EFFERENT-MEDIATED CHANGES IN THE COMPOSITE DISTORTION PRODUCT OTOACOUSTIC EMISSIONS SIGNAL AND ITS COMPONENTS: A POTENTIAL TOOL TO INVESTIGATE AUDITORY PROCESSING DISORDER

BY

SHUKRALLAH ABDELRAZEQ

A dissertation submitted to the Graduate Faculty in Speech-Language-Hearing Sciences in partial fulfillment of the requirements for the degree of Doctor of Philosophy, The City University of New York

2013

This manuscript has been read and accepted for the Graduate Faculty in Speech-Language-Hearing Program in satisfaction of the dissertation requirement for the degree of Doctor of Philosophy.

_____	_____
Date	Glenis R. Long, Ph.D. Chair of Examining Committee
_____	_____
Date	Klara Marton, Ph.D. Executive Officer

Supervisory Committee:

Glenis R. Long, Ph.D.

John J. Guinan, Jr., Ph.D.

Valerie L. Shafer, Ph.D.

THE CITY UNIVERSITY OF NEW YORK

Abstract

Efferent-Mediated Changes in the Composite Distortion Product Otoacoustic Emissions Signal and Its Components: A Potential Tool to Investigate Auditory Processing Disorder

By

Shukrallah Abdelrazeq

Advisor: Glenis R. Long, Ph.D.

One of the hallmarks of auditory processing disorder (APD) is difficulty listening in background noise. This difficulty maybe related to the function of the medial olivocochlear (MOC) efferent system, which is hypothesized to provide an anti-masking effect that might aid in speech processing in noise. To test this hypothesis, we investigated the efferent anti-masking hypothesis via efferent-induced changes in the baseline levels of distortion product otoacoustic emissions (DPOAE) in a group of subjects suspected of having APD with speech-in-noise deficits matched for age and gender with a control group with less speech-in-noise deficits. There was no significant difference in audiometric thresholds between the groups. We examined not only the typical composite DPOAE, but also the two major components (overlap and reflection components), which determine the overall DPOAE level. We hypothesized that the group with speech-in-noise deficits would show reduced efferent effects relative to the control group. The findings did not support the efferent anti-masking hypothesis as efferent-induced changes in the composite DPOAE signal and the overlap component did not differ significantly between the two groups, but the statistical power was low. The separation of the two DPOAE components was beneficial in detecting efferent effects at the high frequency region where the DPOAE levels were lowest, and efferent effects were variable. The mean baseline levels and SNR of composite DPOAE and the overlap component were lower in the group with speech-in-

noise deficits than the control group. This difference was not significant, but the statistical power was low. In addition, no significant correlations were found between performance on speech-in-noise tests and DPOAE change due to efferent activation across groups. Factors that might explain why the efferent anti-masking hypothesis was not supported are discussed.

Acknowledgments

I would like to thank my mentor, Dr. Glenis Long, for her endless support throughout my years at the Graduate Center. At times, it was very difficult to juggle my personal and academic responsibilities, but Dr. Long was instrumental in helping me through my difficult times. I would also like to thank her for standing by me when I fell ill toward the end of my Ph.D. program. I would like to thank Dr. John Guinan for his tremendous support and wealth of knowledge in the efferent system. I could never thank him enough for answering my endless emails. I would like to thank Dr. Shafer for her invaluable input that helped me in my data analysis. Also, I would like to thank Dr. Prieve for participating as an external examiner in my defense and for her important suggestions that helped me immensely in editing my thesis.

Also, I would like to thank Dr. Donna Geffner for her immense support that made it possible for me to recruit my subjects at St. John's University. She is the one who sparked my interest in the area of central auditory processing in Audiology. She is a wealth of knowledge, and I learned so much from her during my tenure at St. John's University. I am very thankful for her guidance and endless support.

Finally, I would like to thank my wife Ana, my daughter Miriam, and my son Samir for their patience and for believing in me throughout my career.

Table of Contents

List of Tables

List of Figures

List of Appendices

Chapter I. Introduction

Auditory processing disorder (APD) is an umbrella term that encompasses different types of deficits (e.g., auditory discrimination, auditory processing in competing conditions, temporal processing) that are thought to be the result of neurobiological abnormalities in the central auditory nervous system (American Speech-Language-Hearing Association [ASHA], 2005). APD has also been described more broadly as a deficit in perceiving verbal and non-verbal auditory stimuli (British Society of Audiology [BSA], 2011). Others have described APD as an impairment in processing non-speech sounds in the absence of a peripheral deficit (Moore, 2006), influenced primarily by top down cognitive processing (Moore et al., 2010), or as a dysfunction in processing auditory information in environments that are not conducive to optimal listening (Jerger and Musiek, 2000). This lack of consensus defining APD contributes to the inability to attain a gold standard for the diagnosis of this disorder (ASHA, 2005; Moore, 2006; American Academy of Audiology [AAA], 2010; BSA, 2011) and highlights the importance of researching its neurobiological underpinnings, which might ultimately lead to better diagnosis and remediation strategies for APD.

APD can either be developmental or acquired (ASHA, 2005; AAA, 2010; BSA, 2011). Developmental APD is thought to be the result of neuro-maturation delay in the auditory system. This view was supported by the findings that performance on central auditory processing tasks was influenced by developmental changes (Moore et al, 2011; O'Beirne et al., 2012). In addition, developmental APD can co-exist with other neuro-developmental disorders (e.g., language, attention) (Bellis, 2003; ASHA, 2005; AAA, 2010; BSA, 2011). Acquired APD can be associated with hearing impairments, head trauma and neurological diseases of the central nervous system (Bellis, 2003; ASHA, 2005; AAA, 2010; BSA, 2011). Therefore, APD is better

understood when one takes into account the complex interaction between bottom up (sensory) and top down processing (cognitive, attention, memory). APD can be thought of as a bottom up disorder that involves a dysfunction in mechanisms that dominate auditory processing prior to higher order cognitive and linguistic operations at the cortical level. However, bottom-up processing does not occur in a vacuum due to the interconnectedness of the auditory modality and other regions in the central nervous system (ASHA, 2005; Musiek et al., 2005; Moore, 2006; AAA, 2010; BSA, 2011). Thus, the co-morbidity between APD and other disorders maybe due to shared neural substrates (AAA, 2010).

There is much controversy surrounding the heterogeneity of developmental APD and the validity of its diagnosis when it co-exists with language disorders (ASHA, 2005; AAA, 2010). The crux of this controversy revolves around a possible confounding linguistic effect on performance in auditory tasks. While linguistic confounds cannot be ruled out in the case of auditory-language co-morbidity, there are three major points that might contribute to resolving this controversy. First, the comparison between APD test battery results and language testing results may help to uncover a possible auditory component underlying the language disorder, which will lead to better understanding of the auditory-language co-morbidity (Bellis, 2003; ASHA, 2005; AAA, 2010). Second, the inclusion of both verbal and non-verbal auditory tasks as part of the APD test battery may help to differentiate between auditory deficits versus a language-related deficit (ASHA, 2005, AAA, 2010). Third, the comparison between performances in auditory tasks presented in an un-manipulated versus manipulated conditions. In essence, if a child can perform the auditory task in the un-manipulated condition (stimulus is intact) but s/he has difficulty in performing the same task when the acoustic signal is manipulated (e.g., stimulus presented in a competing condition or distorted), this discrepancy in

test performance may argue against the influence of linguistic confounds in favor of an auditory deficit underlying the child's APD diagnosis (AAA, 2010).

One of the hallmarks of APD is difficulty listening in the presence of noise (Katz, 1992; Chermak et al., 1999, 2002; Jerger and Musiek, 2000; Bellis, 2003; ASHA, 2005; AAA, 2010). This difficulty maybe related to a dysfunction in the medial olivocochlear (MOC) efferent system, which plays a major role in modifying cochlear response in the presence of noise (reviewed in Guinan, 2011). The MOC system consists of neural fibers originate bilaterally in the medial region of the superior olivary complex and descend to the cochlea, where they synapse directly on the outer hair cells (OHCs) (Warr and Guinan, 1979; Liberman, 1980; Guinan et al., 1983; Guinan et. al., 1984). The characteristic frequency (CF) of afferent fibers is similar in frequency to the best frequency of the MOC fiber innervating that region (Liberman and Brown, 1986).

The MOC system provides an anti-masking effect by acting on the OHCs to reduce cochlear amplification of noise, leading to reduced basilar membrane (BM) motion to the noise (Murugaso and Russell, 1996; Russell and Murugaso, 1997; Dolan et. al. 1997). One consequence is that some of the neurotransmitter supply at the afferent-inner hair cell synapse, normally depleted during noise stimulation in the absence of MOC activation, will be partially preserved (Guinan, 2006), resulting in enhanced auditory nerve dynamic range (Nieder and Nieder, 1970; Dollan and Nuttal, 1987; Winslow and Sachs, 1987; Winslow and Sachs, 1988; Kawase et al., 1993; Kawase and Liberman, 1993). This increased dynamic range is believed to play a major role in improving signal-to-noise (SNR) (Dewson, 1967; Winslow and Sachs, 1987) that can potentially aid in the detection of signals embedded in noise (Winslow and Sachs, 1988; Kawase et al., 1993; Brown et al., 1998). This hypothesis is supported by studies in which

cutting efferent fibers resulted in poorer performance on tasks administered in the presence of noise in both animals (Dewson, 1968; May and McQuone, 1995; Heinz et al., 1998) and humans (Giraud et al., 1997).

In humans, the strength of the MOC system may be estimated non-invasively by measuring changes in evoked otoacoustic emissions (EOAE) (reviewed in Guinan, 2011). EOAE are sound-evoked emissions generated by the healthy cochlea and measured after their reverse transmission through the middle ear to the ear canal (Kemp, 1978). EOAE generation depends on the enhancement of BM motion by OHCs motility (cochlear amplifier) (for review, see Cooper et al., 2008). Because the MOC fibers terminate on the OHCs, they are in a position to alter the dynamics of the cochlear amplifier. As such, the OHCs are considered a functional connection between EOAE and the MOC system because they are influenced by MOC activation and play a major role in the generation of EOAE. This functional connection makes it possible to detect efferent effects via changes in EOAE (reviewed in Guinan, 2011). One important confounding factor, however, that must be accounted for to ensure the validity of estimating efferent-induced changes in EOAE is the possible activation of the middle ear muscle reflex (MEMR) at moderate to high stimulation levels (reviewed in Guinan, 2006). When the MEMR is activated, it affects the properties of the acoustical signal going to and from the cochlea, thereby modifying OAE measurements, which can be erroneously interpreted as efferent effects. Phase analysis and changes in ear canal sound pressure have been used to monitor MEMR activation (e.g., Guinan et al., 2003; Lilaonitkul and Guinan, 2009 a&b; Henin et al., 2011; Henin and Long, 2012).

There are different types of EOAE. Distortion product otoacoustic emissions (DPOAE) are produced when two pure tones (f_1, f_2, $f_2>f_1$), known as primaries, are used to stimulate the cochlea. Because the cochlear response is nonlinear, inter-modulation between the two primaries

gives rise to multiple distortion products, when both stimulate the same cochlea region. The most robust DPOAE is $2f_1$-f_2 generated when $f_2/f_1 = 1.22$.

Theoretical modeling of DPOAE generation (e.g. Shera and Guinan, 1999; Talmadge et al., 1999) has proposed that the DPOAE measured in the ear canal is a composite signal comprised of at least two major components with two distinct mechanisms underlying their generation: the overlap and reflection components (reviewed in Shera and Guinan, 2007). The overlap component (also known as generator, nonlinear or distortion component) is generated by non-linear mechanisms just basal to the region of maximal overlap between the traveling waves generated by the primaries. The phase of this component does not change much when the primaries change while keeping primary ratio unchanged. The overlap region moves along the BM, and the number of traveling waves to peak remains relatively unchanged, giving the overlap component its shallow phase characteristics. In contrast, the reflection component (also known as the CF component) is generated by linear mechanisms at pre-existing perturbations scattered along the BM after a portion of the overlap component energy travels on the BM to reach its CF place (e.g. $2f_1$-f_2). The traveling wave of the reflection component slows down when it approaches the region near its CF, resulting in the reflection component having steep phase characteristics (e.g. Shera and Guinan, 1999; Talmadge et al., 1999). The same linear mechanisms that underlie the generation of the reflection component also generate transient evoked otoacoustic emissions (TEOAE) and stimulus frequency otoacoustic emissions (SFOAE) (e.g., Shera and Guinan, 1999; Kalluri and Shera, 2001; 2007). Amplitude and phase interactions between the two DPOAE components give rise to a pattern of pseudo-fluctuations in the form of minima and maxima seen in the composite DPOAE signal (both components measured together) recorded in the ear canal. This fluctuation pattern is known as DPOAE fine structure (e.g., He

and Schmiedt, 1993; Mauermann et al., 1999a&b).

The two-source model underlying DPOAE generation has been supported by three major findings. First, changes in DPOAE fine structure when the reflection component was suppressed (e.g., Heitmann et al., 1998; Talmadge et al., 1999; Kalluri and Shera, 2001; Mauerman and Kollmeier, 2004; Johnson et al., 2006). Second, concomitant changes in the phase and amplitude of DPOAE fine structure as predicted by mathematical modeling (Talmadge et al., 1999). Third, the unmixing of the composite DPOAE signal based on differences in latencies between the two components (e.g., Kalluri and Shera, 2001; Mauermann and Kollmeier, 2004; Dhar et al., 2005; Long et al., 2008, 2009).

The different origins of the two components suggest that each component might be differentially sensitive to factors affecting cochlear function, such as efferent modification of the cochlear amplifier. However, it is difficult to decipher these differential effects if one just examines the composite DPOAE signal without separating the two components. Furthermore when the two DPOAE components are not separated, both suppression (decrease in OAE amplitude) and enhancement (increase in OAE amplitude) are seen in the composite DPOAE signal during efferent activation due to the interaction between the two components (Wagner et al, 2007; Zhang et al., 2007; Sun, 2008; Abdala et al., 2009; Deeter et al., 2009; Henin et al., 2011). When the components are separated, there is evidence that the reflection component changes more with efferent activation than the overlap component (Abdala et al., 2009; Deeter et al., 2009; Henin et al., 2011). One possible interpretation for the greater sensitivity is due to energy traveling from the overlap region to the DP frequency place being amplified before being reflected back. In contrast, the overlap component does not travel apically after generation and consequently does not get amplified (Talmadge et al., 1999; Shera and Guinan, 1999). In

addition, the reflection component is often lower in amplitude than the overlap component when $f_2/f_1 = 1.22$, which is widely used in clinical and research settings. This difference in amplitude between the two components makes the reflection component potentially more susceptible to the effects of the cochlear amplifier, which plays a greater role at low levels (reviewed in Cooper et al., 2008).

Previous human investigations of the efferent anti-masking hypothesis have yielded mixed results. When the correlation between masking and MOC evoked changes in OAE was examined (summarized in Tables 1, 2), some investigators found no significant correlation (Harkrider and Smith 2005; Mukari and Mamat, 2008; Wagner et al., 2008; Stuart and Butler, 2012), significant negative correlation (Micheyl et al., 1995; Garinis et al., 2011; de Boer et al., 2012) or significant positive correlation (Micheyl and Collet, 1996; Micheyl et al., 1997; Kumar and Vanaja, 2004; Yilmaz et al., 2007; Bhagat and Carter, 2010). Similarity, results were also mixed in studies that investigated the efferent anti-masking hypothesis in individuals with APD or auditory listening problems. Efferent inhibition in such subjects was significantly less than control subjects in some studies (Muchnik et al., 2004; Yalcinkaya et al., 2010), but not in others (Sanches and Carvallo, 2006; Burguetti et al., 2008; Butler et al., 2011) (summarized in Table 3). These inconsistent results may stem from differences in the behavioral task parameters (SNR, type of stimuli), the different types of methods used to estimate efferent magnitude, and the lack of MEMR monitoring. These issues will be covered in more detail in the discussion section.

Although efferent anti-masking hypotheses in individuals with speech-in-noise problems have been investigated before using efferent-induced changes in different types of OAE, efferent-induced changes in DPOAE components have not been reported. Therefore, the goal of this dissertation was to investigate whether a dysfunction in the MOC system could underlie

speech-in-noise deficits in individuals suspected of having APD. We anticipated that estimates of efferent-induced changes in both the composite DPOAE signal and its components might facilitate the evaluation of a potential association between speech-in-noise deficits and efferent function. We hypothesized that individuals with speech-in-noise deficits will show reduced efferent effects when compared with a control group with less speech-in-noise deficits. We also hypothesized that performance on speech-in-noise tests will be significantly correlated with efferent-mediated changes in DPOAE.

Chapter 2. Method

2.1. Subjects

Eighty-five subjects were recruited for this study. All testing was done at St. John's University's Speech and Hearing Center. The majority of the subjects had prior scheduled appointments because they were suspected of having APD. These subjects were administrated a behavioral APD test battery. Other subjects (14 subjects) were recruited by the word of mouth to potentially increase the number of control subjects in the study, and they were only administered two speech-in-noise tests that are part of the APD test battery (with the exception of one subject who was only administered one speech-in-noise test and thus was not included in the study). The Parents/guardians of all children signed a consent form for their children to participate in the study. St. John's University's and the Graduate Center of the City University of New York's Institutional Review Boards approved all procedures and consent forms.

All subjects had to satisfy an inclusion criteria consisting of: Normal hearing thresholds (equal or less than 20 dB HL at .5 - 4 kHz), normal 226 Hz admittance tympanograms (type A) in the right ear, normal stapedial reflexes thresholds (Gelfand et al., 1990), completion of two speech-in-noise tests, no major changes in ear canal primary level used to monitor both calibration and possible MEMR activation, consistent up and down sweeps in DPOAE fine structure and the presence of at least + 6 dB DPOAE SNR. Only 48 subjects out of the total 85 subjects who were tested met the inclusion criteria. Exceptions were made to include three more subjects. One subject was included in both the more restrictive analysis and the more inclusive analysis even though the subject's tympanogram was not assessed due to partial testing. Two subjects were included in the more inclusive analysis. One subject's hearing sensitivity and tympanogram were not assessed due to partial testing and the other subject's tympanogram could

not be obtained due to the subject's very narrow ear canal. Therefore, a total of 51 subjects took part in the study.

