. Halsey et al. (2005) reported a maximum adaptation magnitude of outer hair cell activity in guinea pigs at levels of L1=88 dB SPL, L2=81 dB SPL. However, they defined adaptation magnitude as the largest negative change in outer hair cell activity subtracted from the largest positive change in outer hair cell activity. This may not be a proper measurement as it is not consistent with other studies; other studies define adaptation magnitude as the average amount of change in activity over time. Halsey et al. (2005) also reported a rapid adaptation time constant of 300–500ms which was a longer time constants than other studies, reporting time constants at approximately 60–100ms (Liberman et al., 1996; Kim et al., 2001; Kujawa and Liberman, 2001; Bassim et al., 2003; Brown et al., 2003; Halsey et al., 2005; Smith et al., submitted). It appears that Halsey et al. (2005) compared the difference between DPOAE amplitudes during two

separate trials. This would not be an adaptation magnitude, but a difference in activity of the outer hair cells at two different stimulus presentations. Therefore, their results may not accurately reflect the stimulus levels that produce the greatest magnitude of rapid adaptation.

Meinke et al. (2005) measured the effects of the L1, L2 manipulations on rapid adaptation magnitudes in humans. Their results showed that the largest amount of rapid adaptation occurred at levels of L1=80 dB SPL, L2=75 dB SPL and L1=80 dB SPL, L2=80 dB SPL. However, since they only measured the initial 92ms versus final 92ms in a 1000ms long tone; their methods do not allow estimates of the rapid adaptation time constants. The adaptation they observed may not have solely been from the MOC efferent fibers. The slow component is generally thought to contribute at 1000ms. Therefore, their results could be attributed to the slow adaptation mechanisms. They did not mention slow adaptation mechanisms and only suggested that the MOC efferent reflex contributed to their results.

The purpose of this experiment was to investigate the effects of L1 and L2 levels on rapid adaptation magnitude, rapid adaptation time constants, and absolute level of DPOAEs in humans. The secondary objective was to “optimize” DPOAE collection parameters by increasing DPOAE signal to noise ratios. It is important to optimize the effects in humans because DPOAEs are significantly smaller in humans than they are in experimental animals (Liberman et al. 1996; Kim et al. 2001; Kujawa and Liberman, 2001; Guinan et al., 2003; Martin et al., 2003). We chose the studies by Kujawa and Liberman (2001), Halsey et al. (2005), and Meinke et al. (2005) where the effects of primary tone levels, on DPOAE level and rapid adaptation magnitudes, were explicitly

studied to specify primary tone level combinations that produced the largest rapid adaptation magnitudes. We also used the stimulus levels, L1=70 dB SPL, L2=65 dB SPL, which was previously used in our lab, to determine if these levels produced comparable results (Smith et al., submitted). We attempted to replicate results from these studies and choose a stimulus combination that is optimal for human testing.

### **Methods**

Seventeen human subjects participated in this study. These subjects were asked to read DVD subtitles during the DPOAE recordings. We chose this activity because previous studies have shown the least amount of background noise recorded by requiring the least amount of physical movement (Smith et al., submitted). Also, reading DVD subtitles produced larger absolute DPOAE amplitudes, which, according to Whitehead et al. (1995) and Guinan et al. (2003), results in an increase of rapid adaptation magnitude. Distortion product otoacoustic emissions were graphed by averaging 128 trials for each of the five stimulus L1, L2 level combinations: (1) 70 dB SPL, 65 dB SPL; (2) 75 dB SPL, 70 dB SPL; (3) 75 dB SPL, 68 dB SPL; (4) 80 dB SPL, 75 dB SPL; and (5) 88 dB SPL, 81 dB SPL. The subjects were required to complete all five stimulus combinations to be included in the data analysis.

### **Results**

Table 3-1 shows the minimum, maximum, and average rapid adaptation magnitude that occurred for each level combination. As is apparent, considerable individual differences in rapid adaptation magnitude create wide variations in the measurement of rapid adaptation magnitudes.

Figure 3-1 presents the DPOAE adaptation contours recorded at the five L1, L2 combinations. Based on previous studies, we had expected to see a general increase in

absolute DPOAE amplitude when the combinations of levels were increased. However, this was not the result produced. The absolute DPOAE amplitude does not follow a systematic pattern. The absolute DPOAE amplitude from the combination 70 dB SPL, 65 dB SPL was significantly lower than 75 dB SPL, 70 dB SPL ( $p=0.005$ ). The absolute DPOAE amplitude from the combination 75 dB SPL, 70 dB SPL was significantly higher than 75 dB SPL, 68 dB SPL ( $p<0.0001$ ), and 88 dB SPL, 81 dB SPL ( $p=0.05$ ).

Figure 3-2 shows the relationship between rapid adaptation magnitude and the correlation of fit of the exponential to the DPOAEs. The correlation of fit measures how closely the exponential fits to the DPOAE, with a better fit indicative of a higher signal to noise ratio. The correlation of the fit of the line increases with an increase in stimulus intensity levels up to 80 dB SPL, 75 dB SPL and then decreases to the lowest correlation of fit at the highest primary level combination. The correlation of fit for the stimulus combination 70 dB SPL, 65 dB SPL was significantly lower than combinations; 75 dB SPL, 70 dB SPL ( $p=0.002$ ); 75 dB SPL, 68 dB SPL ( $p<0.0001$ ); 80 dB SPL, 75 dB SPL ( $p=0.003$ ); and higher than 88 dB SPL, 81 dB SPL ( $p=0.017$ ). The correlation of fit for stimulus levels 75 dB SPL, 70 dB SPL was significantly lower than 80 dB SPL, 75 dB SPL ( $p<0.0001$ ), and higher than 88 dB SPL, 81 dB SPL ( $p=0.001$ ). The correlation of fit for stimulus levels 75 dB SPL, 68 dB SPL was significantly higher than 88 dB SPL, 81 dB SPL ( $p=0.0009$ ). The stimulus combination 80 dB SPL, 75 dB SPL had a significantly higher correlation of fit than 88 dB SPL, 81 dB SPL ( $p=0.0001$ ).

Figure 3-2 and Figure 3-3 both compare the rapid adaptation magnitude with Figure 3-3 presenting the rapid adaptation magnitude as a function of time. Figure 3-3 replots the DPOAEs from Figure 3-1 with contours normalized to the onset of the

DPOAE in order to compare the differences in rapid adaptation magnitude and time constants. The rapid adaptation magnitude from levels 70 dB SPL, 65 dB SPL was significant smaller than 75 dB SPL, 68 dB SPL ( $p=0.04$ ), and 80 dB SPL, 75 dB SPL ( $p=0.006$ ). The rapid adaptation magnitude from levels 75 dB SPL, 70 dB SPL was significantly smaller than 80 dB SPL, 75 dB SPL ( $p=0.02$ ). The rapid adaptation magnitude from levels 75 dB SPL, 68 dB SPL was significant smaller than 80 dB SPL, 75 dB SPL ( $p=0.05$ ). The level combination 80 dB SPL, 75 dB SPL had the largest rapid adaptation magnitude. Interestingly, the combination also gave us the highest correlation of fit of the exponential to the DPOAE.

Importantly, there were no significant differences in rapid adaptation time constants when comparing any of the levels. This suggests that while the amplitude of the suppression from the efferent fibers changed, the time it takes to suppress did not. Differences were also observed in slow adaptation. Slow adaptation magnitude at 70 dB SPL, 65 dB SPL was significantly smaller than 75 dB SPL, 68 dB SPL ( $p=0.003$ ), and 80 dB SPL, 75 dB SPL ( $p=0.03$ ). The slow adaptation time constant at 75 dB SPL, 68 dB SPL was significantly faster than 80 dB SPL, 75 dB SPL ( $p=0.05$ ). The slow adaptation time constant showed a trend toward but failed to reach significance when comparing 70 dB SPL, 65 dB SPL and 80 dB SPL, 75 dB SPL ( $p=0.09$ ); 70 dB SPL, 65 dB SPL and 88 dB SPL, 81 dB SPL ( $p=0.06$ ); 75 dB SPL, 70 dB SPL and 80 dB SPL, 75 dB SPL ( $p=0.08$ ); 75 dB SPL, 70 dB SPL and 88 dB SPL, 81 dB SPL ( $p=0.07$ ); and 75 dB SPL, 68 dB SPL and 88 dB SPL, 81 dB SPL ( $p=0.06$ ).