After testing, subjects were divided into two groups based on performance on two speech-in-noise tests. According to certain criteria, subjects were either labeled as "impaired" (impaired group) or control (control group). Subjects who scored at or below the 10^{th} percentile on at least one speech-in-noise test and at or below the 25^{th} percentile on the other test were placed in the impaired group. Subjects who scored at or above the 25^{th} percentile on both tests were placed in the control group. After matching subjects from the impaired group with control subjects for gender and age (within one year with the exception of two subjects who were matched within 14 months and within 20 months), 10 pairs of subjects remained (3 females and 7 males in each group). The mean age of the subjects in the impaired group was 11.33 years (range = 9.59 years; SD = 2.89). The mean age of the control subjects was 11.28 years (range = 10.91 years; SD = 3.09). Three subjects in each of the impaired and control groups had an existing morbid condition according to parent report (in the impaired group: ADHD, Asperger-pervasive developmental disorder-not otherwise specified; in the control group: autism, pervasive developmental disorder-not otherwise specified, seizures). When a less restrictive criterion to separate the impaired and control groups based on speech-in-noise performance was implemented, this resulted in more subject pairs, but less consistency within each group and more overlap in performance on the speech-in-noise tests.

2.2. Behavioral APD Test Battery

The core of the behavioral APD test battery administrated at St. John's University's Speech and Hearing Center consists of: A) The Buffalo Model tests (Katz, 1992; also see Katz, 2007), B) Tests for Auditory Processing Disorders for Children (Scan-3:C, Keith, 2009a) and in

Adolescents and Adults (Scan-3:A, Keith, 2009b). In this dissertation, only the performance from the right ear on the Speech-in-Noise CID-W22 (hereinafter referred to as the CID-W22 test) that is part of the Buffalo Model and the Auditory Figure Ground (AFG) test that is part of the Scan-3 test, were used in order to investigate the efferent anti-masking hypothesis (see Table 4 for behavioral scores on APD tests for the impaired and control subjects in the more restrictive groups).

The CID-W22 test (Modified CID W-22 words, Hirsh, 1952) is recorded on a compact disc (Precision Acoustics, Vancouver, WA) and is used to evaluate the ability to recognize speech embedded in background noise. This test was presented at 40 dB SL above the speech recognition threshold, and consists of 25 monosyllable words presented in quiet first then in the presence of speech spectrum noise at +5 SNR. The AFG test is recorded on a compact disc (Pearson, San Antonio, TX) and it consists of 40 monosyllabic words (20 words in each ear) embedded in a multi-talker speech babble noise presented at +8 dB SNR up to age 12 years and at 0 dB SNR for ages 13 years and above. This test started with practice items and was presented at 50 dB HL. In both tests, subjects were asked to repeat the words they heard and scoring was based on repeating the whole word. No partial credit was given. Because the AFG test is based on scores obtained from both ears, the right and the left ear scores are reported. Only right ear scores are reported from the CID-W22 test.

In the more restrictive group, two impaired subjects complained about static during the administration of the CID-W22 test (one subject in the quiet condition and another subject in the noise condition). In the more inclusive group, two impaired subjects complained about static during the administration of the CID-W22 test in noise and another subject complained about static during the administration of the CID-W22 test in noise and the AFG tests. The test was

then repeated without static and these scores were used in the analysis.

In order to control for the effect of different SNRs in the two speech-in-noise tests, we converted the CID-W22 raw scores into percentile scores by calculating the z scores. No such conversion was necessary for the AFG test as percentile scores were readily available as part of this test's age-normed criteria. Pearson correlation coefficients between the percentile scores of the two speech-in-noise tests as well as between percentile scores and efferent-mediated changes in DPOAE level within and across subject groups were obtained. Correlations within and across groups between the two tests were done to establish whether the two tests were separating the two groups based on speech-in-noise ability.

2.3. DPOAE

2.3.1. DPOAE Recordings

DPOAE were recorded using a sweeping-primary procedure (Long et al. (2008, 2009). The primaries were swept logarithmically over two octaves (f_1 = 820-3280 Hz, f_2 = 1-4 kHz at f_2/f_1=1.22 producing $2f_1$-f_2 at 640-2560 Hz). The levels of the primaries (L_1, L_2 for f_1 and f_2 respectively) were presented to the right ear at 59 and 50 dB SPL respectively (according to the scissors paradigm $L_1 = 0.4*L_2+39$ dB, Kummer et al., 1998). The primary and DPOAE frequency range included frequencies that are crucial for speech processing. The sweep rate was 2 seconds per octave, giving a total of 4 seconds per sweep. Contralateral acoustic stimulation (CAS) (band pass noise, 0.5-6kHz) was presented at 60 dB SPL in the left ear to evoke the MOC system. CAS started 500 ms before the onset of primaries in order to allow the MOC system ample time to be activated before the onset of primaries in the right ear as the build-up time of medial efferent fibers was reported to be around 200 ms (Backus and Guinan, 2006). The primary and CAS levels were chosen to provide a good SNR rate while minimizing possible

activation of MEMR (Henin et al., 2011, 2012).

2.3.2. Data Collection

Signal generation and data recording were done using custom software (written by Carrick Talmadge and described in Long et al, 2008) on a Mac-Book Pro laptop connected via firewire to a MOTU 828 mkII audio-interface (Cambridge, MA) set to 24 bit/ 44100 Hz. The two primaries passed through HB6 headphone buffer before passing through the booth wall and stimulating two ER2 (Etymotic Research, Elk Groove Village, IL) tube phones (to deliver primaries) connected to an ER10 (Etymotic Research, Elk Groove Village, IL) microphone placed in the right ear canal. A third ER2 tube phone (to deliver CAS) was placed in the left ear. The signal picked up by the microphone was pre-amplified by a battery-operated Etymotic preamplifier before being digitized by the MOTU audiointerface and streamed to disk on the laptop to be analyzed offline.

Up (f_2 = 1-4 kHz) and down (f_2 = 4-1 kHz) sweeps with and without CAS were presented in an interleaved manner so that a pair of up and down sweeps without CAS was followed by a pair of up and down sweeps with CAS. There was a minimum of 12 pairs of up and down sweeps with and without CAS, giving a total of at least 48 runs during the recording session. Each recording session lasted approximately 10-15 minutes. Recordings of white noise were done at the beginning and end of the recording session to check probe fit. Probe fit was also evaluated by examining the primary levels from each sweep.

Data were processed offline using an artifact rejection program written by Selesnik and Hajicek (2010) and modified by Simon Henin, a member of our lab at the Graduate Center-City University of New York. The artifact rejection program calculates an estimate based on how the sound stimulus differs from a predicted pattern for the recorded file. This is used to give weights

to each section of the sound files depending on how well it fitted the prediction. When the sound files were averaged, the contribution of each time window from each sound file depended on these weights. This means that for each point, the sound files with the least estimated noise contributed more towards the calculated average in order to get the lowest possible noise (i.e., calculating a "weighted" average).

2.3.3. Extracting Composite DPOAE and Its Components

Wideband least square fit (LSF) analysis (Long and Talmadge, 1997, Dhar et al, 2005; Long et al, 2009) was used to extract the composite DPOAE signal, while narrowband analysis with a latency-dependent filter was used to extract the two DPOAE components (Long et al., 2009; Henin et al., 2011). The LSF method models DPOAE stimulus and the expected signals. These are compared with the ear canal signal. The DPOAE and signal components in the model are then manipulated until the mean square errors between the model and the ear canal signal are minimal. The LSF permits the extraction of either composite DPOAE or separation of the two components by changing the filter bandwidth used in the analysis. The width of the filter depends on the sampling rate and the number of points in analysis window (filter bandwidth = sampling rate / number of analysis points). Composite DPOAE was extracted using wideband analysis relying on both components falling within the resulting wide filter (8 Hz filter). To extract the two components from the ear canal signal, we used narrowband analysis. To achieve this, the number of points in the analysis window was increased (when the analysis window is longer, the filter gets narrower), which resulted in a narrower filter (2 Hz) that resulted in the overlap component being extracted (see Long et al, 2008). Another frequency-dependent filter was used to extract the reflection component (Long et al., 2009; Henin et al., 2011).

The sweep analysis procedure provides detailed information about the change in DPOAE level with frequency. In order to reduce the amount of data collected, the root-mean-square (RMS) of the DPOAE power in 1/3 octave bandwidth were obtained (the center frequency of the bandwidth was incremented in 1/3-octave steps). This minimized the impact of low-level points falling in the vicinity of any DPOAE minima.

2.3.4. Estimating Efferent-Mediated Changes in the Composite DPOAE Signal and Its Components

The strength of efferent function was inferred by calculating differences in the magnitudes (ΔOAE) between the composite DPOAE signal and its components obtained during the No-CAS (baseline) and CAS conditions. The RMS analysis was done on raw ΔOAE values. To minimize the contamination of the data by points near the noise floor, only DPOAE with amplitudes at least +6 dB SNR above the noise floor were included in the analysis. Delta DPOAE values were also binned into three frequency regions: low (up to 1 kHz), middle (1.1-1.4 kHz) and high (above 1.5 kHz) regions. Choosing these frequency bins was based on visual inspection of the data by establishing which frequencies had the largest efferent effects.

Two methods of estimating efferent strength were used: A) dB difference method (ΔdB OAE): this method subtracts the OAE level in dB in the CAS from the OAE Level in dB from the No-CAS conditions, B) Percent change (Δ %Pa OAE): this method calculates ΔOAE as a percent pressure change relative to baseline.

2.3.5. Monitoring MEMR

Changes in primary level in the ear canal with and without the presence of CAS were used to detect whether MEMR activation contaminated the data. Major changes in primary levels in the ear canal were interpreted as being the result of changes in tympanic membrane

compliance and thus indicative of possible MEMR activation (Guinan et al., 2003; Lilaonitkul and Guinan, 2009 a&b; Henin et al., 2011; Henin and Long, 2012).

2.4. Statistical Analysis

Two separate sets of statistical analyses were done. One statistical analysis was based on more restrictive criteria that included 10 impaired subjects suspected of having APD who scored at or below the 10^{th} percentile on at least one speech-in-noise test and at or below the 25^{th} percentile on the other test, and 10 control subjects who scored at or above the 25^{th} percentile on both tests. This was done in order to ensure that all subjects in the impaired group had a deficit in speech discrimination in the presence of background noise. Another statistical analysis was done using less restrictive criteria in order to include more subjects and potentially increase the power of analysis. Subjects whose scores were one standard deviation below the mean (16^{th} percentile) on at least one test were placed in the impaired group and those whose scores were at or above the 16^{th} percentile on both tests were placed in the control group, resulting in 17 subjects in each of the impaired and control groups.

All statistical analyses were done using the SPSS program (version 20). Pearson correlation coefficients between the percentile scores of the two speech-in-noise tests as well as correlations between percentile scores and estimates of efferent magnitude within and across subject groups were obtained. In addition, two-way mixed analyses of variance (ANOVA) with repeated measures (group x frequency) using the general linear model were performed to investigate differences between audiometric thresholds as well as differences in DPOAE baseline level and estimates of efferent magnitude between the impaired and the control groups by analyzing the effects of group (impaired vs. control), frequency and group-by-frequency interaction. The F test results were corrected and degrees of freedom were adjusted when the

sphericity assumptions were found significant and Bonferroni corrections were done to permit post-hoc analysis of within subject effects.

Chapter 3. Results

The analysis with the more inclusive groups resulting from less restrictive criteria showed lower statistical power in the majority of the analyses than the analysis done with fewer subjects but more restrictive criteria leading to groups that differed more in speech and noise ability. The more inclusive analysis also failed to show a significant main effect of frequency in ΔdB OAE in both composite DPOAE and the overlap component that was seen in the more restrictive analysis (see Tables 9-10, 10A-11A, and also see appendix for overall DPOAE measurements binned into three frequency regions in the more restrictive analysis and for the overall results and tables for all subjects in the more inclusive analysis). The statistical analysis based on more restrictive inclusion criteria is presented throughout this paper along with some comparisons with the more inclusive analysis when such comparisons were deemed appropriate.

3.1. Analysis of Behavioral Testing

Table 4 shows the behavioral scores from all subjects used in the more restrictive analysis. Descriptive statistics of the two speech-in-noise percentile test scores for the impaired and control groups are shown in Table 5. Pearson correlation coefficients between the CID-22 and the AFG percentile test scores were not significant *within* the control ($r = -0.07$, $p = 0.86$) and APD ($r = 0.13$, $p = 0.72$) groups. The percentile scores were then combined to include all scores from the APD and control groups for each test. This resulted in all CID percentile scores from both groups in one large group (combined CID group) and another large group that included AFG percentile scores (combined AFG group). Pearson correlation coefficients were *significant* ($r = 0.63$, $p = 0.00$) between the combined CID vs. AFG groups, but no such significant correlation was found in the analysis based on the more inclusive subject group ($r = 0.23$, $p = 0.2$).

Pearson correlation coefficients between speech-in-noise percentile scores and ΔdB OAE for composite DPOAE and the overlap component were not significant when comparisons were made within groups. Pearson correlation coefficients were also not significant when the results from all subjects (impaired and controls) were combined and comparisons were made between performance on each test and efferent magnitude (combined CID vs. combined ΔdB OAE, and combined AFG vs. combined ΔdB OAE) (Table 6). Similar lack of correlations between ΔdB OAE and percentile scores within and across groups were obtained from the more inclusive analysis (Table 7A).

The ANOVA analysis of audiometric thresholds (Figure 1) revealed that the impaired group did not have significantly different thresholds than the control group [$F(1, 18) = 0.41$, $p = 0.53$], determining that any differences between groups was probably not due to differences in audiometric status. However, there was a significant main effect of frequency [$F(2.16, 38.92) = 11.37$, $p = 0.00$] as higher thresholds were seen at the lower frequencies (500, 1000 Hz). This trend was seen in both groups as the group-by-frequency interaction [$F(2.16, 38.92) = 0.76$, $p = 0.48$] was not significant.

3.2. Efferent-Mediated Changes in DPOAE Levels

3.2.1. Composite DPOAE Signal

The baseline levels of the composite DPOAE signal averaged across the frequency range are shown in Table 7. The mean DPOAE level was lower in the impaired group (2.8 dB SPL) than the control group (5.9 dB SPL). Figure 2 displays the mean composite DPOAE baseline level as a function of frequency for both the impaired and control groups. The mean DPOAE levels ranged from -7.75 to 13.55 dB SPL in the impaired group and between -3.5 to 16.44 dB SPL in the control group, but this difference between groups was not significant [$F(1, 18) = 1.83$,

p = 0.19]. The SNR of the composite DPOAE signal was lower in the impaired group compared with the control group across the frequency range (Figure 3). The mean DPOAE baseline level in both the impaired and control groups was highest in the lower frequency region, then it decreased as frequency increased in the middle frequency region, reaching its lowest level above 1.5 kHz. There was a significant main effect of frequency [F(2.76, 49.67) = 61.31, p = 0.00)], but the group-by-frequency interaction was not significant [F(2.76, 49.67) = 0.61, p = 0.6].

Similar patterns of results were seen for the more inclusive analysis of composite DPOAE baseline level as there was a significant main effect of frequency [F(2.79, 89.33) = 85.62, p = 0.00], but the group [F(1, 32) = 1.08, p = 0.31] and the group-by-frequency interactions [F(2.791, 89.33) = 0.66, p = 0.57] effects were not significant.

Estimates of mean efferent strength as indexed by ΔdB OAE and Δ%Pa OAE and averaged across the total frequency range, for the composite DPOAE signal in both the impaired and control groups are shown in Table 8. The mean estimate of efferent magnitude was higher in the impaired group (-0.61 dB and -11.34 % Pa) than in the control group (-0.47 dB and -7.44 % Pa), but this difference between groups was not significant for ΔdB OAE [F(1, 18) = 0.19, p = 0.67] or Δ%Pa OAE [F(1, 18)= 1.2, p= 0.29]. Figure 4 depicts the efferent-mediated changes in the composite DPOAE signal indexed by ΔdB OAE and Δ%Pa OAE as a function of frequency for the impaired and control groups. The frequency main effect was significant for ΔdB OAE [F(4.1, 73.77) = 3.1, p = 0.02], but not for Δ%Pa OAE [F(3.41, 61.32) = 2.22, p = 0.09]. The group-by-frequency interaction was not significant for ΔdB OAE [F(4.1, 73.77) = 1.32, p = 0.27] or Δ%Pa OAE [F(3.41, 61.32) = 0.55, p = 0.67].

In contrast, in the more inclusive analysis, the frequency main effect was *not* significant for ΔdB OAE [F(2.53, 80.82) = 2.07, p = 0.12], although similar to the more restrictive analysis,

the frequency effect was not significant for Δ%Pa OAE [F(2.82, 90.29) = 1.52, p = 0.22]. In addition, similar to the more restrictive analysis, the effects of group for ΔdB OAE [F(1, 32) = 0.01, p = 0.94] and Δ%Pa OAE [F(1, 32) = 0.05, p = 0.83], as well as the group-by-frequency interactions for ΔdB OAE [F(2.53, 80.82) = 0.59, p = 0.59] and Δ%Pa OAE [F(2.82, 90.29) = 0.99, p = 0.4] were not significant.