## **Discussion**

Consistent with previous reports, our data show a significant difference in the DPOAE amplitude and rapid adaptation magnitude when stimulus intensity levels are

changed (Kujawa and Liberman 2001; Halsey et al. 2005; Meinke et al. 2005). Figure 3-3 shows that when the stimulus combinations are increased in intensity level, the rapid adaptation magnitude likewise increases. This suggests that there may be an “optimum” set of stimulus levels used to study the MOC efferent fibers. However, it is unknown whether larger rapid adaptation magnitudes coincide with more activity in the MOC efferent fibers.

There are several methods for determining which primary level combinations are optimal for producing the best response in terms of a combination of largest rapid adaptation magnitude and highest correlation of fit of the exponential. Our individual data suggests that L1=88 dB SPL, L2=81 dB SPL produced the greatest magnitude of rapid adaptation. However, our correlation of fit of the exponential to the DPOAE suggests that, at L1=88 dB SPL, L2=81 dB SPL, a wide variability between subjects results. When looking at individual data, it became apparent that these levels were the most variable out of the selected level combinations producing the largest standard deviation. Five out of seventeen subjects showed the greatest rapid adaptation magnitude at this combination; however, only two out of seventeen showed the best correlation of fit. Because the stimulus levels L1=88 dB SPL, L2=81 dB SPL do not produce consistent results across subjects, we think other stimulus combinations should be used to measure human MOC efferent activity. We do, however suggest that in some individuals, L1=88 dB SPL, L2=81 dB SPL may be the optimum stimulus combination to present because our data suggest that, for some individuals, the data were least variable. Halsey et al. (2005) showed that these levels were best suited for guinea pigs in that they showed large magnitudes of rapid adaptation and it appears that there was a good signal

to noise ratio, yet there was no measured correlation of fit. They did not, however, discuss the variations between animals and may have only used results displaying large rapid adaptation magnitudes and good signal to noise ratios.

Our data suggest that the combination L1=80 dB SPL, L2=75 dB SPL produces the largest average rapid adaptation magnitude and the highest correlation of fit of the exponential to the DPOAE suggesting the best signal to noise ratio. Meinke et al. (2005) argued this level combination as being one of the most efficient combinations because it provided the largest adaptation magnitude of outer hair cell activity. They also saw the lowest standard deviation when comparing rapid adaptation magnitudes suggesting lower variability between subjects. We did not see the same decrease in variability with this combination. With our data, the lowest standard deviation resulted from the lowest stimulus combination suggesting less variability at lower stimulus intensities. However, both our results and Meinke et al.'s (2005) reached the same conclusion with an optimum combination of L1=80 dB SPL, L2=75 dB SPL for human testing.

There is no apparent relationship between rapid adaptation magnitude and absolute amplitude of the DPOAE; we did not observe a systematic increase in rapid adaptation magnitude with increases in DPOAE amplitude as had been expected. Therefore, the present data suggest that the rapid adaptation magnitude does not depend on the absolute amplitude of the DPOAE, and agree with Kujawa and Liberman's (2001) results. Whitehead et al. (1995) showed that stimulus level relationships that produced the largest DPOAE amplitude varied depending on the intensity of the stimulus levels. Our data agree and suggest that the magnitude of rapid adaptation is not driven solely by

stimulus intensity and that absolute DPOAE amplitude and rapid adaptation magnitude may not be related.

It has been suggested that if F1 is increased to levels of approximately 70–75 dB SPL, the two primary regions of excitation are so broad that they may create interference from excitation at places on the basilar membrane (Whitehead et al. 1995). Whitehead et al. (1995) reported a decrease in DPOAE absolute amplitude when stimulus levels above 70–75 dB SPL were presented. It is possible that the active cochlear mechanics do not respond due to activity of the MOC efferent fibers at higher stimulus levels (Avan and Bonfils, 1992; Liberman et al. 1996; Guinan et al., 2003). Avan and Bonfils (1992) suggest that above 70 dB SPL, outer hair cells provide no reliable information on MOC efferent activity and the DPOAEs could arise from other properties of the acoustic system. The present data, however, suggest that MOC efferent activity does change with increases in stimulus levels because we observed a change in absolute DPOAE amplitude and rapid adaptation magnitude with a change in stimulus intensities. However, it is possible the MOC efferent fibers may not act at stimulus levels above 70 dB SPL even though DPOAE measurements imply that it does. The activity of the outer hair cells, in response to stimulus levels above 70 dB SPL, need to be studied directly to determine if the DPOAE rapid adaptation measurements are accurately describing the outer hair cell activity and MOC efferent activity at high stimulus intensities.

Table 3-1. Comparison of the minimum, maximum, and average rapid adaptation magnitude. This table compares the change in DPOAE amplitude for each stimulus combination levels from all 17 subjects.

Level combination	Minimum	Maximum	Average
70 dB SPL, 65 dB SPL	0.15 dB	0.90 dB	0.516 dB
75 dB SPL, 70 dB SPL	0.19 dB	1.41 dB	0.581 dB
75 dB SPL, 68 dB SPL	0.20 dB	1.13 dB	0.619 dB
80 dB SPL, 75 dB SPL	0.08 dB	1.81 dB	0.821 dB
88 dB SPL, 81 dB SPL	0.00 dB	2.19 dB	0.691 dB

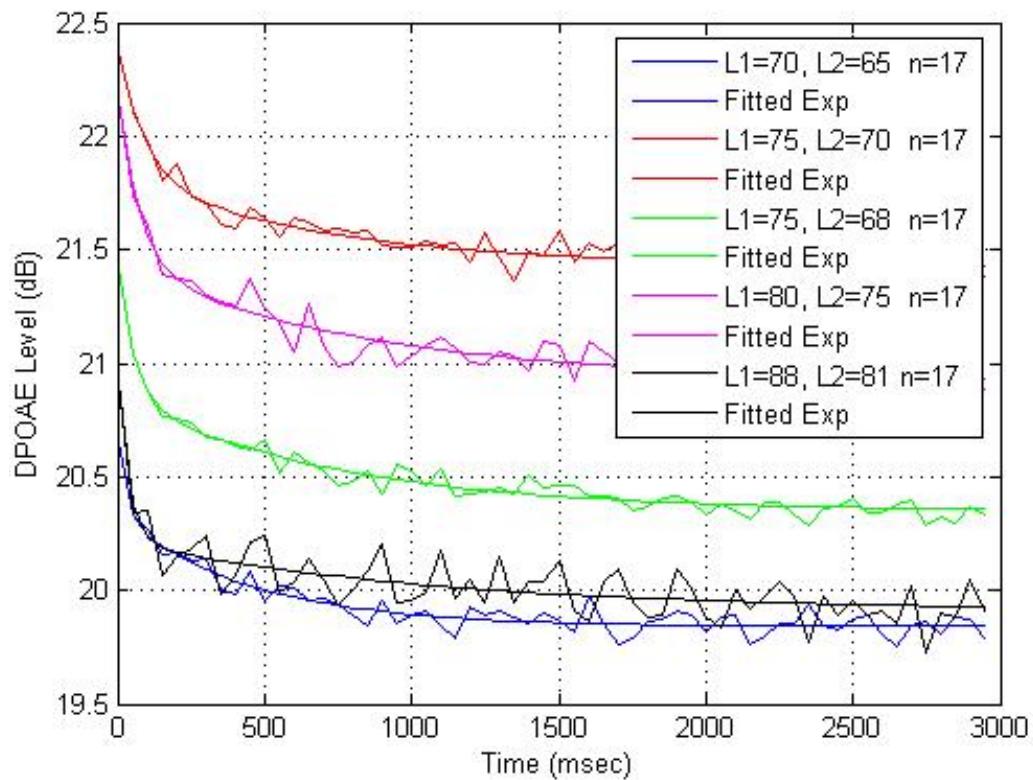


Figure 3-1. Effects of primary stimulus levels on absolute DPOAE amplitudes. This figure compares the absolute DPOAE amplitudes of the five stimulus combinations.

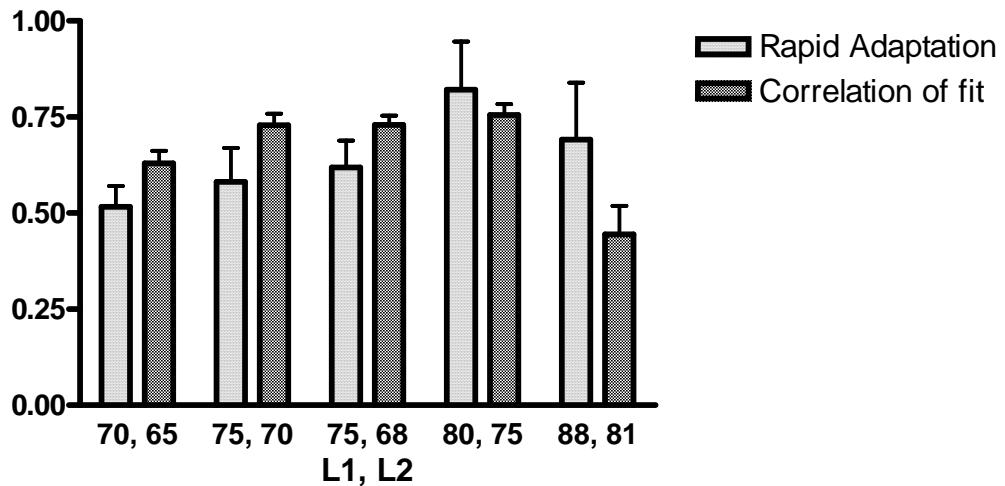


Figure 3-2. Relationship between rapid adaptation magnitude and the correlation of fit of the exponential to the DPOAE as a result of stimulus levels. This graph presents the relationship between rapid adaptation magnitude and the correlation of the fit of the two-component exponential of the five stimulus combinations.

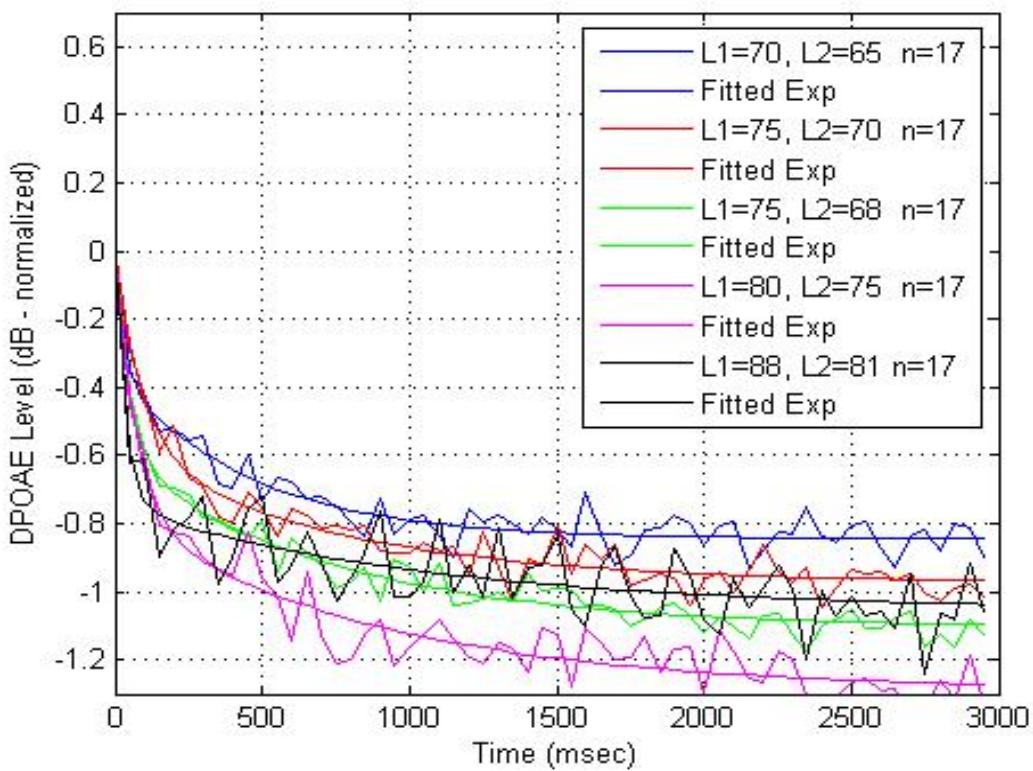


Figure 3-3. Effects of stimulus levels on rapid adaptation magnitude and time constants. These contours compare the five stimulus combinations normalized to the DPOAE onset, and show the differences in rapid adaptation magnitude and time constants as well as the slow adaptation magnitude and time constants.

## CHAPTER 4 EXPERIMENT 2

### Introduction

As previously described, one proposed medial olivocochlear (MOC) function is a peripheral influence in the process of mediating a peripheral component of selective auditory attention—increasing the salience of one, attending stimulus, at the expense of a second, ignored stimulus. We can selectively attend to or away from an auditory stimulus, which is thought to be regulated by a top-down process (Meric and Collet, 1994a). Several studies have looked at the effects of attention at different levels on the central nervous system; as well as on otoacoustic emission (OAE) measurements relating to the outer hair cell and MOC efferent activity at the auditory periphery.

Most studies recording brain activity reported increases in activity when subjects attended to an auditory stimulus. Woldorff et al. (1993) measured event-related potentials (ERPs) complimented by recordings of neuromagnetic fields (ERFs) as subjects attended to an auditory stimulus. They reported increased activity of the auditory cortex at the supratemporal plane when subjects were asked to attend to an auditory stimulus in the contralateral ear from measurement compared to when subjects were attending to an auditory stimulus in the ipsilateral ear. They concluded that auditory attention exerts control over early sensory processing. Pugh et al. (1996) studied auditory selective attention using functional magnetic resonance (fMRI). With fMRIs, they reported a systematic increase in parietal lobe activity when task demand increased, which was strongest in the inferior parietal lobule. Electroencephalograms (EEGs) have

shown changes in activity resulting from changes in attention as well (Galbraith et al., 2003). Galbraith et al. (2003) compared EEG activity during two specific attentional tasks, subjects attending to an auditory stimulus and subjects attending to a visual stimulus. Brain response amplitudes in the auditory brainstem were larger while the subjects attended to an auditory stimulus, compared with when they attended to the visual stimulus.

A few studies reported no effects of attention on brain activity. Tzourio et al. (1997) compared brain activity using positron emission tomography (PET) when subjects passively listened to an auditory stimulus in both ears, to when they attended to an auditory stimulus in one ear and ignored the other. They did not see significant differences in activity. However, their attending conditions appeared to be conflicting. Their non-attending condition consisted of subjects listening to a stimulus in both ears, while their attending condition required subjects to listen for tones in one ear. It is possible that their subjects focused on the same tones during both conditions, resulting in no difference across conditions. Hoormann et al. (2000) studied the effect of attention with auditory-evoked potentials (AEP) and frequency-following potential (FFP) while subjects attended to a target auditory stimulus in one ear compared to subjects passively listening to different tones in both ears. They reported no effects of attention conditions using FFP, yet AEP measurements show a negative displacement during attended conditions. Again, these conditions did not require subjects to attend to different stimuli. These studies suggest that changing attention to a different modality affects brain activity in that they show a change in brain activity when comparing measurements during

attention to an auditory stimulus to attention toward a visual stimulus. The studies also suggest that there is no change when no visual stimulus is presented.

In a more recent fMRI study, Petkov et al. (2004) suggested that the auditory cortex may be segregated into two sections, a mesial region that processes sound regardless of attention, and a lateral attention zone that is dependent on attention to an auditory stimulus. The lateral zone is made up of the superior temporal gyrus, superior temporal plane, and temporal-parietal junction. In this zone, responses are enhanced by auditory attention. This conception may explain why some studies found no attentional differences in responses, possibly looking at the mesial zone which respond to all auditory stimuli regardless of attention, while others show changes related to attention, possibly looking at the lateral zone.

Attentional conditions have also been shown to affect OAE amplitude. Medial olivocochlear efferent activity may influence the outer hair cell activity in response to attentional conditions (Michie et al., 1996). Influenced by outer hair cell activity, it has been reported that OAEs are affected by attention (Puel et al., 1988; Froehlich et al., 1990; Froehlich et al., 1993; Giard et al., 1994; Meric and Collet, 1994b; Maison et al., 2001; Smith et al., submitted). Manipulations of attention have resulted in variable conclusions regarding the effects on transient evoked otoacoustic emission (TEOAE) and distortion product otoacoustic emission (DPOAE) measurements. Previous results with TEOAEs showed significant reductions in absolute amplitude when subjects attended to a visual stimulus (Puel et al., 1988; Meric and Collet, 1994b) and an increase in absolute amplitude when subjects attended to an auditory stimulus (Giard et al., 1994). These reports contradict some findings of an increase in absolute amplitude when subjects were

attending to a visual stimulus (Froehlich et al., 1990) and a decrease in OAE amplitude when subjects attended an auditory stimulus (Michie et al., 1996; Maison et al., 2001).

Several studies have tried to explain the differences in previous results. Avan and Bonfils (1992) suggested that previous TEOAE studies on attention really have no “listening” task. The stimulus used to elicit a TEOAE is not an adequate stimulus for the subjects to attend to (Avan and Bonfils, 1992; Guinan et al., 2003); therefore, there is not a sufficient separation between tasks. Poor choice of stimuli may be the reason why their results fail to show a statistical difference between attention conditions. Maison et al. (2001) asked subjects to identify a target stimulus in noise for their attending condition and were given no task instructions for a non-attending condition. Here, they found when subjects were given a more demanding auditory task to focus their attention to; there was a significant reduction in TEOAE amplitude during the attending condition, supporting Avan and Bonfils’ (1992) theory.