The impaired group showed both suppression and enhancement when CAS stimulation evoked efferent activation at the high DPOAE frequencies (Figure 4). In order to further investigate the effect of frequency, efferent estimates were binned into three frequency regions: low (up to 1 kHz), middle (1.1-1.4 kHz) and high (1.5-2.2 kHz) frequency regions, and a separate ANOVA analysis was done. Table 1A presents the data from individual subjects. There was a significant main effect of frequency for ΔdB OAE [F(1.98, 35.67) = 7.29, p = 0.00] and Δ%Pa OAE [F(1.86, 33.51) = 6.58, p = 0.01]. Figure 5 depicts the efferent-mediated changes in the composite DPOAE signal indexed by ΔdB OAE and Δ%Pa OAE as a function of the three frequency bins for the impaired and control groups. The impaired group had more suppression in ΔdB OAE and Δ%Pa OAE in the low and middle frequency regions than the control group. This group-by-frequency interaction was not significant for ΔdB OAE [F(1.98, 35.67) = 2.84, p = 0.07, with the observed power = 0.52], but there was a *significant* group-by frequency contrast [F(1, 18) = 4.96, p = 0.04, with the observed power = 0.56). Enhancement was seen in ΔdB OAE in the high frequency region in the impaired group. Such enhancement could be related to the interaction between the two DPOAE components, as this effect disappeared when the two DPOAE components were separated (see below). The group-by-frequency interaction was not significant for Δ%Pa OAE [F(1.86, 33.51) = 0.74, p = 0.47].

3.2.2. Unmixing of the DPOAE Signal

In both the impaired and control groups, the mean baseline level of the overlap component was higher in amplitude than the reflection component across the frequency range (Figures 6A, B). As a result, the SNR of the overlap component was greater than the reflection component (Figures 7A, B). Consequently, estimates of efferent-mediated changes in the overlap component were much more reliable and consistent (Figures 8A, B) than estimates based on the reflection component (Figures 9A, B), which varied considerably due to its lower SNR. The effects of noise floor contamination on efferent-mediated changes in the reflection component was evident by the presence of more than 100 Δ%Pa OAE at some frequencies (figure 9B). For this reason, efferent-mediated changes in the reflection component were excluded from further analysis.

The mean baseline levels of the overlap component averaged across the frequency range are shown in Table 6. The mean of the overlap component level was lower in the impaired group (1.86 dB SPL) compared with the control group (5.34 dB SPL). Figure 6A displays the mean of the overlap component level as a function of frequency for the impaired and control groups. The mean of the overlap component ranged from -8.95 to 12.37 dB SPL in the impaired group and between -4.03 to 15.13 dB SPL in the control group, but this difference between groups was not significant [$F(1,18) = 2.03$, $p = 0.17$]. The overlap component level in both the impaired and the control groups was highest in the lower frequency region and decreased as frequency increased in the middle frequency region, reaching its lowest level in the higher frequency region. There was a significant main effect of frequency [$F(2.14, 38.51) = 55.03$, $p = 0.00$], but the group-by-frequency interaction was not significant [$F(2.14, 38.51) = 0.76$, $p = 0.48$].

Similar results were found in the overlap component level from the more inclusive analysis; there was a significant main effect of frequency [$F(2.39, 76.61) = 71.09$, $p = 0.00$], but

the group [F(1, 32) = 1.1, p = 0.3] and the group-by-frequency interactions [F(2.39, 76.61) = 0.5, p = 0.64] effects were not significant.

Estimates of efferent strength, as indexed by ΔdB OAE and Δ%Pa OAE averaged across frequency for the overlap component in both the impaired and control groups, are shown in table 8. The mean efferent magnitude was higher in the impaired group (-1.21 dB and -15.18 % Pa) than the control group (-0.82 dB and -10.58 % Pa), but this difference between groups was not significant for either ΔdB OAE [F(1, 18)=1.04, p = 0.32] or Δ%Pa OAE [F(1, 18) = 1.11, p = 0.31]. Figures 8A, B depict the mean efferent-mediated changes in the overlap component indexed by ΔdB OAE and Δ%Pa OAE as a function of frequency for the impaired and control groups. The main effect of frequency was significant for ΔdB OAE [F(3.11, 55.97) = 2.7, p = 0.05], but not for Δ%Pa OAE [F(3.48, 62.7) = 1.82, p = 0.14]. The group-by-frequency interaction was not significant for ΔdB OAE [F(3.11, 55.97) = 0.94, p = 0.43] or Δ%Pa OAE [F(3.48, 62.7) = 0.86, p = 0.48].

In contrast, the frequency main effect for mean ΔdB OAE [F(3.03, 97.03) = 1.36, p = 0.26], was *not* significant in the second more inclusive analysis, although similar to the more restrictive analysis, the frequency effect was not significant for Δ%Pa OAE [F(2.91, 93.13) = 0.94, p = 0.42]. In addition, similar to the more restricted analysis, the effects of group for ΔdB OAE [F(1, 32) = 0.02, p = 0.9] and Δ%Pa OAE [F(1, 32) = 0.02, p = 0.89], as well as the group-by-frequency interactions for ΔdB OAE [F(3.03, 97.03) = 1.34, p = 0.27] and Δ%Pa OAE [F(2.91, 93.13) = 1.62, p = 0.19] were not significant.

The effect of frequency was further investigated by binning efferent-mediated changes in the overlap component into the same three frequency regions used for analyzing composite DPOAE in order to allow for a meaningful comparison between the two analyses. The ANOVA

on this data revealed that there was a main effect of frequency for ΔdB OAE [F(1.53, 27.51) = 5.9, p = 0.01] and Δ%Pa OAE [F(1.75, 31.46) = 3.56, p = 0.05]. Figure 10 depicts the efferent-mediated changes in the overlap component indexed by ΔdB OAE and Δ%Pa OAE as a function of the three frequency bins for the impaired and control groups. The individual data for each subject are presented in Tables 2A. The overlap component showed consistent suppression across the frequency range in contrast to estimates from the composite DPOAE. The ΔdB OAE enhancement in the high frequency region in composite DPOAE (Figure 4A) was not seen in the overlap component, probably stemming from the separation of the DPOAE components and the resulting improvement in SNR in the overlap component when compared with the composite DPOAE signal (Figures 3, 7A). In addition, close visual inspection of the efferent-mediated changes in the overlap component revealed more efferent suppression in the low and middle frequency regions in both groups, but the impaired group had more suppression in these two regions than the control group. However, the group-by-frequency interaction was not significant for ΔdB OAE [F(1.53, 27.51) = 0.23, p = 0.74] or Δ%Pa OAE [F(1.75, 31.46) = 0.34, p = 0.68].

3.3. Monitoring MEMR

We monitored changes in primary level in the ear canal with and without the presence of CAS to detect possible activation of the MEMR. If major changes in primary level in the ear canal were seen, they were interpreted as being the result of changes in tympanic membrane compliance and thus indicative of possible MEMR activation, which could affect the signals traveling to and from the cochlea (Guinan et al., 2003; Lilaonitkul and Guinan, 2009 a&b; Henin et al., 2011; Henin and Long, 2012). Figure 11 shows one of the best examples from one subject (control subject 29) depicting nearly identical primary levels with and without CAS, suggesting that the MEMR effect, if present, was minimal.

Chapter 4. Discussion

Efferent strength in subjects with speech-in-noise deficits and control subjects matched in age and gender was estimated by determining changes in DPOAE level with contralateral stimulation. Correlations between percentile scores on each of the speech-in-noise tests that were used to classify subjects as either impaired or controls were significant, indicating that the two tests were measuring similar underlying skills. In addition to examining the levels of the composite DPOAE signal, the two major DPOAE components were separated to ensure that interactions between the two components did not limit evaluation of efferent strength. This was done using continuously-sweeping primaries (Long et al. 2008). When 1/3-octave RMS averaged DPOAE levels were calculated, there were no significant main effects of subject group on baseline DPOAE levels in either the composite DPOAE signal or the overlap component. However, there was a significant main effect of frequency. DPOAE were larger at frequencies below 1.5 kHz and reduced at higher frequencies. This dependence of DPOAE level on frequency was the same in both groups (the frequency-by-group interactions was not significant). Mean baseline DPOAE levels and the SNR of both the composite DPOAE and the overlap component were lower in the impaired group than the control group. Differences in DPOAE levels between groups were not due to differences in hearing. In order to ensure that the apparent differences in baseline DPOAE level did not contaminate estimates of efferent strength, we evaluated efferent strength not only by subtracting the level in dB of the DPOAE with CAS from the equivalent level without CAS (ΔdB OAE), but also by evaluating the percentage change in DPOAE pressure (Δ%Pa OAE). There were no significant main effects of subject group on efferent-induced changes in either the composite DPOAE signal or the overlap component. However, there was a significant main effect of frequency in ΔdB OAE in both groups with

efferent changes being greater below 1.5 kHz. The group-by-frequency interactions were not significant with the 1/3-octave bins, but when efferent estimates from the composite DPOAE signal were binned into three frequency regions [low (up to 1 kHz), middle (1.1-1.4 kHz) and high (1.5-2.2 kHz)], the group-by-frequency contrast for ΔdB OAE was significant ($p = 0.04$, power = 0.56). The contrast stemmed from an increase in mean DPOAE level (enhancement) in the high frequency region during CAS stimulation in the APD group. This enhancement was only found when the impact of CAS was calculated from the composite DPOAE, and thus it could be due to interaction between the two DPOAE components. When the overlap component was extracted, there was no mean enhancement in any frequency bin, indicating that separation of DPOAE components can improve the validity of estimates of efferent effects (Deeter et al., 2009; Abdala et al., 2009; Henin et al., 2011; Abdala and Dhar, 2012). Overall, the statistical power of the main effects of frequency was the highest (~ 0.5 and above), but the statistical power of group effects and frequency-by-group interactions were lower (less than 0.5) for the remaining comparisons (Tables 9-13).

Based on the anti-masking hypothesis it was predicted that the impaired subjects with speech-in-noise deficits would have less reduction in DPOAE level during CAS stimulation than the controls subjects. Our results did not support this claim. In addition, it was also predicted that there would be significant correlations between mean ΔdB OAE in each subject group and percentile performance on speech-in-noise tests. The correlations were not significant. Our results are in agreement with previous human investigations whose findings were not consistent with the efferent anti-masking hypothesis (Micheyl et al., 1995; Harkrider and Smith, 2005; Sanches and Carvallo, 2006; Mukari and Mamat, 2008; Wagner et al., 2008; Burguetti et al., 2008; Garinis et al., 2011; Butler et al., 2011; de Boer et al., 2012; Stuart and Butler, 2012), but

not with others which supported the anti-masking hypothesis (Michely and Collet, 1996; Micheyl et al., 1997; Kumar and Vanaja, 2004; Muchnik et al. 2004; Yilmaz et al., 2007; Yalcinkaya et al., 2010; Bhagat and Carter, 2011).

Our ability to evaluate the anti-masking hypothesis was limited by the numbers of subjects. Although we started out with a large number of subjects, we were only able to find 10 pairs of matched subjects who were clearly different in their speech-in-noise abilities. Three subjects in the impaired and control groups had an existing morbid condition according to parent report (in the impaired group: ADHD, Asperger-pervasive developmental disorder-not otherwise specified; in the control group: autism, pervasive developmental disorder-not otherwise specified, seizures). Thus, the impaired and control groups may have not been completely heterogeneous. As a consequence, the lack of statistical significance in some comparisons does not necessarily indicate a lack of relationships between the measured variables, but rather that such relationships could not be established due to the small number of subjects and the large variability of the data stemming from the selection of subjects in the present study. The only way that the number of subjects could be increased was to change the criteria for assignment of subjects to the impaired and control groups, which resulted in more overlap in speech-in-noise performance in the two groups. When this more inclusive analysis was done, the variance was larger, leading to a failure to detect the main effect of frequency in ΔdB OAE.

We will discuss the evidence for differences in DPOAE level and efferent strength between our impaired and control groups. We will also discuss certain factors that might explain the discordant findings regarding the role of efferent activation on masking. Such factors include the influence of key parameters, such as SNR and type of stimuli, and the effect of using different types of methods to estimate efferent strength. Finally, comparisons will be made between our

impaired and control groups with previous studies that investigated individuals with APD or auditory listening problems.

4.1. Efferent-Mediated Changes in DPOAE Levels

4.1.1. Composite DPOAE

The pattern of DPOAE levels with frequency was similar to that previously reported when a similar paradigm was implemented (Abdala and Dhar, 2012). DPOAE level was highest in the low and middle frequencies (below 1.5 kHz), then it decreased as frequency increased reaching its lowest level at the higher frequencies (above 1.5 kHz). The mean composite DPOAE level and SNR were lower for the impaired group than for the control group at all frequencies (Figures, 2, 3), but the differences between the groups were not significant.

When efferent-mediated changes in the composite DPOAE signal were averaged across all frequencies, there were small but not significantly greater changes in the impaired group (-0.61 ΔdB, -11.34 Δ%Pa) than in the control group (-0.47 ΔdB, -7.44 Δ%Pa). This is opposite to the predicted reduced efferent magnitude in the impaired group. There was evidence of enhancement at the higher frequencies, which could be due to the interaction between the two DPOAE components when efferent activation differentially affected them. For instance, when total destructive interference between the two components occurs when both components are 180 degrees out of phase and similar in amplitude, it results in a deep DPOAE fine structure minimum. If efferent activity affects the phase of one component but not the other, this results in increased DPOAE levels at some frequencies (enhancement) because the frequency where the two components are out of phase (and thus the dip) will change (Henin et al., 2011).

Our estimates of efferent strength were based on subtracting RMS estimates of DPOAE levels with and without CAS, which included both DPOAE maxima and minima, which would

reduced the range of DPOAE levels. In the low and middle frequency regions, mean reductions of level of up to 1 dB were seen in the both impaired and control groups. This reduction was similar to previous research (Bassim et al., 2003; James et al., 2005; Zhang et al., 2007; Wagner et al., 2008; Mukari and Mamat, 2008; Butler et al., 2011) using a similar paradigm (Abdala et al., 1999). However, the efferent-induced changes in the DPOAE composite signal were lower than the 1.5-1.75 ΔdB OAE of Garinis et al. (2011), who estimated efferent activity only at fine-structure maxima, thus avoiding the impact of frequency changes in fine structure that have greatest impact near fine-structure minima (Henin et al, 2011).

4.1.2. The Overlap Component

The frequency-dependent trend in the overlap component's baseline level was similar to the one seen in the composite DPOAE suggesting that the composite DPOAE signal was dominated by the overlap component. This is not surprising, given the low amplitude of the reflection component (Figure 6B). Since statistical power was low, further research is needed to determine the implications of the lower DPOAE level in the impaired group compared with the control group. Since cochlear amplifier effects (reviewed in Robles and Ruggero, 2001) play a major role in generating EOAE (c.f., Shera and Guinan, 1999), it possible that this seemingly reduced OAE level in the impaired group and its indication of reduced cochlear amplification might underlie their speech-in-noise deficits.

Separation of the DPOAE components revealed a clearer picture of efferent activity, especially for the high frequency region where DPOAE levels were lowest. The overlap component had greater and consistent suppression. The enhancement in ΔdB OAE in the high frequency region in composite DPOAE (Figure 5A) was not seen in the overlap component, which could be due to the separation of the DPOAE components. In addition, the process of

separating the two DPOAE components resulted in the improvement of the SNR when compared with the composite DPOAE signal (Figures 3, 7A), due to the removal of the reflection component. Thus, the separation of the two DPOAE components appears to improve the validity of estimating efferent function, in agreement with previous findings (Deeter et al., 2009; Abdala et al., 2009, Henin et al., 2011; Abdala and Dhar, 2012).

Similar to the composite DPOAE, when efferent effects were binned into three frequency regions (Figure 10), more efferent suppression was seen in the low and middle frequency regions, which is in agreement with previous studies (Collet et al., 1990; Moulin et al., 1993; Yilmaz et al., 2007; Lilaonitkul and Guinan, 2009a; Bhagat and Carter, 2011; Butler et al., 2011; Henin and Long, 2012). These greater changes at the low and middle frequency regions may not have been predicted because medial efferent innervations are denser at the basal end of the cochlea (Guinan et al., 1984). However, cochlear innervations of low-CF neurons may be more basal than their CF (Liberman, 1988). Alternatively, greater efferent impact at the low frequencies maybe due to central influences that affect the MOC system firing response (Lilaonitkul and Guinan, 2009a).

4.1.3. The Reflection Component

In both the impaired and control groups, the baseline level of the reflection component across the frequency range was lower than the overlap component (Figures 6A, B). Consequently, the SNR of the reflection component was also lower (Figures 7A, B). Although the reflection component was reported to be more susceptible to the efferent activity in adults in previous investigations that used a similar paradigm (Deeter et al., 2009; Abdala et al., 2009; Henin et al., 2011), efferent-mediated changes in the reflection component were found to be contaminated by noise floor effects (Figures 9A, B) and hence very variable. Contamination by

the noise floor resulted in estimates of more than 100 Δ%Pa OAE at some frequencies (Figure 9B). Therefore, efferent-mediated changes in the reflection component were not analyzed further for this dissertation.

4.1.4. Monitoring MEMR

Activation of the MEMR can affect estimation of MOC activation (Borg et al., 1971; Relkin et al., 2005; Goodman and Keefe, 2006) because the resulting changes in the middle ear transfer function could modify sounds traveling to and from the cochlea. The neurons controlling the MEMR originate from the same region in the brainstem as the MOC system (Joseph et al., 1985; Liberman and Guinan, 1998). Changes in primary levels at the entrance to the ear canal were used to monitor MEMR activation. We did not have fixed criteria to monitor possible MEMR activation, but we looked at each subject's data on a case-by-case basis. There were no major changes in primary levels in the selected subjects across the frequency region. We realize that we may have missed changes near MEMR threshold levels, but our method is much more sensitive than the clinical measurements of MEMR. Clinical MEMR measurements may not be valid because they are done before the start of testing with no averaging. Consequently, they are not optimal for detecting small changes in ear canal pressure and ignore the influence of the primaries on reflex activation (Guinan, 2006). In contrast, our method was more sensitive because it reduced noise by averaging and monitored MEMR during data collection using the same stimuli that generated DPOAE with and without CAS. This is crucial because MEMR measurements do not depend just on contralateral stimulation, but they also depend on the bilateral acoustic simulation (Kawase et al., 1997), as it is the case during MOC activation (i.e., OAE probe in the ipsilateral ear and CAS in the opposite ear). Figure 11 shows a good example

from one subject depicting nearly identical primary levels with and without CAS, suggesting that the MEMR effect in this subject was minimal.