Another interesting finding, by Meric and Collet (1994b), suggests that the presence of spontaneous OAEs (SOAEs) changes results in attentional conditions. Meric and Collet (1994b) conducted a study separating subjects into two groups; one consisted of individuals who have SOAEs and another of individuals who do not have SOAEs. Their results showed that TEOAE amplitude during a visual attention task decreased for the group who did not have SOAEs. They concluded that the MOC efferent fibers may play a role in attention for those individuals that do not have SOAEs, while those who do have SOAEs may use the MOC efferent fibers for other cochlear functions.

Froehlich et al. (1993) suggested that attention plays different roles in different parts of the cochlea. They saw a decrease in TEOAE amplitude when comparing

responses to auditory and visual stimuli, but the effects were dependent on the particular frequency under study. There was a significant decrease in absolute amplitude when attending to visual stimuli compared to auditory stimuli at 930–1920Hz, and a significant decrease in absolute amplitude when attending to auditory stimuli compared to visual stimuli at 1920–2880Hz. The MOC system is not equally distributed throughout the cochlea and, therefore, the system may control outer hair cell activity differently at the different testing frequencies, which may explain differences in results across studies.

Data concerning the effects of attention on DPOAEs has been limited. Avan and Bonfils (1992) found no significant difference in DPOAE amplitude across attention conditions; however, variability increased during a visual task. Recently, Smith et al. (submitted) reported a significant difference, in absolute DPOAE amplitude, with different attention conditions. They instructed their subjects to attend to an auditory stimulus by asking them to count brief tones in a random sequence of short and long tones. The non-attending condition required subjects to attend to a visual stimulus by reading DVD subtitles or a book. Their results showed a significant increase in absolute DPOAE amplitude when the subject focused their attention toward a visual stimulus, suggesting an increase in outer hair cell activity. These data agree with TEOAE data from Froehlich et al. (1990), Michie et al. (1996) and Maison et al. (2001), however, they conflict with the results from Puel et al. (1988), Meric and Collet (1994b), and Giard et al. (1994). Unfortunately, there are the only two documented studies using DPOAEs to measure the activity of the outer hair cells by manipulating selective attention (Avan and Bonfils, 1992; Smith et al., submitted). Additional studies must be conducted to determine the results of attention on DPOAE measurements.

Increasing the task complexity has been shown to affect brain activity. Several studies have reported an increase in brain activity correlating to an increase in task complexity (Pugh et al., 1996; Dyson et al., 2005). Pugh et al. (1996) increased an auditory task from an easy binaural task, the same stimulus in both ears, to a more complex dichotic task, different stimuli in each ear. They reported increases in activation with an increase in the difficulty of the task using fMRI measurements. Dyson et al. (2005) reported that subjects tended to be slower and more error prone to harder tasks. Using ERP measurements, they showed a decrease in activity in one area in the brain while showing a concurrent increase in activity to another brain area, suggesting that the sensory systems may interact during presentations of stimuli.

The purpose of this experiment was to study the effects of different attentional loads on MOC efferent function as measured by DPOAE amplitude and rapid adaptation magnitude. We chose to use the paradigm previously selected by Smith et al. (submitted), which required subjects to attend to the tones by counting the brief tones from a series that varied randomly in duration and attend to a visual stimulus by either reading a book or DVD subtitles. This experiment attempted to replicate the previous study and also add a third condition of increased attentional load to the visual stimulus. This condition consisted of playing a video game (Tetris®). The hypothesis was an increase in DPOAE amplitude coinciding with the increased brain activity due to an increased task complexity of playing a video game.

## Methods

Thirty-one human subjects participated in this experiment. Sixty-eight percent of the subjects were female and 87% were in the age group ranging from 18–22. The transducers were calibrated and a distortion product otoacoustic emission gram (DPgram)

was measured at the beginning of each session. A stimulus frequency combination was chosen, as described previously. Prior to the collection of attentional data, frequency levels were optimized by presenting different stimulus levels. The optimization technique mirrored Experiment 1; however, only DPOAEs from 32 stimulus presentations of each level combination were measured. The chosen level combination resulted in DPOAEs with a higher absolute level, larger magnitude of rapid adaptation, a better correlation of fit of the exponential to the DPOAE, or a combination of all three.

Each subject participated in three separate attentional conditions and the subjects were divided into two groups. Group 1 (n=17) consisted of subjects that attended to a visual stimulus by reading DVD subtitles (auditory ignoring), attended to the auditory tones (auditory attending) by counting the number of 3-second long tones in a random sequence of 3- and 6-second long tones, and played a video game (Tetris® on Gamecube®) (auditory ignoring/attention increase) with a wireless controller. Group 2 (n=16) consisted of subjects that attended to a visual stimulus by reading a book (auditory ignoring), attended to the auditory tones (auditory attending) by counting the number of 3-sec long tones in a random sequence of 3- and 6-sec long tones, and played a video game (Tetris® on Gamecube®) (auditory ignoring/attention increase) with a wireless controller. Tetris® was selected as it is a relatively easy game to play without sound that would interfere with DPOAE measurements, little instruction, and only slight physical movement. Distortion product otoacoustic emissions were measured in each condition and graphs were averaged among 128 stimulus presentations. The order of the conditions varied randomly across subjects to control for any extraneous factors such as fatigue.

## Results

Figure 4-1 shows a comparison of the DPOAE contours of subjects, from Group 1, who read DVD subtitles, counted tones, and played Tetris®. The absolute DPOAE amplitude from when subjects were reading DVD subtitles was significantly higher than DPOAE amplitude when counting tones ( $p=0.05$ ), and playing Tetris® ( $p=.025$ ). There was no significant difference in absolute amplitude of the DPOAE when subjects were counting tones and playing Tetris®. The correlation of the fit of the exponential to the DPOAE when subjects were playing Tetris® was significantly lower than reading DVD subtitles ( $p=0.001$ ), and counting tones ( $p=0.001$ ) suggesting more variability of the DPOAEs when subjects played Tetris®. There was no significant difference in the correlation of the fit of the exponential between counting tones and reading DVD subtitles which was previously reported by Smith et al. (submitted).

Figure 4-2 presents DPOAE contours normalized to the DPOAE onset in order to directly compare the rapid adaptation magnitude and time course across attention conditions. There were no significant differences in the rapid adaptation magnitude or time constant across the three conditions. Statistical comparisons across conditions suggest that the DPOAE amplitude was the only measure that changed across attention conditions.

Figure 4-3 presents DPOAEs measured, from Group 2, when subjects read a book, counted tones, and played Tetris®. Comparing the difference in absolute DPOAE amplitude, reading a book was significantly higher than counting tones ( $p= 0.05$ ), and playing Tetris® ( $p=0.02$ ). There was no significant difference in absolute DPOAE amplitude when subjects were counting tones compared to playing Tetris® suggesting that the outer hair cell activity was greater while subjects read a book compared to other

attention conditions. Comparing the correlation of the fit of the exponential to the DPOAE, the correlation was significantly lower when subjects were playing Tetris® compared to when they were reading a book ( $p=0.002$ ), and counting tones ( $p=0.04$ ). This suggests that playing Tetris® increases variability of the DPOAE compared to the other conditions, which might be related to physical movement required to play the game. There was no significant difference in the correlation of the fit of the exponential between counting tones and reading a book.

Figure 4-4 presents DPOAE contours normalized to the onset of the DPOAE to compare rapid adaptation magnitude and time constants across the three attention conditions. There were no significant differences across conditions regarding rapid adaptation magnitude and rapid adaptation time constants. This suggests that MOC efferent system consistently suppresses outer hair cell activity across all conditions.

It is important to note the differences in absolute DPOAE amplitude between Figure 4-1 (Group 1) and Figure 4-3 (Group 2). Because the subjects were divided into two groups, individual differences make up the difference in absolute DPOAE amplitude between the groups. There were several subjects in Group 2 who had extremely high absolute DPOAE amplitudes, for all conditions. This resulted in the increased average DPOAE amplitudes shown in Figure 4-3.