4.2. Possible Factors Leading to Differences in Published Evidence Related to the Efferent Anti-Masking Hypothesis

We will now consider certain factors that might lead to different conclusions regarding the validity of efferent anti-masking hypotheses obtained from human subjects in the publications summarized in Tables 1and 2.

4.2.1 SNR

The SNR of stimuli plays an important role in investigations MOC function because it has to be optimal for detecting such activity (Guinan, 2011). In line with this view, tasks with moderate SNR (e.g., within +10 dB) would be more likely to provide clear evidence of efferent activation. This is because the efferent system can potentially aid in the detection of an intermittent signal, such as speech, when it is moderately above the level of a background noise it is embedded in. Because the cochlear amplifier has a greater impact on lower level stimuli (reviewed in Robles and Ruggero, 2001), the cochlear response to the lower level noise will be more inhibited than the more intense speech signal, resulting in better detection of the intermittent speech signal. In contrast, efferent activity is not expected to provide much benefit in tasks with high SNR because signal is much higher than the noise (i.e., tasks are too easy). Similarly, efferent activity is not expected to provide much benefit in tasks with very low SNR (i.e., tasks that are too difficult) because the noise and the intermittent speech signal are very close in level and thus both will be similarly inhibited by the MOC system.

In this dissertation, the two speech-in-noise tests had different SNRs. The SNR in the CID-W22 test was +5 dB, while two different SNRs were used in the AFG test (+8 dB up to age

12 years; 0 dB ages 13 years and over). We used mostly moderate SNRs (only 3 subjects in the APD group and 2 subjects in the control groups were over the age of 12, and thus were given the AFG test at a very low SNR of 0 dB), and the correlation *between* the two tests across experimental groups was significant ($p = 0.00$). Yet, no significant correlations were found between each of these tests and mean ΔdB OAE when comparisons were made across experimental groups (Table 6). This lack of correlation, although not consistent with the assumption that efferent activity is most beneficial in tasks with moderate SNRs, may be due to the type of stimuli used in these tests (see below).

When behavioral tasks had either high SNR (Kumar and Vanaja, 2004) or very low SNR (Harkrider and Smith, 2005) near threshold (Micheyl et al., 1995; Garinis et al., 2011), the efferent anti-masking hypothesis was not supported. Tasks with moderate SNRs were positively correlated with efferent activity in some studies (Kumar and Vanaja, 2004; Yilmaz et al., 2007) but not in others (de Boer et al., 2012). However, Kumar and Vanaja's (2004) results may have been confounded by a major factor, which is the linguistic ability of their subjects. Children in their study were not native speakers of English. Therefore, the presence of noise in their behavioral task may have been was more disruptive to their subjects, which might explain the major drop in their speech-in-noise scores (e.g., a mean score of only 7.6 % in the right ear in the +10 dB SNR condition with ipsilateral noise without CAS, see their Table 1). This major drop was not seen in our study with native speakers of English (one subject in our study was trilingual), as speech-in-noise scores measured using comparable stimuli, did not decrease as precipitously in the presence of background noise (e.g., the lowest mean score was 64% in the CID-W22 test was found in the impaired group).

4.2.2. Type of Stimuli

For efferent activity to be beneficial, the continuity and duration of the masker relative to the signal of interest, such as speech, must be considered (Guinan, 2011). Efferent activity is expected to provide benefit when the noise is sustained and the signal of interest, such as speech, is intermittent. The sustained noise signal will be more susceptible to reductions in the gain of the cochlear amplifier, resulting in better discrimination of the intermittent speech signal. This may explain why the efferent-anti-masking hypothesis was not supported when target stimuli and continuous maskers of the same duration were used (Garinis et al., 2011). However, Bhagat and Carter (2011) supported the efferent anti-masking hypothesis when differences between absolute and masked thresholds of 1 kHz tone were significantly correlated with efferent activity, even though the masker and the tone were of equal durations. Furthermore, Stuart and Butler (2012) found that masked thresholds, measured in either interrupted or continuous noises, were not correlated with efferent activity. Other aspects of the experimental design must have determined the pattern of results

We presented monosyllabic words intermittently in continuous noise, and no significant correlations were found between each of the two tests and mean ΔdB OAE when comparisons were made across experimental groups (Table 6). This could be due to the complex characteristics of the speech signal (i.e. containing variations in frequency and amplitude), which may not have been equally affected by efferent activity in the presence of noise. Indeed, the complexity of the behavioral stimuli may explain the failure of some studies to support the efferent anti-masking hypothesis (Table 1). It is possible that the type of stimuli (multi-tone complex containing 1, 1.5 and 2 kHz in Micheyl et al., 1995; a challenging phonemic contrast continuum task in de Boer et al., 2012) may have contributed to their failure to support the efferent anti-masking hypothesis.

Some researchers reported positive correlations between *improvements* in performance using different types of behavioral stimuli and efferent activity (Micheyl and Collet, 1996; Micheyl et al. 1997; Kumar and Vanaja, 2004). However, they correlated efferent activity estimated via changes in EOAE during CAS with the *improvement* in performance when CAS was presented during the ipsilateral presentation of behavioral stimuli embedded in noise. In essence, this is equivalent to comparing potential *bilateral* activation of MOC system but only correlating this activation with *contralateral* MOC effects. Thus, this approach may not be optimal to investigate the contralateral efferent activity because the MOC effects have been reported to be bigger with bilateral stimulation than contralateral stimulation (Guinan et al., 2003; Lilaonitkul and Guinan, 2009a). A more accurate approach would be to compare improvements in behavioral performance during *bilateral* compared to *ipsilateral* activation of MOC system with improvements from *bilateral* compared to *ipsilateral* estimation of the MOC activation.

It has been suggested that the estimation of the MOC function could be optimized by implementing a procedure in which behavioral measurements and efferent estimation are done simultaneously using the same stimuli (Garinis et al., 2011). Francis and Guinan (2011) attempted to implement such a procedure when they presented an intensity discrimination task after the offset of the stimulus that measured TEOAE, but more work needs to be done to improve the analysis of this testing paradigm.

4.2.3. Method Used to Estimate MOC Strength

Another factor that might contribute to the conflicting evidence regarding the efferent anti-masking hypothesis is the type of method used to index efferent strength. The most common method is the arithmetic difference in OAE level (ΔdB) measured with and without efferent

activation (reviewed in Guinan, 2011). However, Tables 1 and 2 show that the position in fine structure at which ΔdB was measured differed between studies and different metrics were used to estimate efferent effects. In DPOAE studies, the two DPOAE components were not separated and efferent activation was estimated at either the DPOAE fine-structure minima (Wagner et al., 2008) or maxima (Garinis et al., 2011), at discrete frequencies where the researchers did not know where they fell in the fine structure (Mukari and Mamat, 2008), or using input/output compression thresholds (Bhagat and Carter 2011). Others estimated efferent activity by measuring changes in the TEOAE input/output slope (Micheyl et al., 1995; Micheyl and Collet, 1996; Micheyl et al., 1997; de Boer et al. 2012). This lack of consistency using a uniform method to estimate efferent strength may contribute to the discordant findings of behavioral studies that investigated the efferent anti-masking hypothesis.

4.3. Previous Research in Children with APD or Auditory Listening Problems

Although we only classified subjects as impaired or controls solely based on performance on two speech-in-noise tests, we will *quantitatively* and *qualitatively* compare our results with previous APD studies that investigated the efferent anti-masking hypothesis (Muchnik et al., 2004; Sanches and Carvallo, 2006; Burguetti et al., 2008; Butler et al., 2011) because speech-in-noise impairment is one of the hallmark of APD (ASHA, 2005; AAA, 2010). We will also compare our results with other studies that investigated the efferent anti-making hypothesis in individuals with auditory listening problems solely identified by questionnaires (Yalcinkaya et al., 2010). First, it is important to acknowledge that the APD studies placed subjects into either APD or control groups based on performance on APD test batteries according to a certain inclusion criteria. These inclusion criteria, and the battery chosen, differed between studies (Table 3). Although ASHA (2005) APD technical report has recommended that APD diagnosis

be based on scoring 3 SD below the mean on at least one test or 2 SD below the mean on at least two tests, currently, there are no gold standards for APD testing or diagnosis. All of the published APD studies *only* used one speech-in-noise test. We used *two* speech-in-noise tests to ensure the presence of such deficit in our subject group that we labeled as being impaired. It is important to note, however, that three subjects in each of our impaired and control groups had an existing morbid condition according to parent report (in the impaired group: ADHD, Asperger-pervasive developmental disorder-not otherwise specified; in the control group: autism, pervasive developmental disorder-not otherwise specified, seizures). The presence of morbid conditions in individuals suspected of having APD with speech-in-noise deficits, as it is the case in our impaired group, necessitates the implementation of a more comprehensive experimental design that will take into account the influence of top-down factors on estimating MOC function (see section 4.4 below).

Table 3 depicts the number of APD subjects, test battery administered to all subjects, as well as the type of MOC index in several previous APD studies that investigated the efferent anti-masking hypothesis. The most pertinent comparison to our study is Butler et al. (2011) because they investigated the efferent anti-masking hypothesis using composite DPOAE. There are methodological differences in how DPOAE were elicited between the two studies. We swept the primaries logarithmically over two octaves, while Butler et al. (2011) used fixed f_2 (2, 3, 4 kHz) while sweeping f_1 linearly over a narrower frequency range. The APD group in Butler et al. (2011) had lower DPOAE SNR than the control group. We also found lower SNR in our impaired group compared with controls. However, the APD group in Butler et al. (2011) had a higher mean DPOAE baseline level than their control group, but our impaired group had lower levels than our control group at comparable frequencies. These differences in relative amplitudes

may be due to the fact that Butler et al. (2011) only used one test to evaluate speech discriminability in noise, while we opted to consider two speech-in-noise tests. Consequently, their APD group and our impaired group may not have been equivalent in terms of speech-in-noise ability.

Butler et al. (2011) failed to find a significant difference in efferent effects between the APD and control groups. They reported a similar mean reduction in DPOAE of about 1 dB at 2 and 3 kHz and 0.5 dB at 4 kHz at fixed f_2 frequencies in both their APD and control groups. Similarly, we also found almost identical mean efferent effects between our impaired and controls groups in the more inclusive analysis that separated the two groups based on the failure on at least one speech-in-noise test (Table 9A). However, the mean efferent-induced changes in composite DPOAE was higher in our impaired group compared with the control group in the analysis with more restrictive inclusion criteria to separate the two groups. A comparison of efferent-mediated changes in the overlap component between the present study and Butler et al. (2011) is not possible since Butler et al. (2011) did not separate the two DPOAE components.

Comparison of efferent strength between the present study and APD studies (Muchnik et al., 2004; Sanches and Carvallo, 2006; and Burguetti et al., 2008), as well as other studies that investigated the efferent anti-masking hypothesis in individuals with auditory listening problems (Yalcinkaya et al., 2010) using TEOAE, is limited because the composite DPOAE and the overlap component used in our study and TEOAE are generated by different mechanisms (reviewed in Shera and Guinan, 2007). Muchnik et al. (2004) and Sanches and Carvallo (2006) all used a behavioral APD test battery that included only *one* speech-in-noise test. Some APD studies did not specify their inclusion criteria (Burguetti et al., 2008) for APD diagnosis and others did not match their APD and control subjects for age and gender (Sanches and Carvallo,

2006; Burguetti et al., 2008). Matching subjects is crucial as performance on the APD test battery is influenced by maturation (Moore et al, 2011; O'Beirne et al., 2012).

Furthermore, in some of the TEOAE studies, individuals with APD (Muchnik et al., 2004) or those with auditory listening problems (Yalcinkaya et al., 2010) had significantly lower estimates of efferent activation than controls, but this difference was not significant in other studies (Sanches and Carvallo, 2006; Burguetti et al., 2008). With the exception of Burguetti et al. (2008) study in which the click level used to elicit TEOAE was not specified, all of these studies used a click level that was high enough to potentially activate the MOC system in the ipsilateral ear, which affects the estimation of efferent activity (Veuillet et al., 1991; Guinan et al., 2003). Taken together, differences in inclusion criteria to separate the APD from the control group, the lack of subject matching, and the use of high click levels might explain the different findings in previous TEOAE studies investigating efferent effects in both the APD populations or in individuals with auditory listening problems. Finally, none of these studies that investigated individuals with APD or those with auditory listening problems monitored MEMR activation during testing. Instead they relied on MEMR threshold measurements done by clinical equipment, which are not always able to detect small changes in middle ear pressure (Guinan, 2006). We implemented a much more sensitive method to detect possible MEMR activation by monitoring changes in ear can primary level with and without CAS during data collection.

4.4. Implications for Future Studies

4.4.1. Developing a Potential Comprehensive Procedure to Optimize the Evaluation of the MOC Function: Considering Bottom-Up vs. Top-Down Processing

The influence of top-down factors, such as the state of attention must be considered when investigating the MOC function as one would assume that the degree of attention needed to

perform a behavioral task would increase when the difficulty of the task's parameters mentioned in section 4.2 increases (e.g., decreasing SNR and increasing the complexity of stimulus type). Thus, in order to optimize the evaluation of MOC system, one must consider the influence of both bottom-up and top-down processes on estimation of the MOC function. Figure 12 illustrates the complex interaction between bottom-up and top-down factors as they relate to the MOC system. Although bottom-up processing (sensory) dominates at a level prior to top-down processing (e.g., cognition, attention, memory), there is a constant exchange of neural information between the two processes. This is crucial since the MOC system receives projections from the inferior colliculus (Thompson and Thompson, 1993; Vetter et al., 1993) and OAE measurements were altered by deep brain stimulation indicating input from higher brain centers (Perrot et al., 2006). In addition, there were greater changes in auditory nerve responses when inferior colliculus and acoustic stimulation were combined (Mulders and Robertson, 2002). Furthermore, frequency-specific changes in efferent magnitude were seen when attention to the auditory modality was manipulated alone (Giard et al., 1994; Maison et al., 2001) and with combined manipulations of both the auditory and visual modalities (Froehlich et al., 1993; Ferber-Viart et al., 1995).

Thus, considering the influence of top down factors, such as attention, might help to uncover if the interaction between bottom-up and top- down processes would result in either the summation or cancellation of MOC effects. This is because the efferent anti-masking effect might have an inhibitory effect, whereas the influence of the state of attention may have an excitatory effect on estimating MOC function.

The same issues related to the influence of top-down control on optimizing the detection of efferent effects are also important when investigating the efferent anti-masking hypothesis in

individuals suspected of having APD because there is much controversy regarding the validity of APD diagnosis when it co-occurs with ADHD (ASHA, 2005; AAA, 2010). In our study, subjects suspected of having APD were a very heterogamous group whose performance varied considerably on APD tests and some had existing morbid conditions (see individual subject data in Tables 4, 3A, 4A). The hypothesized dual role of the MOC system in providing an anti-masking effect and in selective attention maybe a common denominator that can be investigated to better understand the neurophysiological processing underlying the co-morbidity of APD with other disorders.

4.4.2. Recruiting Healthy Controls without Existing Morbid Conditions

We realize that we labeled our subjects and placed them in either the impaired or control groups based solely on performance on two speech-in-noise tests. This resulted in some subjects suspected of having APD who had an existing morbid condition (e.g., ADHD, autism) being placed in both the impaired or control groups. Therefore, it would be optimal to recruit a control group of healthy individuals with normal auditory performance based on more comprehensive testing and without existing morbid conditions. This would permit extending the investigation of the efferent anti-masking hypothesis to determine whether significant differences in DPOAE level and efferent activation can be detected for individuals with speech-in-noise problems and two control groups (with and without morbid conditions).

4.5 Conclusion

There were no significant differences in efferent-induced changes in composite DPOAE or the overlap component between our impaired group with speech-in-noise deficits and our control group with less speech-in-noise deficits. In addition, no significant correlations were found between estimates of efferent strength and speech-in-noise performance. Separation of the two

DPOAE components improved the estimation of efferent magnitude at high frequencies where DPOAE level was lowest. In addition, mean DPOAE level was lower in the impaired group than the control group, although this difference between groups was not significant. The failure to support the anti-masking hypothesis should be interpreted with caution, as the power of statistical analysis was mostly low due to the small number of subjects and the variability stemming from the subject selection. Implementing a procedure that takes into account the influence of the state of attention on both behavioral performance and the estimation of efferent strength may provide a better test for the efferent anti-masking hypothesis.

5. Tables

Table 1. Stimulus parameters of threshold tasks (type of task, laterality of noise) and the MOC index used in several publications that investigated the correlation between masked threshold or masked threshold shifts (improvements with CAS) and the MOC function in human subjects.

Publication	Masking		OAE	
	Measurement	Laterality of Noise	MOC Index	Correlation
Micheyl et al. (1995)	Threshold detection and threshold shift of multi- tone (1, 1.5, 2 kHz)	Ipsilateral with CAS	Difference in TEOAE I/O regression lines	Significant negative correlation
Micheyl and Collet (1996)	Threshold detection and threshold shift (measured with CAS) using 1, 2 kHz tone pips.	Ipsilateral Ipsilateral with CAS	I/O equivalent attenuation of TEOAE	Significant positive correlation between MOC and threshold shift at 1, 2 kHz, and detection threshold at 2kHz.
Micheyl et al. (1997)	Intensity difference limen of masked thresholds of 1kHz pips	Ipsilateral Ipsilateral with CAS Contralateral	TEOAE I/O slope	Significant positive correlation.
Mukari and Mamat (2008)	Sentence reception threshold under headphones simulating sound field environment (head-related function)	Ipsilateral Contralateral Front	ΔdB DPOAE at discrete f_2 frequencies	No significant correlations
Wagner et al. (2008)	Masked sentence recognition threshold in sound field.	Ipsilateral	ΔdB DPOAE at fine structure minima.	No significant correlation
Garinis et al. (2011)	Masked thresholds of 1kHz tone embedded in maskers (BBN, fixed, random).	Ipsilateral	ΔdB in DPOAE at fine structure maxima	Significant negative correlations between MOC and thresholds measured in random masker.
Bhagat and Carter (2011)	Difference between absolute and masked thresholds of 1, 2 kHz tones.	Ipsilateral	I/O compression thresholds in composite DPOAE	Significant positive correlation at 1 kHz only.
Stuart and Butler (2012)	Sentence reception threshold in interrupted and continuous noises	Ipsilateral Bilateral	ΔdB TEOAE	No significant correlations

Table 2. Stimulus parameters of speech-in-noise tasks (SNR, laterality of noise) and the MOC index used in several publications that investigated the correlation between performance in noise with CAS (shift) or without CAS and the MOC system in human subjects.