## **Discussion**

The current study sought to characterize the effects of selective auditory attention on absolute DPOAE amplitude and rapid adaptation magnitude while also determining the effects of attentional load by increasing the complexity of a task. Distortion product otoacoustic emissions have been studied extensively in non-human animals (Liberman et al., 1996; Sun and Kim, 1999; McGee et al. 2000; Kujawa and Liberman, 2001; Luebke

et al., 2002). The study of selective attention, however, has focused exclusively on humans (Avan and Bonfils, 1992; Smith et al., submitted). In this study, we examined DPOAEs under several attention conditions that required the subject to attend to an auditory or a visual stimulus. The present results replicated previous results showing an increase in absolute DPOAE amplitude when subjects attended to a visual stimulus by reading DVD subtitles or a book (Smith et al., submitted). Our results showed remarkably consistent results across subjects, though our data contrast sharply with the results obtained when using a TEOAE paradigm in that those studies reported increased amplitude when attention was focused to an auditory stimulus (Giard et al., 1994) or a decrease in amplitude when attention was focused on a visual stimulus (Puel et al., 1988; Meric and Collet, 1994b). We suggest that the TEOAE stimulus may not be an effective stimulus to study the effects of selective auditory attention because of its short duration of about 4–20ms. Because the rapid adaptation time constant is 60–100ms, the TEOAE eliciting stimulus is not sufficiently long to produce the MOC reflex (Avan and Bonfils, 1992; Guinan et al., 2003) and it has been suggested that tone duration plays a part in determining the results of an attentional effect (Maison et al., 2001). Distortion product otoacoustic emissions, with longer eliciting tones of approximately 5s, may provide a more effective stimulus, as the MOC reflex should occur before the eliciting stimulus has ended.

Previous investigators have suggested that auditory selective attention alters the sensory perception of auditory stimuli in the central nervous system (Froehlich et al., 1990; Avan and Bonfils, 1992; Giard et al., 1994; Meric and Collet, 1994a; Michie et al., 1996; Puel et al., 1988; Smith et al., submitted). Our results, showing that, during

attention conditions, MOC activity alters the outer hair cell activity within the cochlea (i.e., prior to the transduction process), support this idea.

The suggestion that selective attention has a peripheral component remains controversial. Our results, as well as others, suggest that the outer hair cell activity changes depending on attentional task (Puel et al., 1988; Froehlich et al., 1990; Giard et al., 1994; Meric and Collet, 1994b; Maison et al., 2001; Smith et al., submitted); however, some studies did not show any effects of selective attention on outer hair cell activity (Avan and Bonfils, 1992). We think the differences across studies in outer hair cell activity, in relation to attention conditions, are due to differences in methods in each study. A main difference between studies is the instructions given to the subjects. Several studies request subjects attend to a visual stimulus as a non-auditory attending condition (Puel et al., 1988; Froehlich et al., 1990; Froehlich 1993; Smith et al., submitted) while other studies instructed the subjects to attend to auditory tones in the opposite ear than measuring (Giard et al., 1994; Maison et al., 2001), and some studies only had one real task and compared it to a condition of subjects sitting passively (Puel et al., 1988; Froehlich et al., 1990; Avan and Bonfils, 1992; Froehlich et al., 1993; Meric and Collet 1994b; Maison et al., 2001). It is unclear, however, as to how well subjects followed the instructions, which may lead to inconsistent results between studies.

Task difficulty can lead to changes in activity in the brain. An increase of activity in the parietal lobe has been shown when subjects increased their task difficulty (Pugh et al., 1996). This brain region may control selective attention in audition. Task difficulty may also affect mechanisms peripherally. Meric and Collet (1994a) suggested that asking the participants to perform a task puts a strain on the middle ear of the subject,

which reduces OAE amplitude. Martins et al. (2005) confirmed both results by reporting an increase centrally and a decrease peripherally with an increase in the complexity of a task. In our study, we increased the complexity of our visual task by asking subjects to play a video game. According to Martins et al. (2005), playing a video game should increase the activity in the brain and, therefore, decrease the activity in the periphery. Our data, indicating a statistically significant decrease in DPOAE amplitude with an increase in task complexity when playing Tetris® compared with reading DVD subtitles or a book, support this assertion.

Medial olivocochlear efferent fibers are known to suppress in response to constant and internally generated noise (Kawase and Liberman, 1993; Kawase et al., 1993). Interference may occur with internally generated muscle movements associated with playing Tetris®. Though we instructed our subjects to minimize physical movement while playing Tetris®, we would expect increases of myogenic noise created by the constant movement required to play a video game. Myogenic influences have been shown to affect brain activity measurements as well (Fifer and Novak, 1990; Brunner et al., 1996; Zimmermann and Scharein, 2004). Fifer and Novak (1990) have shown interference with electrical auditory brainstem response (EABR). With an increase in muscle movement, myogenic artifacts increased in EABR recordings, and any identification of auditory responses became impossible. They also reported that anesthetizing these animals alleviated the myogenic interferences. EEG studies have also shown an increase in brain activity with increases in muscular activity (Brunner et al., 1996; Zimmermann and Scharein, 2004). If one role of the MOC efferent system is to suppress background and internally generated noise, as a means of increasing the salience

of transients, it is possible that with sufficient myogenic noise, the MOC efferent fibers caused a reduction in outer hair cell responses to the eliciting tones while the subjects were playing Tetris®, resulting in a decreased absolute DPOAE amplitude. Further studies, without movement, will determine if myogenic artifacts affect DPOAE amplitudes.

This experiment demonstrated that attention influences DPOAEs. Because of the innervation pattern of the cochlea, this effect could only be mediated through the activity of the MOC efferent tracts to the outer hair cells. However, attentional increases in our study produced surprising responses. The use of other activities that manipulate and increase attention without creating myogenic artifacts should be studied.

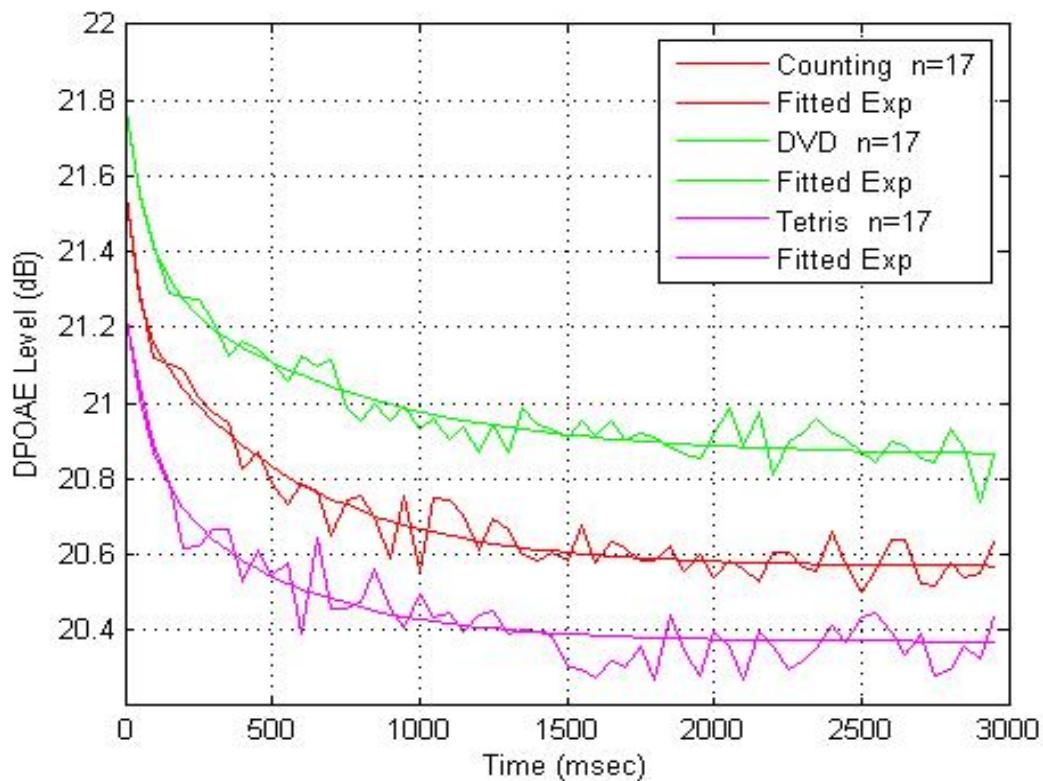


Figure 4-1. Effects of attention on absolute DPOAE amplitudes in Group 1. This figure shows the absolute amplitudes for the three conditions of reading DVD subtitles, counting tones, and playing a video game.

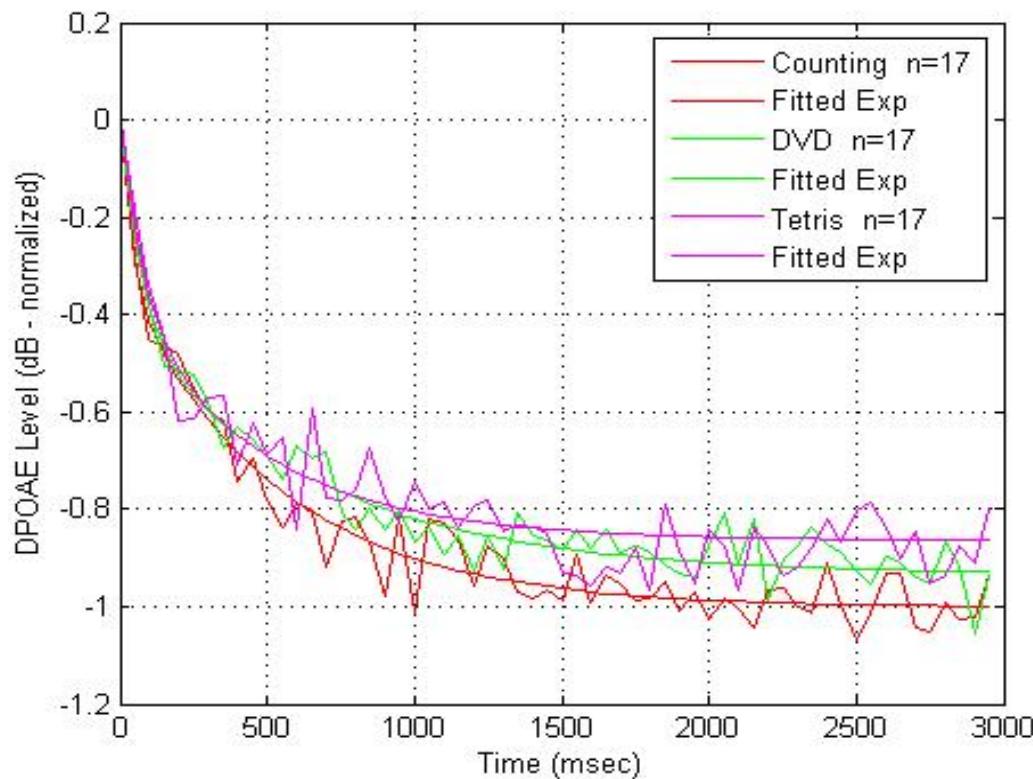


Figure 4-2. Effects of attention on rapid adaptation magnitudes and time constants in Group 1. This figure shows DPOAE contours normalized to the onset of the DPOAE during the three conditions of reading DVD subtitles, counting tones, and playing a video game to compare rapid adaptation across conditions.

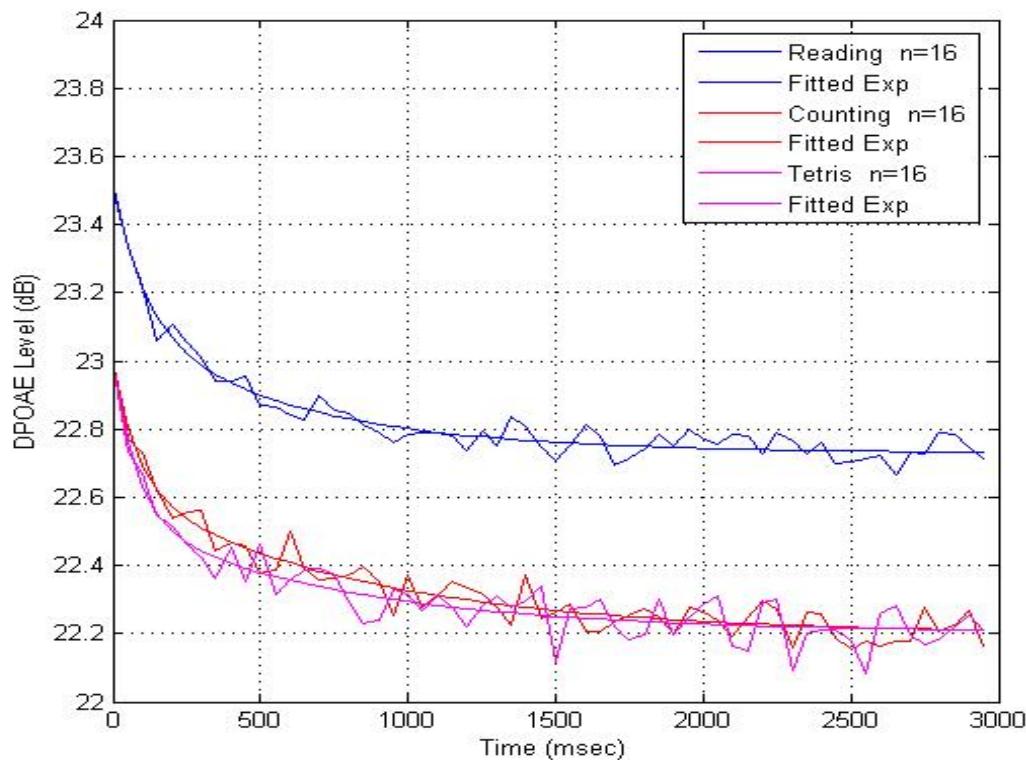


Figure 4-3. Effects of attention on absolute DPOAE amplitudes in Group 2. This figure shows the absolute DPOAE amplitudes for the three conditions of reading a book, counting tones, and playing a video game.

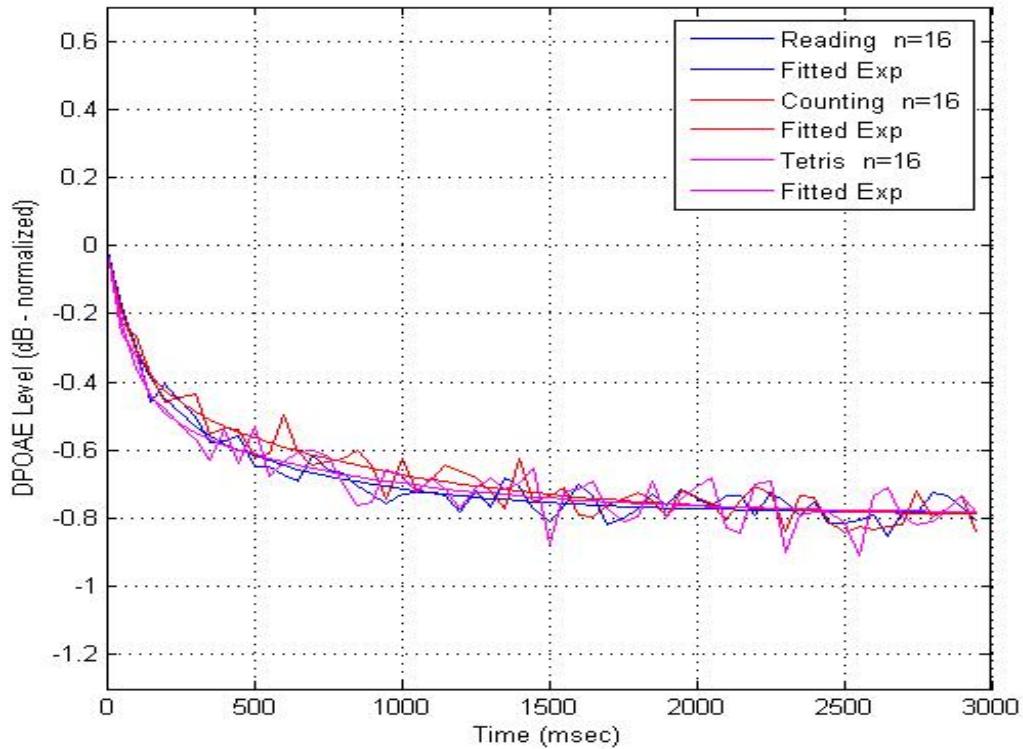


Figure 4-4. Effects of attention on rapid adaptation magnitudes and time constants in Group 2. This figure shows DPOAE contours normalized to the onset of the DPOAE during conditions of reading a book, counting tones, and playing a video game to compare rapid adaptation across conditions.

## CHAPTER 5 EXPERIMENT 3

### Introduction

One aspect of the medial olivocochlear (MOC) efferent function that has not been studied explicitly is whether the activity of these fibers changes due to familiarity and experience with the stimulus or task. Anecdotal evidence (Smith, personal communication) has shown that subjects who returned for subsequent testing had decreased absolute distortion product otoacoustic emission (DPOAE) amplitudes and rapid adaptation magnitudes; suggesting that familiarity and experience affects DPOAE measurements. Meric and Collet (1993) performed a study repeating transient evoked otoacoustic emission (TEOAE) testing on subjects. They noted an increase in TEOAE amplitude, which plateaus during the session 2 and session 3. May et al. (2002) suggested that their mice learn strategies that created inflated results due to highly routine testing procedures. They thought that it was possible that repeated testing could result in normal sensitivity for highly practiced tones but show deficits when presented with an unexpected tone suggesting that practice and experience could change the sensitivity of the ear. They noted that comparing data from a study averaged over five days with their data averaged over several weeks created incongruent results. They concluded that results may vary over time and argued that possible changes over several days of testing can alter results making them appear inconsistent with other studies.