Publication	Masking			OAE	
	Speech-in-Noise Task	SNR	Laterality of Noise	MOC Index	Correlations Between Behavioral Testing and MOC
Kumar and Vanaja (2004)	Shift in speech scores between quite and noise conditions.	+10, +15, +20	Ipsilateral with CAS	ΔdB TEOAE	Significant positive correlation.
Harkrider and Smith (2005)	Acceptable Noise Level (ANL)- Phonemic Recognition in Noise	0 dB (Phonemic Recogniti on Task)	Ipsilateral (Phonemic Recognition Task)	ΔdB TEOAE	No significant correlation
Yilmaz et al. (2007)	Monosyllabic words in noise.	+10 dB	Ipsilateral	ΔdB TEOAE	Significant positive correlation at TEOAE bands at1 kHz in right ear and at 2 kHz in left ear.
de Boer et al. (2012)	/d/, /g/ continuum	+10 dB	Ipsilateral	TEOAE I/O slope and ΔdB	Significant negative correlation

Table 3. The number of subjects, test battery (tasks and criteria for diagnosis) and the MOC index in several publications that investigated differences in efferent effects between individuals with APD or auditory listening problems (ALP) and controls.

Publication	Number of Subjects and Diagnostic Criteria			OAE	
	APD Test Battery	Criteria for Subject Placement in APD Group	Number of Subjects in APD and Control Groups	MOC Index	Statistical Difference in Efferent Magnitude between the APD-ALP and Control Groups
Muchnik et al. (2004)	Speech-in-noise Competing Sentences Threshold interference	Scoring 2 SD below the mean on at least one test.	15 (controls) 15 (APD)	ΔdB TEOAE	Significant
Sanches and Carvallo (2006)	Speech-in-Noise (S/N) Staggered Spondaic Words (SSW) Pediatric Speech Intelligibility Nonverbal Dichotic Task Sound Localization Verbal Sequential Memory Nonverbal Sequential Memory	< 85% on SSW <68% on S/N in APD-I and >68% in APD-II	15 (controls) 20 (APD-I) 16 (APD-II)	ΔdB TEOAE	Not Significant
Burguetti et al. (2008)	Speech-in-Noise Staggered Spondaic Word	Not Specified.	38 (controls) 50 (APD)	ΔdB TEOAE	Not Significant
Yalcinkaya et al. (2010)	Questionnaire	N/A.	12 (controls) 12 (APD)	ΔdB TEOAE	Significant at 1, 2 kHz.
Butler et al.(2011)	Staggered Spondaic Words Auditory Fusion-Revised, Words Ipsilateral Competition Pitch Pattern Sequence Filtered Speech	Scoring 2 SD below the mean on at least two tests.	8 (controls) 8 (APD)	ΔdB DPOAE at fixed f_2: 2, 3, 4 kHz.	Not significant.

Table *4.* Behavioral performance on APD tests from the impaired and control subjects included in the more restrictive analysis. PTA = pure tone average (right Ear 1-4 kHz), SSW = staggered spondaic words, PS = phonemic synthesis, CID = CID-W22 in Noise-Right Ear, FW = filtered words, AFG = auditory figure ground, CW = competing words, CS = competing sentences, TCS = time compressed speech, C = composite, N/A = not administered, ID = identified, WNL = within normal limits.

			Buffalo Test Battery (Raw Scores When Applicable)			Scan-3 (Percentile Scores)						
Subject	Group	PTA	SSW	PS	CID	FW	AFG	CW	CS	TCS	C	Morbid Condition
15	Impaired	5	ID	18 (WNL)	17	25	9	9	37	5	10	
22	Impaired	8.33	ID	20 (ID)	15	84	25	16	75	25	50	ADHD
40	Impaired	6.67	N/A	N/A	20	N/A	16	N/A	N/A	N/A	N/A	
47	Impaired	10	ID	16 (ID)	13	2	0.1	1	9	0.4	0.2	
48	Impaired	13.33	ID	13 (ID)	14	2	0.1	1	25	5	0.1	
51	Impaired	8.33	N/A	N/A	17	25	5	5	75	25	10	ADHD
53	Impaired	6.67	ID	20 (WNL)	19	9	9	2	16	0.1	3	
55	Impaired	10	N/A	N/A	12	N/A	16	0.4	9	2	N/A	
65	Impaired	8.33	WNL	18 (ID)	14	37	5	1	84	25	13	
70	Impaired	1.67	ID	20 (ID)	19	5	2	2	1	0.1	0.4	PDD.NOS Asperger
13	Control	6.67	ID	18 (WNL)	20	50	75	9	16	50	25	
17	Control	6.67	ID	11 (ID)	20	84	37	50	37	37	53	
18	Control	10	ID	18 (ID)	21	37	25	16	37	5	19	
20	Control	11.67	N/A	N/A	22	N/A	98	N/A	N/A	N/A	N/A	Autism
29	Control	5	N/A	N/A	24	N/A	75	N/A	N/A	N/A	N/A	
34	Control	8.33	N/A	N/A	22	N/A	37	N/A	N/A	N/A	N/A	
35	Control	10	N/A	N/A	20	N/A	75	N/A	N/A	N/A	N/A	Seizures
39	Control	20	N/A	N/A	20	N/A	25	N/A	N/A	N/A	N/A	
46	Control	5	N/A	N/A	21	63	91	9	16	37	39	
57	Control	1.67	ID	16 (ID)	22	25	63	5	9	0.1	13	PDD.NOS

Table 5. Range, mean, standard error of mean (SE) and standard deviation (SD) for the CID and AFG percentile test scores in the impaired and control groups (N=10).

Statistic	Control		Impaired	
	CID	AFG	CID	AFG
Range	85.77-24.51=61.26	98-25=73	18.67-0.01=18.66	25-0.1=24.9
Mean	49.35	60.1	3.85	8.72
SE	7.74	8.56	1.98	2.57
SD	24.46	27.07	6.27	8.11

Table 6. Pearson correlations coefficients between CID / AFG percentile test scores and ΔdB OAE averaged across the frequency range within (N=10) and in the combined impaired and control groups (N=20) (p values are represented between parenthesis).

MOC Index	Control		Impaired		Combined	
	CID	AFG	CID	AFG	CID	AFG
Composite ΔdB OAE	0.42 (0.22)	-0.08 (0.83)	0.13 (0.72)	-0.44 (0.21)	0.21 (0.37)	-0.01 (0.98)
Overlap ΔdB OAE	0.46 (0.18)	-0.07 (0.85)	0.01 (0.99)	-0.39 (0.27)	0.29 (0.21)	0.12 (0.63)

Table 7: Mean and standard error (SE) of the averaged up- and down-sweeps across the frequency range for composite DPOAE and the overlap component levels in dB SPL without (No-CAS) and with contralateral 60 dB SPL noise (CAS) in the impaired and control groups (N=10).

Statistic	Control				Impaired			
	Composite		Overlap		Composite		Overlap	
	No-CAS	CAS	No-CAS	CAS	No-CAS	CAS	No-CAS	CAS
Mean	5.9	5.06	5.34	4.44	2.8	1.58	1.86	0.59
SE	1.62	1.74	1.73	1.86	1.62	1.74	1.73	1.86

Table 8. Mean and standard error of the mean (SE) of the averaged up- and down-sweeps across the frequency range for composite DPOAE and overlap component in ΔdB OAE and Δ%Pa OAE in the impaired and control groups (N=10).

Statistic	Control				Impaired			
	Composite		Overlap		Composite		Overlap	
	ΔdB	Δ%Pa	ΔdB	Δ%Pa	ΔdB	Δ%Pa	ΔdB	Δ%Pa
Mean	-0.47	-7.44	-0.82	-10.58	-0.61	-11.34	-1.21	-15.18
SE	0.24	2.52	0.27	3.09	0.24	2.52	0.27	3.09

Table 9. Main effects and interactions of two-way repeated measures ANOVA for ΔdB and Δ%Pa in composite DPOAE.

Statistic	ΔdB			Δ%Pa		
	F	Sig	Power	F	Sig	Power
Group	0.19	0.67	0.07	1.2	0.29	0.18
Frequency	**3.09**	**0.02***	0.79	2.22	0.09	0.57
Group X Frequency	1.32	0.27	0.4	0.55	0.67	0.16

(* p<0.05)

Table 10. Main effects and interactions of two-way repeated measures ANOVA for ΔdB and Δ%Pa in the overlap component.

Statistic	ΔdB			Δ%Pa		
	F	Sig	Power	F	Sig	Power
Group	1.04	0.32	0.16	1.11	0.31	0.17
Frequency	**2.7**	**0.05***	0.64	1.82	0.14	0.49
Group X Frequency	0.94	0.43	0.25	0.86	0.48	0.24

(* p≤0.05)

Table 11. Main effects and interactions of two-way repeated measures for composite DPOAE and the overlap component baseline level.

Statistic	Composite DPOAE Baseline Level			Overlap Component Baseline Level		
	F	Sig	Power	F	Sig	Power
Group	1.83	0.19	0.25	2.03	0.17	0.27
Frequency	**61.31**	**0.00****	1.00	**55.03**	**0.00****	1.00
Group X Frequency	0.61	0.6	0.16	0.76	0.48	0.17

(p<0.01)**

Table 12. Main effects and interactions of two-way repeated measures ANOVA for the frequency bins analysis for ΔdB and Δ%Pa in composite DPOAE.

Statistic	ΔdB			Δ%Pa		
	F	Sig	Power	F	Sig	Power
Group	0.19	0.67	0.07	1.2	0.29	0.18
Frequency	**7.29**	**0.00***	0.91	**6.58**	**0.01***	0.87
Group X Frequency	2.84	0.07	0.52	0.74	0.47	0.16

($p \leq 0.01$**)**

Table 13. Main effects and interactions of two-way repeated measures ANOVA for the frequency bins analysis for ΔdB and Δ%Pa in the overlap component.

Statistic	ΔdB			Δ%Pa		
	F	Sig	Power	F	Sig	Power
Group	1.07	0.31	0.17	1.15	0.3	0.17
Frequency	**5.9**	**0.01****	0.77	**3.56**	**0.05***	0.58
Group X Frequency	0.23	0.74	0.08	0.34	0.68	0.1

(*p≤0.05)
(p≤0.01)**

6. Figures

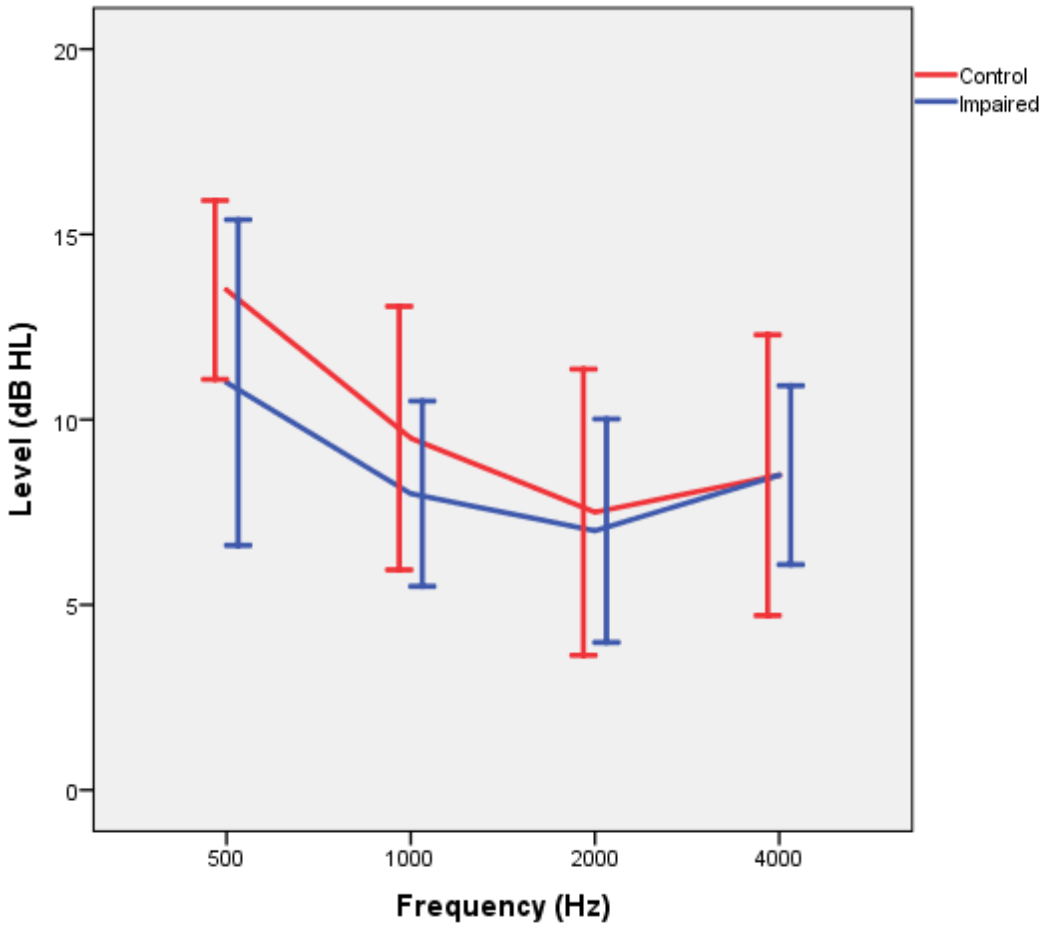


Figure *1*. Behavioral thresholds levels as a function of frequency for the impaired and control groups (error bars represent the stand error of the mean).

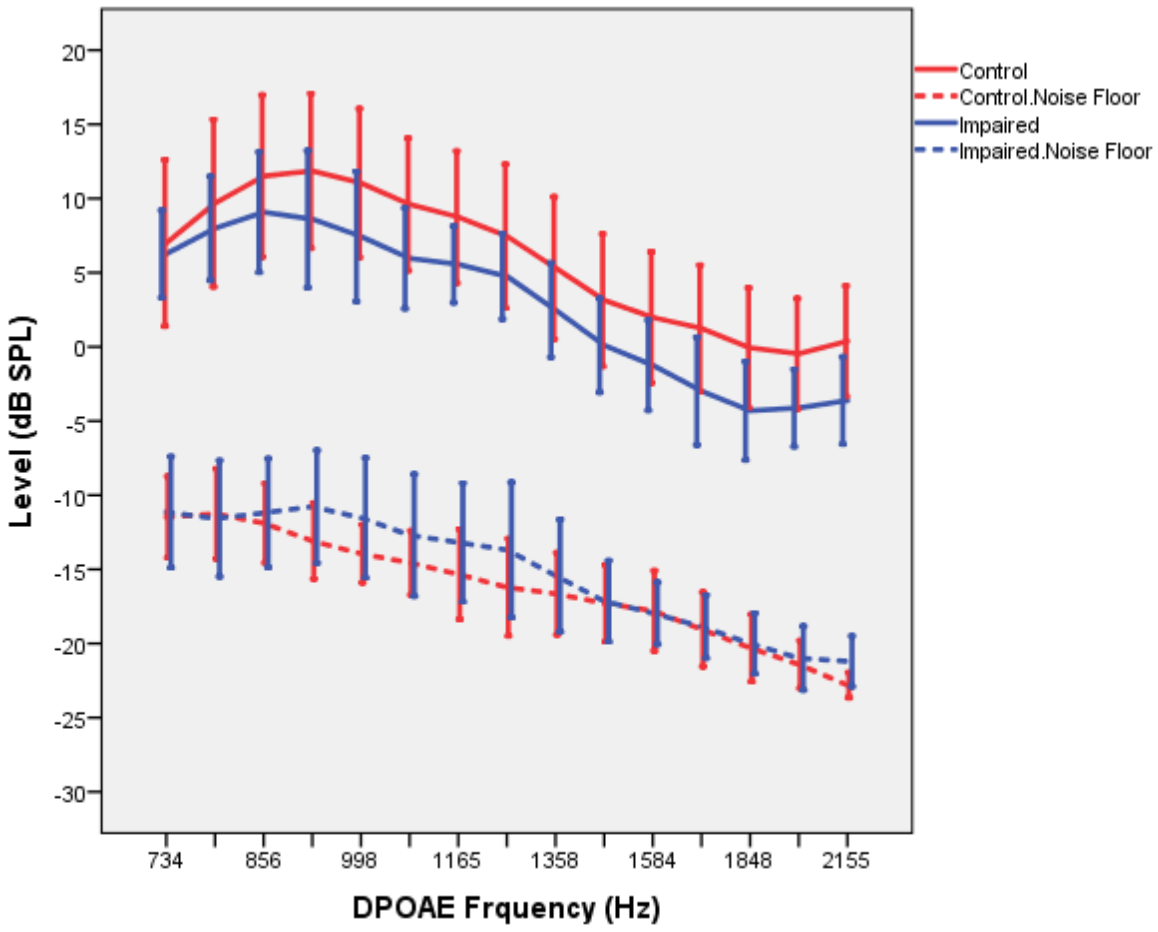


Figure 2. Composite DPOAE baseline level in 1/3-octave RMS bandwidths in the impaired and controls groups (error bars represent the standard error of the mean).