Psychophysical studies in humans have shown similar effects of experience. The psychophysical measurement of overshoot deals with the phenomenon in which the

probability of detecting a tone in background noise is greater if that tone is delayed from the onset of the noise (Zwicker, 1965). It has been argued that overshoot is mediated by an MOC efferent process (Zeng et al., 2000). Zeng et al. (2000) have shown that overshoot is decreased or lost altogether when the MOC efferent fibers are sectioned in human vestibular neurotomy patients; confirming that the MOC efferent reflex plays a role in overshoot. As previously mentioned, rapid adaptation occurs with a time constant of approximately 150ms. Several studies have shown that detection of a transient signal in noise increases when the signal is delayed relative to the onset of a simultaneous masker by approximately 100ms (Carlyon and Sloan, 1988; McFadden, 1989; Bacon, 1990). Schairer (personal communication) has reported decreases in the “overshoot” effect with retesting. Schairer noticed that psychophysical measurements of overshoot get smaller when subjects return for repeated sessions suggesting some influence of experience. Accordingly, if overshoot measurements are changing over time, DPOAE measurements of rapid adaptation magnitude and absolute DPOAE amplitude should change as well.

The purpose of this experiment was to study the effects of experience and familiarity of a stimulus on DPOAE measurements of rapid adaptation. We wanted to determine if this effect is measurable with DPOAEs as it is with TEOAEs and overshoot. We expect to see a decrease in rapid adaptation magnitude and absolute DPOAE amplitude as Smith (personal communication) had suggested.

## Methods

Eighteen human subjects participated in this experiment. We requested the subjects who produced a correlation of fit of the exponential of 0.7 and above on Experiment 1 or 2 to return for 2 additional testing sessions. We chose 0.7 as a criterion

because, presumably, the correlation of fit of the exponential to the DPOAE contour reflects a relatively good signal to noise ratio. The subjects were asked to engage in the same attentional task during each test session. Likewise, the same optimized stimulus parameters were used for each recording. DPOAE responses were averaged for 128 stimulus presentations. Only data from subjects who completed all three sessions were included in the results.

## Results

Figure 5-1 shows a comparison of DPOAE contours averaged across all subjects recorded during the three sessions. The absolute DPOAE amplitude from session 1 was significantly higher than session 2 ( $p=0.01$ ), and session 3 ( $p=0.01$ ). There was no significant difference between session 2 and 3, suggesting that the outer hair cell activity was equivalent during sessions 2 and 3. The correlation of the fit of the exponential to the DPOAE in session 1 was significantly higher than session 2 ( $p=0.007$ ), and session 3 ( $p=0.02$ ). There was no significant difference in the correlation of the fit of the exponential to the DPOAEs between sessions 2 and 3. This suggests that, in session 2 and 3, we measured the same amount of background noise; and session 2 and 3 had a lower signal to noise ratio than session 1.

Figure 5-2 replots the DPOAE contours from Figure 5-1, normalized to the onset of the DPOAE, to compare the rapid adaptation magnitude and time constant across sessions. There were no significant differences in the rapid adaptation magnitude; however, a slight trend showing a decrease in rapid adaptation magnitude over time was observed. There were no significant differences in time constants across the three sessions, suggesting that the suppression of the outer hair cell activity did not change over time even though the absolute DPOAE amplitude did change.

## Discussion

To our knowledge, this is the first study to explicitly test the effects of experience on the DPOAE measurements of absolute amplitude and rapid adaptation magnitude. Our results show a decrease in absolute DPOAE amplitude when subjects returned for subsequent visits. This suggests that outer hair cell activity decreased with repeated testing possibly due to familiarity with the stimulus. Our results confirm the suggestion that activity can change over several days of testing (Meric and Collet, 1993; May et al. 2002, Shraier, personal communication; Smith personal communication). These findings raise questions concerning studies where auditory data are collected for the same stimuli over repeated sessions and all data are averaged together.

Our data contrast with Meric and Collet's (1993) results using short stimuli to produce TEOAEs. They saw an increase in absolute TEOAE amplitude when subjects participated in multiples sessions. In contrast, our data exhibit a decrease in activity with a floor effect at the same point their data plateaued. Again, we see TEOAE measurements contradicting DPOAE measurements with opposite results. These opposing results may be related to the short stimulus duration. The eliciting stimulus is not sufficient for the MOC efferent reflex to occur (Avan and Bonfils, 1992; Guinan et al. 2003). Therefore, Meric and Collet's (1993) change in absolute TEOAE amplitude across sessions may not be due to the MOC efferent fiber activity.

May et al. (2002) suggested that animals respond differently with experience. Kirk and Smith (2003) argued that the MOC efferent fibers are important for biologically relevant stimuli. They suggest that experienced sounds such as wind and water are suppressed by the MOC efferent fibers to detect noises from oncoming predators. Our data agree with this claim and suggest that once a stimulus is labeled safe by the central

nervous system, MOC efferent fibers will suppress the outer hair cell response on future presentations to be able to detect unknown stimuli.

We think that additional studies need to be conducted in order to determine if the MOC efferent fibers suppress outer hair cell activity additionally to our measured sessions; as well as determine if experience has the same effects across attentional conditions. With further testing sessions, a statistical significance may be found comparing rapid adaptation magnitudes over more sessions as a trend toward smaller magnitudes over time was observed. Also, the effect of introducing a new stimulus within the presentation of experienced stimuli needs to be studied using human subjects and a DPOAE measurement to determine if there are any effects with novel auditory stimuli.

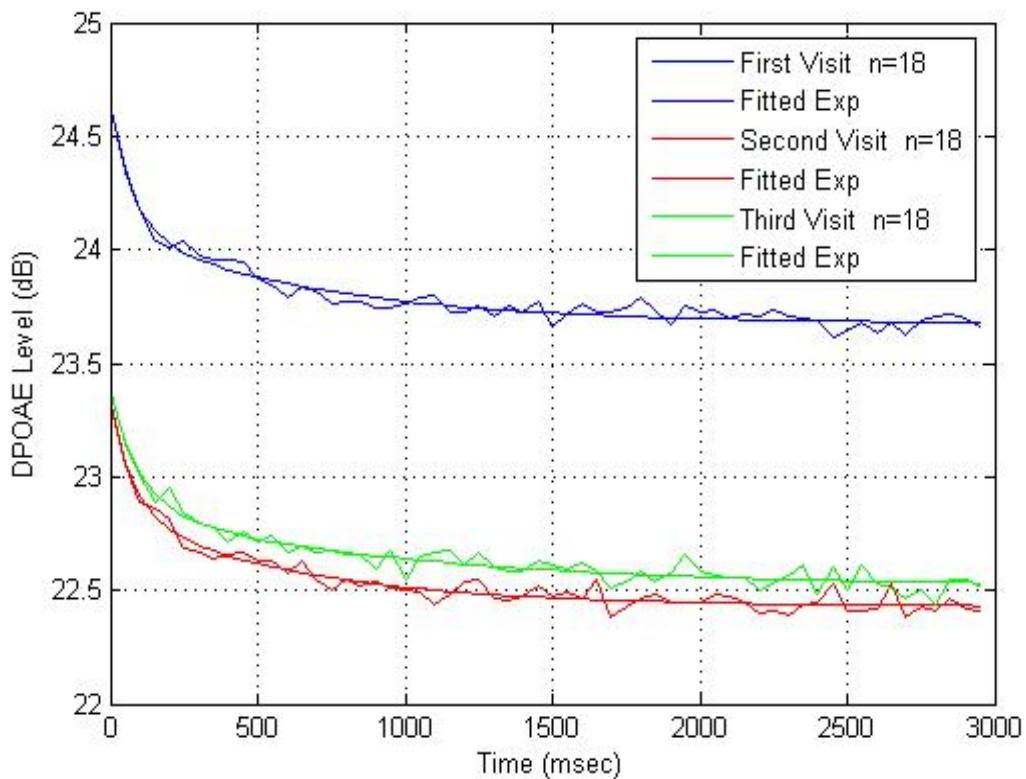


Figure 5-1. Effects of experience on DPOAE amplitudes. This figure compares the absolute DPOAE amplitudes for three subsequent sessions.

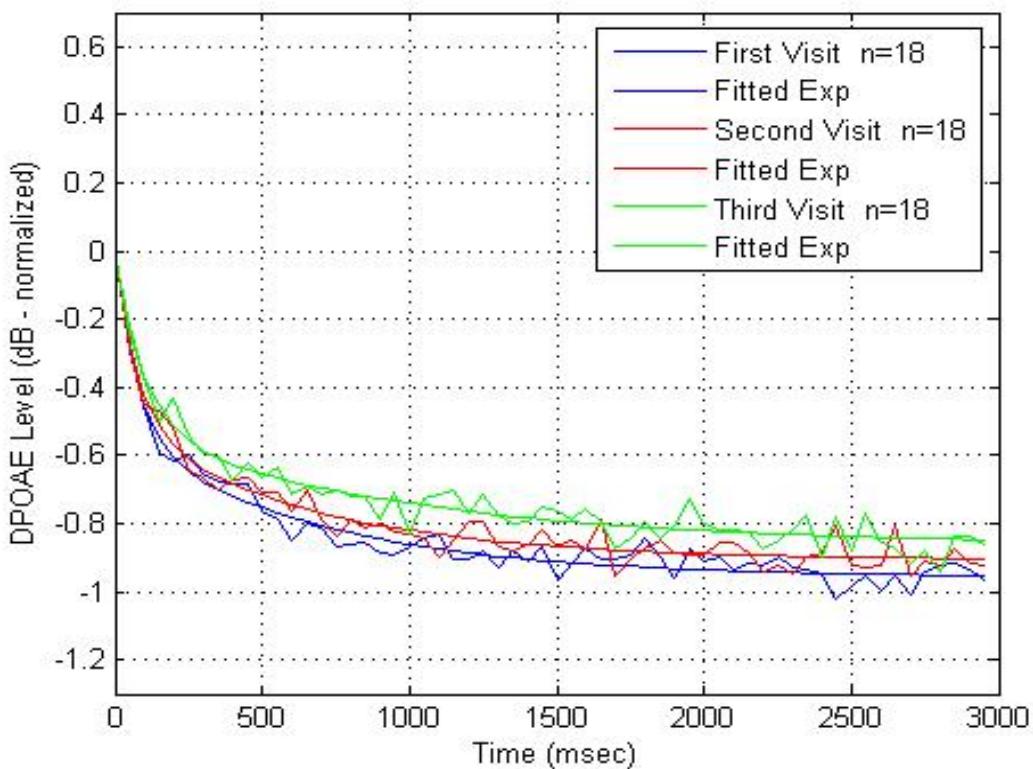


Figure 5-2. Effect of experience on rapid adaptation magnitude and time constants. This figure shows the DPOAE contours normalized to the onset of the DPOAE to compare the rapid adaptation magnitude and time constants across sessions.

## CHAPTER 6 GENERAL CONCLUSIONS

In this master's thesis, we studied the effects of changing stimuli, attentional parameters, and experience on distortion product otoacoustic emission (DPOAE) measurements of absolute amplitude and rapid adaptation. These parameters were explicitly designed to study the effects of the activity of the medial olivocochlear (MOC) efferent system on cochlear activity. Experiment 1 focused on changing the stimulus presentation levels and examining the effects on absolute DPOAE amplitude and MOC mediated rapid adaptation. We observed a general increase in rapid adaptation magnitude when increasing the stimulus levels; suggesting that the MOC efferent suppression increased with an increase in stimulus levels. We also noticed an interaction of slow adaptation, which is not controlled by the MOC efferent fibers; arguing there may be other mechanisms influencing the overall effect of the MOC efferent system on DPOAE measurement. We reported no trend between absolute DPOAE amplitude and rapid adaptation magnitudes disagreeing with Whitehead et al. (1995) and Guinan et al. (2003)

Experiment 2 studied the effect of attentional load on DPOAE measurements. Our results showed an increase in absolute DPOAE amplitude when subjects focused on a visual stimulus consisting of reading DVD subtitles or a book compared to when subjects attended to an auditory stimulus; however, absolute DPOAE amplitudes did not increase when the subjects had increased their attentional load by attending to a visual stimulus and playing a video game. Other studies suggest that myogenic artifacts create additional

suppression from the MOC efferent fibers to suppress internally generated noise (Fifer and Novak, 1990; Kawase and Liberman 1993; Kawase et al., 1993; Bruner et al., 1996; Zimmermann and Scharein, 2004). The internally generated noise resulting from playing a video game may have interfered with our DPOAE amplitudes. The issue can be clarified in future studies by development of tasks that increase attentional load and do not require physical movement, therefore, abolishing the myogenic artifacts associated with our video game task.

Experiment 3 studied the effects of repeated stimulation on DPOAEs. We observed a decrease in absolute DPOAE amplitude with repeated testing of the same stimulus. There appears to be a floor effect in absolute DPOAE amplitude, where the absolute DPOAE amplitudes remained relatively constant between sessions 2 and 3. These data suggest that the MOC efferent fibers either suppress the outer hair cell activity when presented with the same stimuli on subsequent sessions or increase the outer hair cell activity during the first presentation of a stimulus.

It is important to note that our results conflict with previous studies using transient evoked otoacoustic emission (TEOAE) measures (Puel et al., 1988; Froehlich et al., 1993; Meric and Collet, 1993; Meric and Collet, 1994b; Giard et al., 1994). When comparing Experiment 2 to the previous studies, our data and other DPOAE data (Smith et al., submitted) suggest an increase in outer hair cell activity, as evidenced by an increase in absolute DPOAE amplitude, when the subjects were attending to a visual stimulus compared to an auditory stimulus. Transient evoked otoacoustic emission data contrast our data with increases in activity to an auditory stimulus or decreases in activity to a visual stimulus (Puel et al., 1988; Froehlich et al., 1993; Giard et al., 1994; Meric and

Collet, 1994b). The results from Experiment 3 suggest that outer hair cell activity decreases during session 2 and 3. Transient evoked otoacoustic emission data by Meric and Collet (1993) show the opposite effect, with absolute TEOAE amplitude increasing and plateauing after the first visit. We think the conflicting results are due to the short-duration of the TEOAE stimulus of 4ms, which is shorter than the suppression reflex at 60–100ms (Avan and Bonfils, 1992; Guinan et al., 2003). This suggests that DPOAE studies can measure the MOC efferent reflex, however, TEOAE studies cannot. These methodological issues need to be kept in mind when comparing TEOAE and DPOAE studies.

The function of the MOC efferent fibers that connect to the outer hair cells is still under review. Several functions of the MOC system have been discussed; the first proposed function suggests that the MOC efferent fibers act to protect the ear from acoustic over-stimulation (Maisong and Liberman, 2000; Rajan, 2001; Vazquez et al., 2001; Le Prell et al., 2003). According to this theory, the MOC efferent fibers suppress the activity of the outer hair cells to protect the ear from noise-induced traumas. Subsequent work, however, has shown that protection cannot be an evolved function of the MOC system (Kirk and Smith, 2003; Smith et al., submitted). Almost all mammals have MOC efferent fibers, though few natural environments contain the required high level acoustic stimuli necessary to damage the inner ear.

The second proposed function is that MOC efferent fibers serve to increase the signal to noise ratio and allow for easier detection of signals in background noise (Winslow and Sachs, 1988; Morlet et al., 1999; Shera, 2002; Brown et al., 2003; May et al., 2004). When MOC efferent fibers are stimulated, transient signals are easier to detect

in background noise (Winslow and Sachs, 1988). Yet when MOC efferent fibers are cut, there is a decreased detection of speech in noise compared with normal patients (Giraud et al., 1997; Kuman and Vanaja, 2004). This function is thought to be important in the natural environment to detect biologically relevant stimuli embedded in natural noise (Kirk and Smith, 2003).

The third proposed function is that MOC efferent fibers provide a peripheral control for an auditory selective attention mechanism (Puel et al., 1988; Froehlich et al., 1990; Avan and Bonfils, 1992; Froehlich et al., 1993; Giard et al., 1994; Meric and Collet, 1994b; Michie et al., 1996; Maison et al., 2001; Smith et al., submitted). These authors reported results showing that absolute OAE amplitude, and presumably MOC efferent activity, changed depending on whether the subjects attend to or away from an auditory stimulus. The data from Experiment 2 confirmed the idea that DPOAEs and, therefore MOC efferent activity, change when attention is directed to an auditory stimulus versus when attention is directed to a visual stimulus. Our results showed, with remarkable consistency, an increase in absolute DPOAE amplitude when subjects were attending to a visual stimulus by reading DVD subtitles or a book. This suggests that outer hair cell activity, which is controlled by MOC efferent fibers, increases during these activities. However, the function of the MOC efferent fibers is still under consideration. Future studies look to verify or contradict these three proposed functions.

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