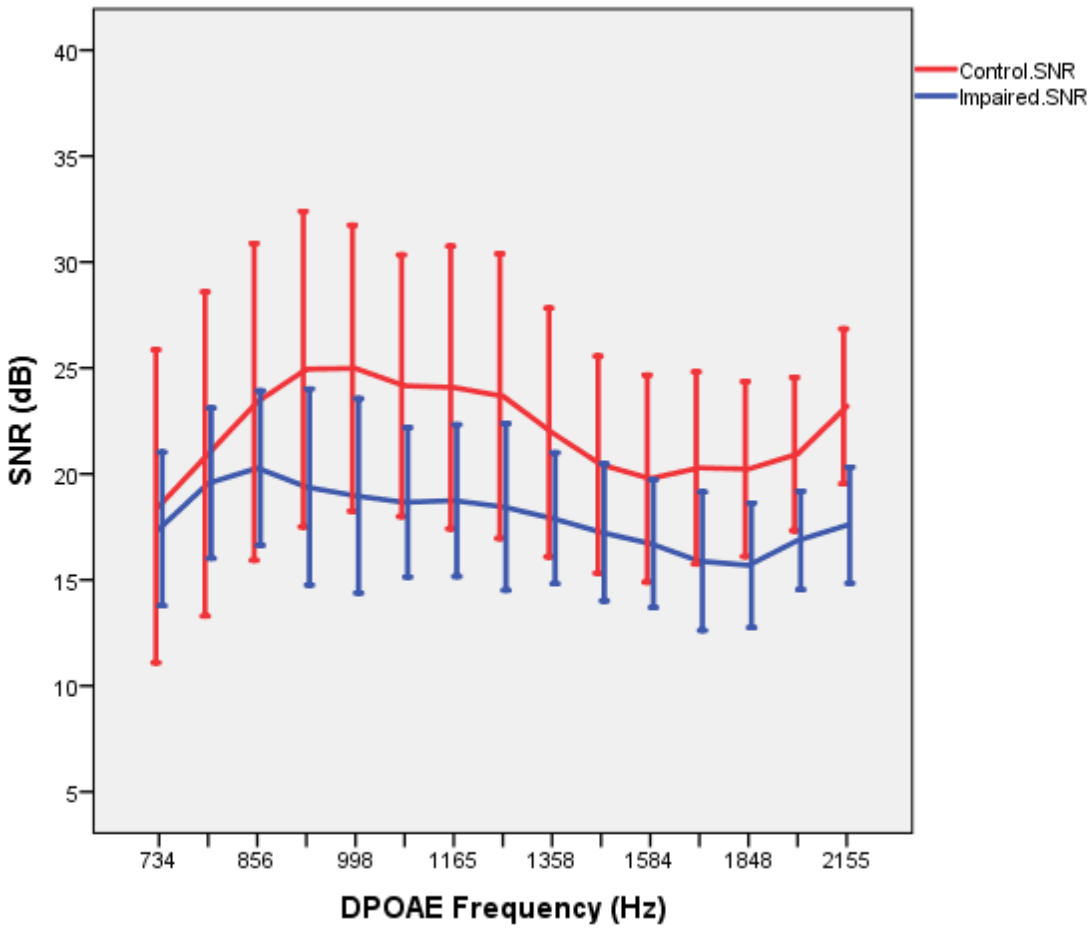
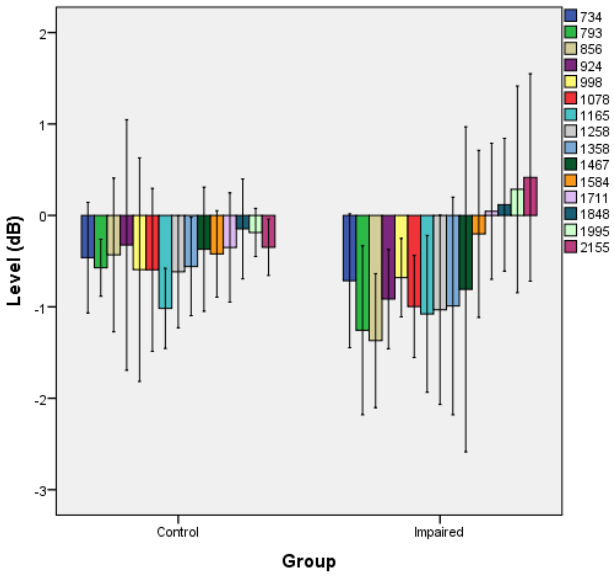


Figure 3. Signal-to-noise ratio (SNR) of the composite DPOAE signal in 1/3-octave RMS bandwidths in the impaired and controls groups (error bars represent the standard error of the mean).

A



B

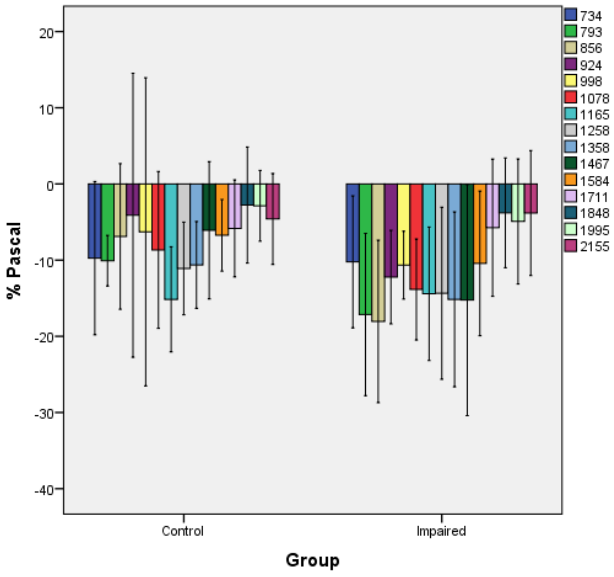
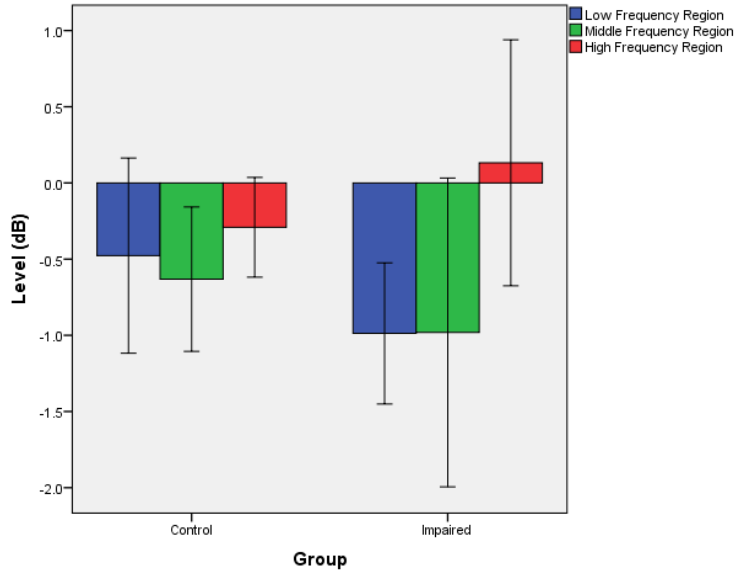


Figure 4. RMS difference in 1/3-octave bandwidths between No-CAS and CAS conditions in dB (top) and percent Pascal (bottom) for composite DPOAE level in the impaired and control groups (error bars represent the standard error of the mean).

A



B

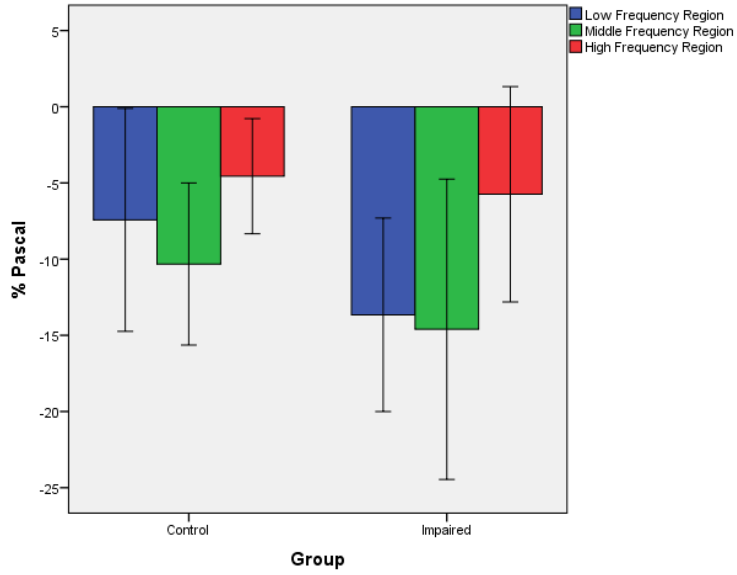
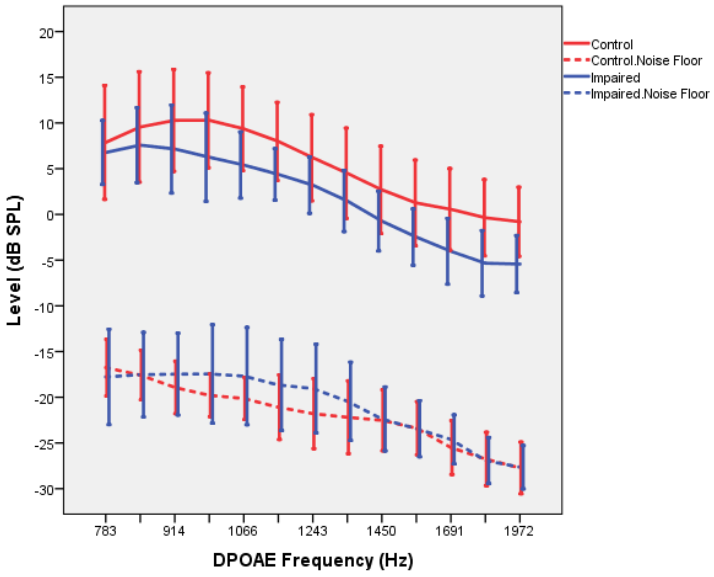


Figure 5. RMS difference between No-CAS and CAS conditions in dB (top) and percent Pascal (bottom) in 1/3-octave bandwidths binned into three frequency regions (low: up to 1 kHz; middle: 1.1-1.4 kHz; high: above 1.5.kHz) for composite DPOAE in the impaired and control groups (error bars represent the standard error of the mean).

A



B

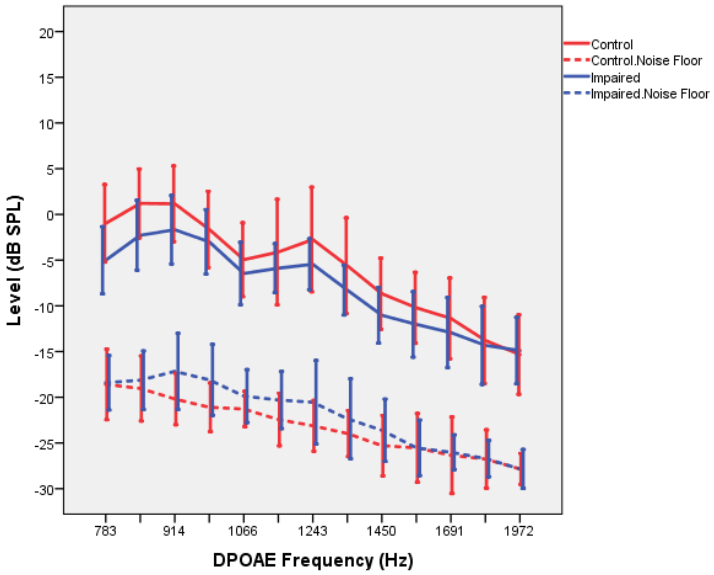
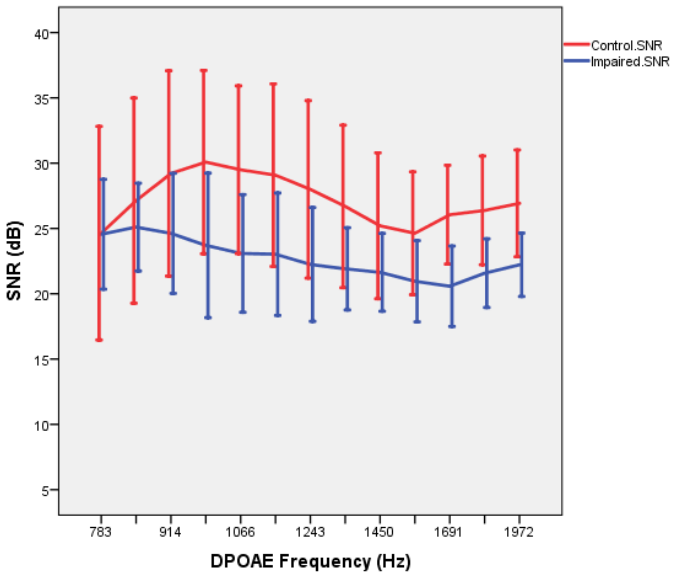


Figure 6. Baseline level in 1/3-octave RMS bandwidths for the overlap component (top) and the reflection component (bottom) in the impaired and control groups (error bars represent the standard error of the mean).

A



B

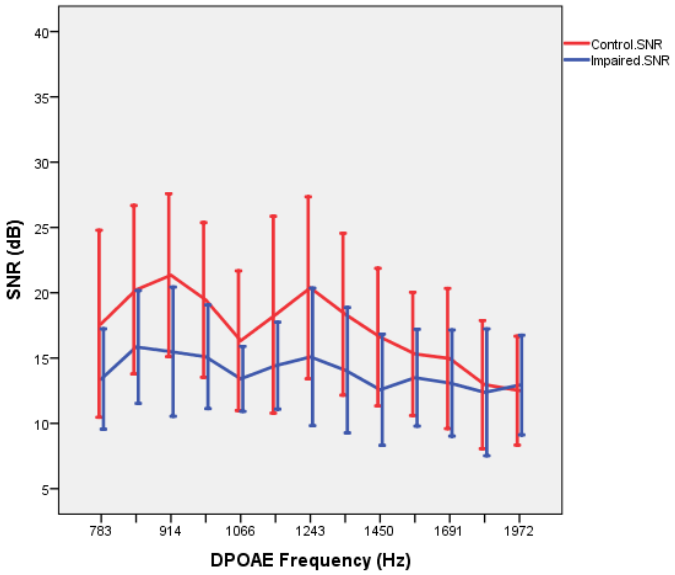
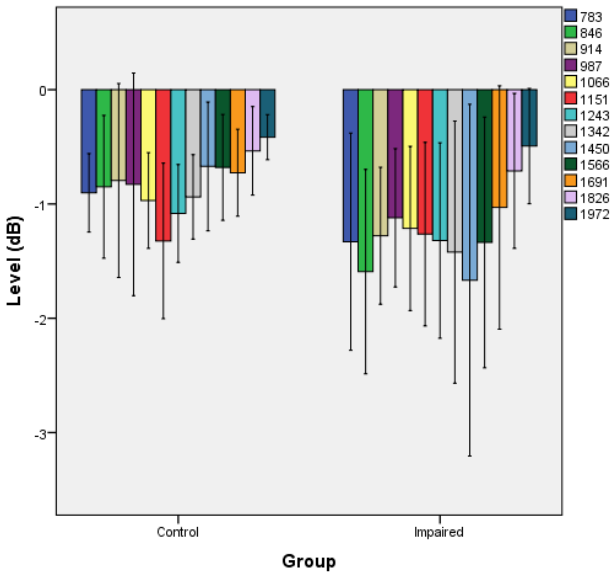


Figure 7. Signal-to-noise ratio (SNR) of the overlap component (top) and the reflection component (bottom) in 1/3-octave RMS bandwidths in the impaired and control groups (error bars represent the standard error of the mean).

A



B

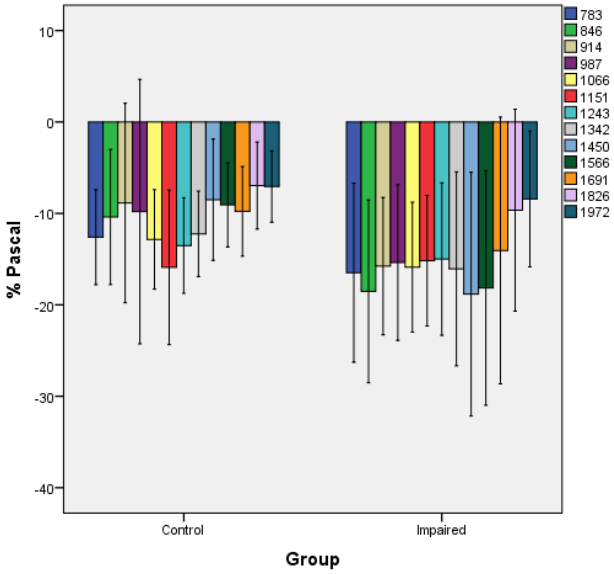
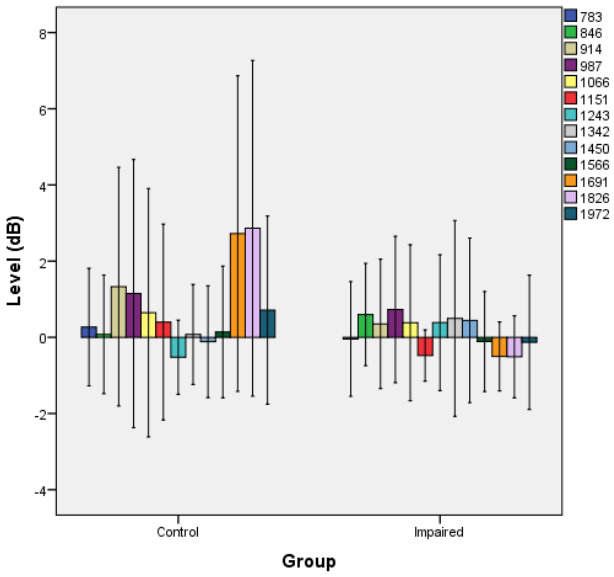


Figure 8. RMS difference in DPOAE level 1/3-octave bandwidths between No-CAS and CAS conditions in dB (top) and percent Pascal (bottom) for the overlap component in the impaired and control groups (error bars represent the standard error of the mean).

A



B

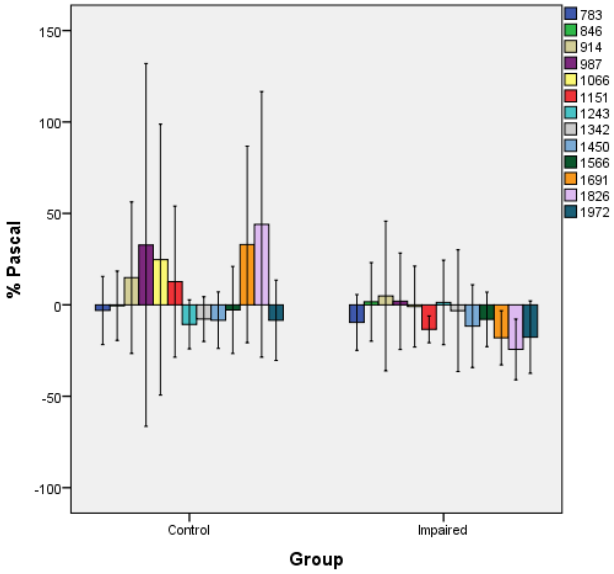
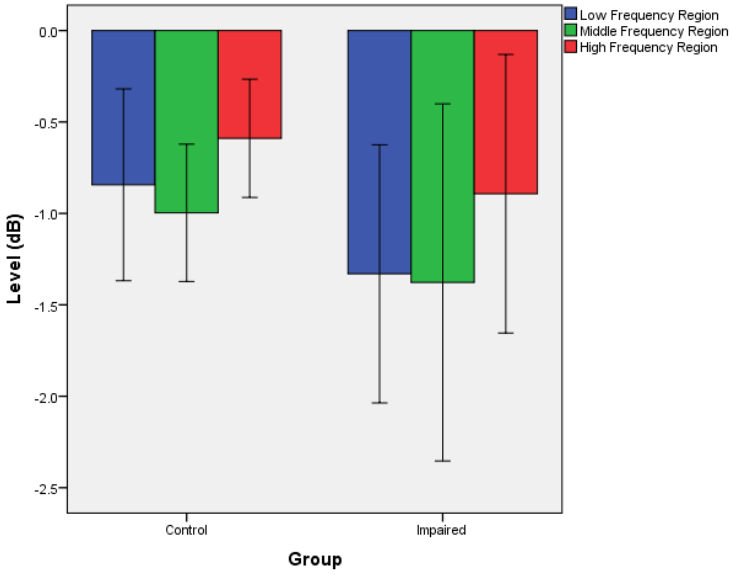


Figure 9. RMS difference in DPOAE level 1/3-octave bandwidths between No-CAS and CAS conditions in dB (top) and percent Pascal (bottom) for the reflection component in the impaired and control groups (error bars represent the standard error of the mean).

A



B

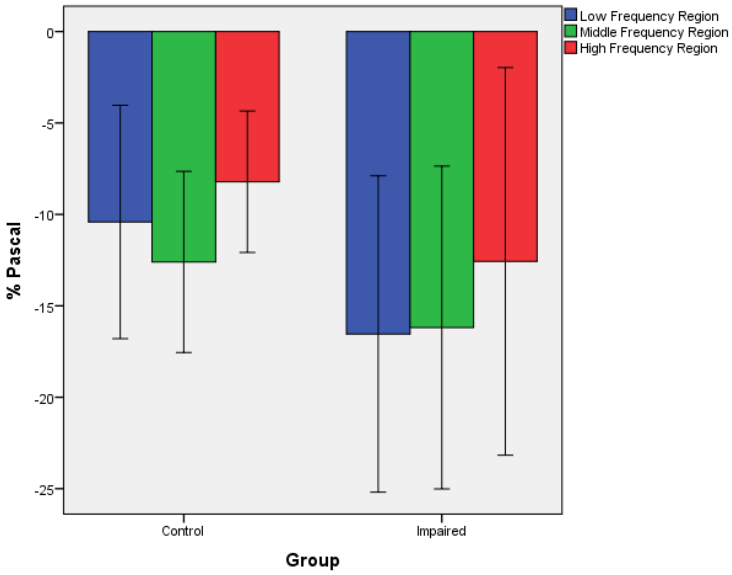


Figure 10. RMS difference between No-CAS and CAS conditions in dB (top) and percent Pascal (bottom) in 1/3-octave bandwidths binned into three frequency regions (low: up to 1 kHz; middle: 1.1-1.4 kHz; high: above 1.5.kHz) for the overlap component in the impaired and control groups (error bars represent the standard error of the mean).

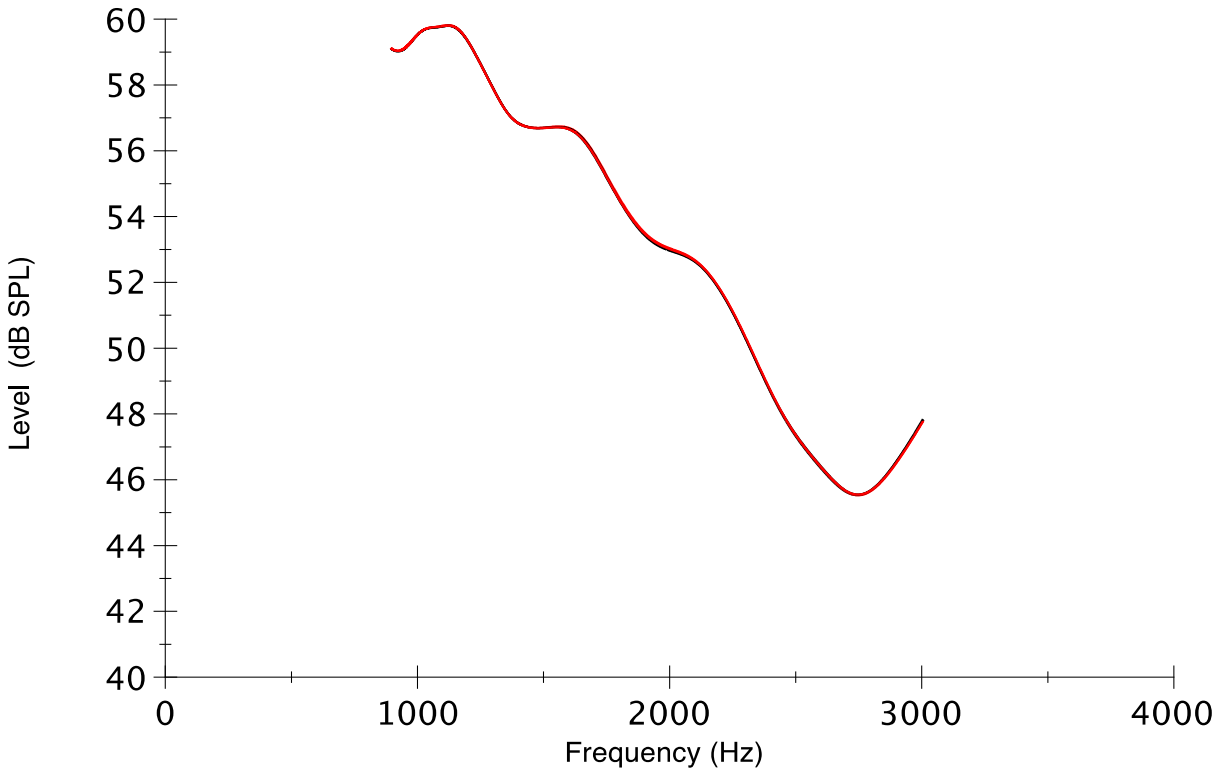


Figure 11. The primary level of f_1 with (red line) and without CAS (black line) measured in the ear canal in control subject 29 using narrowband analysis (note the overlap between the lines in the two conditions suggesting that the MEMR effect, if present, was minimal).

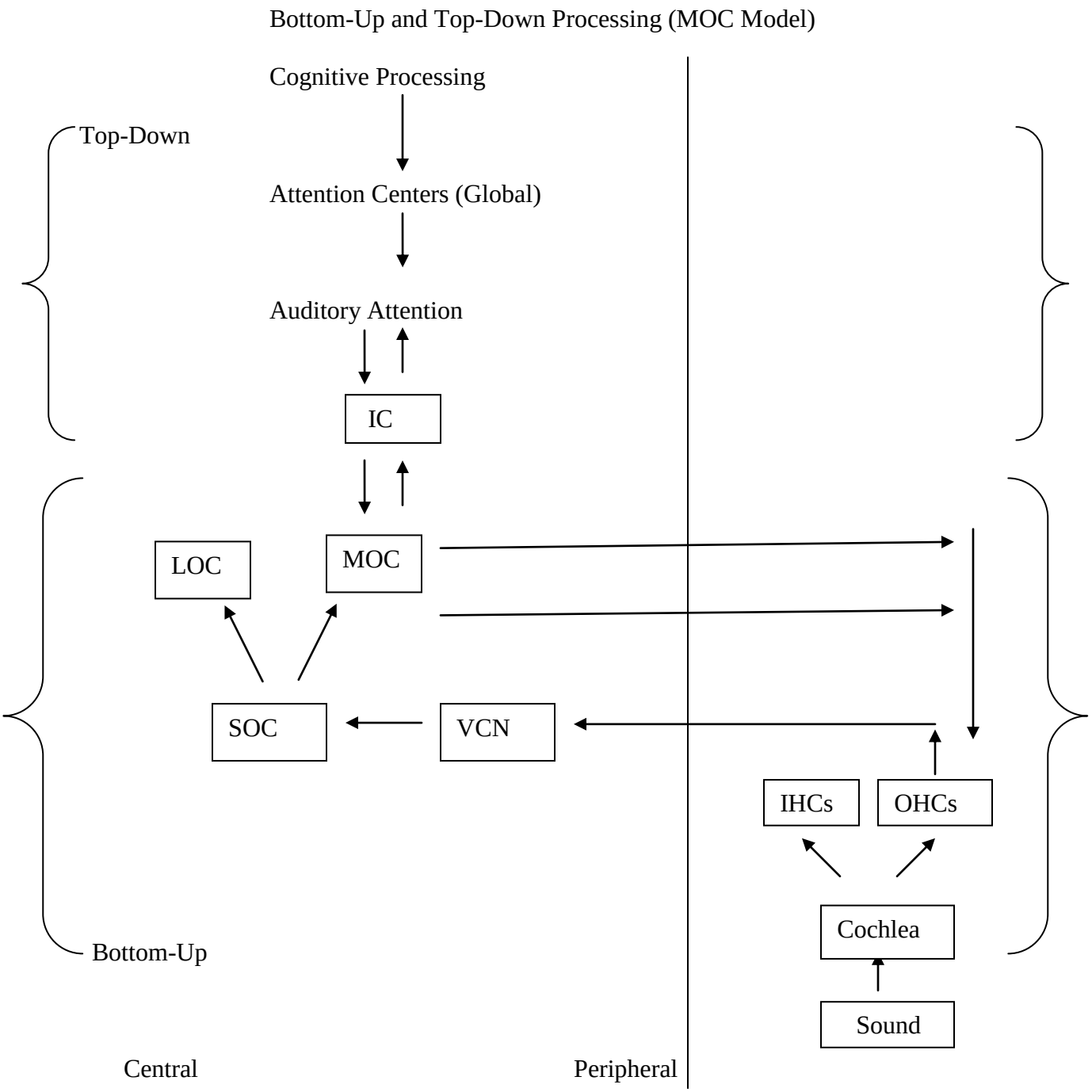


Figure 12. Simplistic schematic of a proposed MOC model as it relates to bottom up and top down processes. OHC = Outer hair cell, IHC = Inner hair cell, VCN = Ventral cochlear nucleus, SOC = Superior olivary complex, LOC = Lateral olivocochlear, MOC = Medial olivocochlear, IC = Inferior colliculus.

7. Appendices

Table *1A.* Baseline, noise floor and ΔdB OAE values of composite DPOAE binned into three-frequency regions (low = up to 1 kHz, middle = 1.1-1.4 kHz, high = more than 1.5 kHz) from subjects included in the more restrictive analysis. C = Control, I = Impaired.

	Composite DPOAE Baseline Level (dB SPL)			Composite DPOAE Noise Floor (dB SPL)			Composite DPOAE ΔdB OAE		
Subject	Low	Mid	High	Low	Mid	High	Low	Mid	High
I.15	14.58	9.59	3.56	-13.07	-13.48	-20.28	-0.82	-0.86	-0.73
I.22	9.33	5.68	-1.93	-15.75	-18.82	-21.16	-0.38	-0.99	0.12
I.40	-4.39	-2.52	-12.03	-16.16	-20.42	-22.76	-2	-4.09	-0.98
I.47	6.47	0.4	-2.95	-14.07	-16.54	-21.25	-1.51	-0.28	-0.59
I.48	7.7	3.62	-3.64	-11.98	-18.52	-22.21	-0.83	0.35	1.16
I.51	5.43	-1.32	-4.53	-10.53	-15.38	-18.1	-1.66	-1.04	-0.23
I.53	10.22	4.14	-4.78	-10.22	-8	-19.82	0.03	0.94	0.76
I.55	12.97	8.62	1.21	2.02	-3.86	-14.3	-1.5	-2.42	-1.19
I.65	10.2	7.43	-2.39	-9.04	-12.44	-16.7	-0.65	-1.02	0.53
I.70	6.25	2.12	-5.06	-13.64	-16.83	-21.44	-0.55	-0.39	2.47
C.13	2.8	5.18	-0.34	-12.61	-15.98	-20.62	-1.2	-1.92	-1.1
C.17	11.11	5.53	2.37	-15.62	-16.58	-21.54	-0.74	-0.75	0.23
C.18	13.52	12.66	3.46	-12.99	-16.26	-20.29	-0.59	-0.52	-0.25
C.20	17.84	10.96	0.96	-15.35	-17.85	-22.04	-0.54	-0.59	-0.01
C.29	21.4	16.39	9.19	-14.76	-21.27	-21.53	-0.72	-0.78	-0.49
C.34	13.61	8.39	2.28	-11.38	-13.62	-19.53	-0.54	0.12	-0.32
C.35	14.98	10.21	0.76	-14.9	-17.62	-21.63	-0.93	-0.75	-0.75
C.39	0.27	2.18	-5.11	-9.11	-15.34	-20.6	-0.07	-1.37	-0.42
C.46	4.95	-5.11	-11.32	-12.11	-18.43	-21.74	-1.29	0.08	0.49
C.57	1.73	2.15	3.9	-4.49	-7.12	-13.2	1.87	0.16	-0.28

Table *2A*. Baseline, noise floor and ΔdB OAE values of the overlap component binned into three-frequency region (low = up to 1 kHz, middle = 1.1-1.4 kHz, high = more than 1.5 kHz) from subjects included in the more restrictive analysis. C = Control, I = Impaired.

	Overlap Baseline Level (dB SPL)			Overlap Noise Floor (dB SPL)			Overlap ΔdB OAE		
Subject	Low	Mid	High	Low	Mid	High	Low	Mid	High
I.15	13.54	8.8	3.45	-17.76	-18.13	-24.05	-0.88	-0.9	-0.68
I.22	8.5	5.37	-3.61	-23.46	-26.97	-27.65	-0.55	-1.05	-0.65
I.40	-7.24	-4.92	-13.01	-24.87	-25.25	-28.9	-3.11	-4.71	-3.49
I.47	6.01	-0.27	-4.44	-20.42	-22.75	-27.58	-1.83	-0.55	-1.03
I.48	7.23	1.88	-6.04	-16.36	-22.73	-28.86	-0.78	-0.76	-0.64
I.51	4.43	-2.13	-5.03	-18.21	-20.15	-22.5	-2	-1.36	-0.6
I.53	9.74	3.71	-5.78	-17.88	-14.36	-27.01	0.01	-0.08	-0.1
I.55	12.83	8.15	1.32	-0.86	-6.3	-18.61	-2.53	-2.75	-1.8
I.65	9.56	5.03	-2.85	-14.74	-16.64	-23.29	-0.92	-0.99	0.11
I.70	4.82	1.83	-7.23	-21.02	-23.12	-28.08	-0.71	-0.61	-0.04
C.13	2.83	4.71	-0.31	-17.16	-21.33	-25.13	-2.35	-2.04	-1.42
C.17	9.25	5.06	0.36	-23.51	-22.31	-28.29	-0.73	-0.81	-0.29
C.18	13.63	12.08	4.19	-19.39	-21.88	-26.86	-0.71	-0.53	-0.33
C.20	17.76	10.61	0.74	-21.22	-22.32	-28.32	-0.6	-0.64	-0.09
C.29	21.23	15.86	9.35	-20.39	-28.02	-25.32	-0.77	-0.78	-0.53
C.34	13.6	7.39	1.71	-17.95	-20.13	-26.53	-0.56	-0.56	-0.46
C.35	14.64	9.13	0.92	-18.57	-22.09	-25.14	-0.98	-0.82	-0.92
C.39	-1.43	1.57	-5.4	-15.38	-19.79	-27.36	-0.71	-1.8	-1.22
C.46	4.47	-5.74	-12.95	-18.49	-26.08	-29.27	-1.55	-0.77	-0.15
C.57	-0.93	0.8	2.97	-10.55	-11.5	-16.19	0.52	-1.24	-0.48

Table *3A*. Behavioral performance on APD tests from subjects included in the more inclusive analysis. PTA = pure tone average (right Ear 1-4 kHz), SSW = staggered spondaic words, PS = phonemic synthesis, CID = CID-W22 in Noise-Right Ear, FW = filtered words, AFG = auditory figure ground, CW = competing words, CS = competing sentences, TCS = time compressed speech, C = composite, N/A = not administered, ID = identified, WNL = within normal limits.

			Buffalo Test Battery (Raw Scores When Applicable)			Scan-3 (Percentile Scores)						
Subject	Group	PTA	SSW	PS	CID	FW	AFG	CW	CS	TCS	C	Morbid Condition
14	Impaired	Not Done	WNL	N/A	23	75	5	37	50	84	30	
15	Impaired	5	ID	18 (WNL)	17	25	9	9	37	5	10	
16	Impaired	6.67	ID	14 (ID)	19	37	2	2	16	0.1	3	ADHD
22	Impaired	8.33	ID	20 (ID)	15	84	25	16	75	25	50	ADHD
31	Impaired	10	N/A	N/A	22	N/A	1	N/A	N/A	N/A	N/A	
40	Impaired	6.67	N/A	N/A	20	N/A	16	N/A	N/A	N/A	N/A	
42	Impaired	13.33	ID	22 (WNL)	24	25	1	16	16	25	4	ADHD
44	Impaired	10	ID	20 (ID)	21	37	5	50	37	25	19	ADHD
47	Impaired	10	ID	16 (ID)	13	2	0.1	1	9	0.4	0.2	
51	Impaired	8.33	N/A	N/A	17	25	5	5	75	25	10	ADHD
53	Impaired	6.67	ID	20 (WNL)	19	9	9	2	16	0.1	3	
54	Impaired	10	N/A	11 (ID)	18	0.4	9	0.1	0.1	N/A	<0.1	Abnormal brain MRI
55	Impaired	10	N/A	N/A	12	N/A	16	0.4	9	2	N/A	
61	Impaired	6.67	ID	15 (ID)	18	2	9	5	25	5	3	Articulation Problem
66	Impaired	5	WNL	21 (ID)	20	16	25	2	50	16	10	ADHD
70	Impaired	1.67	ID	20 (ID)	19	5	2	2	1	0.1	0.4	PDD.NOS Asperger
80	Impaired	6.67	WNL	24 (WNL)	20	50	37	50	75	25	53	ADHD
13	Control	6.67	ID	18 (WNL)	20	50	75	9	16	50	25	
17	Control	6.67	ID	11 (ID)	20	84	37	50	37	37	53	
18	Control	10	ID	18 (ID)	21	37	25	16	37	5	19	
19	Control	3.33	ID	24 (WNL)	21	63	16	16	63	37	30	
20	Control	11.67	N/A	N/A	22	N/A	98	N/A	N/A	N/A	N/A	Autism
21	Control	10	ID	11 (ID)	19	37	25	0.1	0.1	1	1	
23	Control	6.67	ID	14 (ID)	21	84	16	0.4	5	37	7	
29	Control	5	N/A	N/A	24	N/A	75	N/A	N/A	N/A	N/A	
30	Control	5	N/A	N/A	21	N/A	25	N/A	N/A	N/A	N/A	
34	Control	8.33	N/A	N/A	22	N/A	37	N/A	N/A	N/A	N/A	
35	Control	10	N/A	N/A	20	N/A	75	N/A	N/A	N/A	N/A	Seizures
36	Control	6.67	N/A	N/A	19	N/A	37	N/A	N/A	N/A	N/A	ADHD-Autism
38	Control	5	N/A	N/A	22	N/A	25	N/A	N/A	N/A	N/A	Blood Pressure
39	Control	20	N/A	N/A	20	N/A	25	N/A	N/A	N/A	N/A	
46	Control	5	N/A	N/A	21	63	91	9	16	37	39	
57	Control	1.67	ID	16 (ID)	22	25	63	5	9	0.1	13	PDD.NOS
63	Control	6.67	ID	24 (WNL)	20	63	16	25	25	37	23	

Table *4A*. Behavioral performance on APD tests from all 51 subjects participated in the study and who were placed in either the impaired or the control group based on the more inclusive analysis before matching. PTA = pure tone average (right Ear 1-4 kHz), SSW = staggered spondaic words, PS = phonemic synthesis, CID = CID-W22 in Noise-Right Ear, FW = filtered words, AFG = auditory figure ground, CW = competing words, CS = competing sentences, TCS = time compressed speech, C = composite, N/A = not administered, ID = identified, WNL = within normal limits.

			Buffalo Test Battery (Raw Scores When Applicable)			Scan-3 (Percentile Scores)						
Subject	Group	PTA	SSW	PS	CID	FW	AFG	CW	CS	TCS	C	Morbid Condition
14	Impaired	Not Done	WNL	N/A	23	75	5	37	50	84	30	
15	Impaired	5	ID	18 (WNL)	17	25	9	9	37	5	10	
16	Impaired	6.67	ID	14 (ID)	19	37	2	2	16	0.1	3	ADHD
22	Impaired	8.33	ID	20 (ID)	15	84	25	16	75	25	50	ADHD
28	Impaired	Audiogram not clear*	ID	17 (WNL)	19	50	9	0.1	9	9	3	ADHD
31	Impaired	10	N/A	N/A	22	N/A	1	N/A	N/A	N/A	N/A	
32	Impaired	Audiogram not clear*	ID	20 (WNL)	22	16	5	37	91	1	25	
40	Impaired	6.67	N/A	N/A	20	N/A	16	N/A	N/A	N/A	N/A	
42	Impaired	13.33	ID	22 (WNL)	24	25	1	16	16	25	4	ADHD
44	Impaired	10	ID	20 (ID)	21	37	5	50	37	25	19	ADHD
45	Impaired	6.67	N/A	N/A	23	N/A	2	N/A	N/A	N/A	N/A	
47	Impaired	10	ID	16 (ID)	13	2	0.1	1	9	0.4	0.2	
48	Impaired	13.33	ID	13 (ID)	14	2	0.1	1	25	5	0.1	
50	Impaired	8.75	ID	9 (ID)	13	0.1	0.4	0.1	9	0.1	<0.1	
51	Impaired	8.33	N/A	N/A	17	25	5	5	75	25	10	ADHD
53	Impaired	6.67	ID	20 (WNL)	19	9	9	2	16	0.1	3	
54	Impaired	10	N/A	11 (ID)	18	0.4	9	0.1	0.1	N/A	<0.1	Abnormal brain MRI
55	Impaired	10	N/A	N/A	12	N/A	16	0.4	9	2	N/A	
59	Impaired	Audiogram not clear*	WNL	20 (WNL)	17	16	84	50	95	16	73	
61	Impaired	6.67	ID	15 (ID)	18	2	9	5	25	5	3	Articulation Problem
65	Impaired	8.33	WNL	18 (ID)	14	37	5	1	84	25	13	
66	Impaired	5	WNL	21 (ID)	20	16	25	2	50	16	10	ADHD
67	Impaired	3.33	ID	21 (WNL)	17	5	25	5	5	2	3	ADHD
70	Impaired	1.67	ID	20 (ID)	19	5	2	2	1	0.1	0.4	PDD.NOS Asperger
72	Impaired	0	ID	20 (ID)	20	50	37	16	75	37	37	
73	Impaired	5	ID	22 (WNL)	18	37	9	5	25	25	9	
80	Impaired	6.67	WNL	24 (WNL)	20	50	37	50	75	25	53	ADHD
81	Impaired	5	ID	22 (ID)	20	37	37	9	25	1	16	Autism
13	Control	6.67	ID	18 (WNL)	20	50	75	9	16	50	25	
17	Control	6.67	ID	11 (ID)	20	84	37	50	37	37	53	
18	Control	10	ID	18 (ID)	21	37	25	16	37	5	19	
19	Control	3.33	ID	24 (WNL)	21	63	16	16	63	37	30	
20	Control	11.67	N/A	N/A	22	N/A	98	N/A	N/A	N/A	N/A	Autism
21	Control	10	ID	11 (ID)	19	37	25	0.1	0.1	1	1	
23	Control	6.67	ID	14 (ID)	21	84	16	0.4	5	37	7	

24	Control	6.67	WNL	25 (WNL)	21	63	25	37	84	84	53	ADHD
29	Control	5	N/A	N/A	24	N/A	75	N/A	N/A	N/A	N/A	
30	Control	5	N/A	N/A	21	N/A	25	N/A	N/A	N/A	N/A	
34	Control	8.33	N/A	N/A	22	N/A	37	N/A	N/A	N/A	N/A	
35	Control	10	N/A	N/A	20	N/A	75	N/A	N/A	N/A	N/A	Seizures
36	Control	6.67	N/A	N/A	19	N/A	37	N/A	N/A	N/A	N/A	ADHD-Autism
38	Control	5	N/A	N/A	22	N/A	25	N/A	N/A	N/A	N/A	Blood Pressure
39	Control	20	N/A	N/A	20	N/A	25	N/A	N/A	N/A	N/A	
43	Control	Audiogram not clear*	ID	10 (WNL) picture	18	5	16	N/A	N/A	N/A	N/A	
46	Control	5	N/A	N/A	21	63	91	9	16	37	39	
52	Control	8.33	WNL	25 (WNL)	23	50	16	50	50	N/A	93	
57	Control	1.67	ID	16 (ID)	22	25	63	5	9	0.1	13	PDD.NOS
63	Control	6.67	ID	24 (WNL)	20	63	16	25	25	37	23	
75	Control	0	N/A	N/A	22	N/A	37	N/A	N/A	N/A	N/A	
76	Control	1.67	N/A	N/A	22	N/A	16	N/A	N/A	N/A	N/A	
77	Control	5	N/A	N/A	21	N/A	50	N/A	N/A	N/A	N/A	

[* Although original audiograms showed threshold levels within 20 dB HL (500-4000 Hz), there is no access to original audiograms for these subjects and copies of audiograms put in subjects' files did not clearly indicate threshold levels].

Table 5A. Range, mean, standard error of mean (SE) and standard deviation (SD) for the CID and AFG percentile test scores in the impaired and control groups from the more inclusive analysis (N=17)*.

Statistic	Control		Impaired	
	CID	AFG	CID	AFG
Range	85.77-18.67=67.1	98-16=82	96.25-0.01=96.24	37-0.1=36.9
Mean	42.83	44.76	22.02	10.36
SE	5.45	6.82	7.53	2.51
SD	22.49	28.13	31.04	10.36

(* Three subjects complained about static during the administration of the CID-W22 and AFG tests. Two of these complained about static during the administration of CID-22 test in noise. The test was repeated once for one subject and 4 times for the other subject in order to obtain results not contaminated by static. The third subject complained about static during the administration of both CID-W22 and the AFG tests in noise and both tests were repeated without static. In all cases, the scores from the static-free tests were included in the analysis).

Table 6A. Range, mean, and standard deviation (SD) for subjects' age in each of the impaired and control groups from the more inclusive analysis (N=17)*.

Statistic	Range	Mean	SD
APC	10.91	11.17	3.36
APD	9.59	10.98	3.02

(* According to parent report, 10 impaired subjects had morbid conditions: Asperger-pervasive developmental disorder-not otherwise specified, articulation and abnormal MRI brain scan. The remaining seven impaired subjects had ADHD. Five controls had morbid conditions: pervasive developmental disorder-not otherwise specified, autism, seizures, blood pressure and the remaining subjects had both ADHD and autism).

Table 7A. Pearson correlations coefficients from the more inclusive analysis between CID / AFG percentile test scores and ΔdB OAE averaged across the frequency range within (N=17) and in the combined impaired and control groups (N=34) (p values are represented between parenthesis).

MOC Index	Control		Impaired		Combined	
	CID	AFG	CID	AFG	CID	AFG
Composite ΔdB OAE	0.25 (0.32)	-0.02 (0.93)	0.18 (0.48)	0.07 (0.79)	0.2 (0.26)	0.01 (0.94)
Overlap ΔdB OAE	0.38 (0.13)	0.23 (0.37)	0.23 (0.37)	0.01 (0.98)	0.24 (0.17)	0.06 (0.72)

Table 8A. Mean and standard error (SE) of the averaged up- and down-sweeps across the frequency range for composite DPOAE and the overlap component levels in dB SPL without (No-CAS) and with contralateral 60 dB SPL noise (CAS) in the impaired and control groups from the more inclusive analysis (N=17).

Statistic	Control				Impaired			
	Composite		Overlap		Composite		Overlap	
	No-CAS	CAS	No-CAS	CAS	No-CAS	CAS	No-CAS	CAS
Mean	5.08	4.06	4.28	3.21	2.87	1.81	1.87	0.8
SE	1.51	1.55	1.62	1.69	1.51	1.55	1.62	1.69

Table 9A. Mean and standard error of the mean (SE) of the averaged up- and down-sweeps across the frequency range for composite DPOAE and the overlap component in ΔdB OAE and Δ% Pa OAE in the impaired and control groups from the more inclusive analysis (N=17).

Statistic	Control				Impaired			
	Composite		Overlap		Composite		Overlap	
	ΔdB	Δ% Pa	ΔdB	Δ% Pa	ΔdB	Δ% Pa	ΔdB	Δ% Pa
Mean	-0.45	-8.48	-0.99	-12.38	-0.47	-9.09	-0.96	-11.91
SE	0.22	2.04	0.2	2.28	0.22	2.04	0.2	2.28

Table 10A. Main effects and interactions of two-way repeated measures ANOVA for ΔdB and Δ%Pa in composite DPOAE from the more inclusive analysis.

Statistic	ΔdB			Δ%Pa		
	F	Sig	Power	F	Sig	Power
Group	0.01	0.94	0.05	0.05	0.83	0.06
Frequency	2.07	0.12	0.47	1.52	0.22	0.38
Group X Frequency	0.59	0.59	0.16	0.99	0.4	0.25

Table 11A. Main effects and interactions of two-way repeated measures ANOVA for ΔdB and Δ%Pa in the overlap component from the more inclusive analysis.

Statistic	ΔdB			Δ%Pa		
	F	Sig	Power	F	Sig	Power
Group	0.02	0.9	0.05	0.02	0.89	0.05
Frequency	1.36	0.26	0.35	0.94	0.42	0.25
Group X Frequency	1.34	0.27	0.35	1.62	0.19	0.41

Table 12A. Main effects and interactions of two-way repeated measures ANOVA for composite DPOAE and the overlap component baseline level from the more inclusive analysis.

Statistic	Composite DPOAE Baseline Level			Overlap Component Baseline Level		
	F	Sig	Power	F	Sig	Power
Group	1.08	0.31	0.17	1.1	0.3	0.18
Frequency	**85.62**	**0.00****	1.00	**71.09**	**0.00****	1.00
Group X Frequency	0.66	0.57	0.18	0.5	0.64	0.14

(p<0.01)**

8. References

Abdala, C. and Dhar, S. (2012). Maturation and aging of the human cochlea: A view through the DPOAE looking glass. Journal of the Association for Research in Otolaryngology, 13, 403-421.

Abdala, C., Ma, E., and Sininger, Y. (1999). Maturation of medial efferent system function in humans. Journal of the Acoustical Society of America, 105, 2392-2402.

Abdala, C., Mishra, S. K., & Williams, T. L. (2009). Considering distortion product otoacoustic emission fine structure in measurements of the medial olivocochlear reflex. Journal of the Acoustical Society of America, 153, 1584-1594.

American Academy of Audiology (AAA) (2010).*Guidelines for the Diagnosis, Treatment and Management of Children and Adults with Central Auditory Processing Disorder*. http://www.audiology.org/resources/documentlibrary/Documents/CAPD%20Guidelines%208-2010.pdf208-2010.pdf.

American Speech-Language-Hearing Association (ASHA) (2005).*(Central) Auditory Processing Disorders*. Technical report. http://www.asha.org/members/deskref journals / deskref/default.

Backus, B. C. and Guinan, J. J., Jr. (2006). Time course of the human medial olivocochlear reflex. Journal of the Acoustical Society of America, 119, 2889-2904.

Backus, B.C. and Guinan, J. J., Jr., (2007). Measurement of the distribution of medial olivocochlear acoustic reflex strengths across normal-hearing individuals via otoacoustic emissions. Journal of the Association for Research in Otolaryngology, 8, 484-496.

Bassim M.K., Miller R.L., Buss E. & Smith D.W. (2003). Rapid adaptation of the 2f1-f2 DPOAE in humans: Binaural and contralateral stimulation effects. Hearing Research, 182, 140-152.

Bellis, T.J., (2003). Assessment and management of central auditory processing disorders in the educational setting: From science to practice (2nd ed.). Clifton Park, N.Y: Delmar Learning.

Bhagat, S.P. and Carter, P.H. (2010). Efferent-induced change in human cochlear compression and its influence on masking of tones. Neuroscience Letters, 485,94-97.

Borg, E. (1971).Efferent inhibition of afferent acoustic activity in the unanesthetized rabbit. Experimental Neurology, 31, 301-312.

British Society of Audiology. (2011). Position Statement - Auditory processing disorder (APD).Available at http://www.thebsa.org.uk/images/stories/docs / BSA_APD_PositionPaper_31March11_FINAL .pdf.

Brown, M, Kujawa, S., and Duca, M. (1998).Single olivocochlear neurons in the guinea pig. I. Binaural facilitation of responses to high-level noise. Journal of Neurophysiology, 79, 3077-3087.

Burguetti, F, Mota, R. and Carvallo, M. (2008). Efferent auditory system: its effect on auditory processing. Brazilian Journal of Otorhinolaryncology, 74, 737-745.

Butler, B., Purcell, D. and Allen, P. (2011). Contralateral inhibition of distortion product otoacoustic emissions in children with auditory processing disorders. International Journal of Audiology, 50, 530-539.

Chermak GD, Hall JW, and Musiek F. (1999). Differential diagnosis and management of central auditory processing disorder and attention deficit hyperactivity disorder. Journal of the American Academy of Audiology, 10, 289-303.

Chermak, G., Tucker, E., and Seikel, J. (2002). Behavioral characteristics of auditory processing disorder and attention deficit hyperactivity disorder: Predominantly inattentive type. Journal of the American Academy of Audiology, 13, 332-338.

Collet, L., Kemp, D. T., Veuillet, E., Duclaux, R., Moulin, A., and Morgon, A. (1990). Effect of contralateral auditory stimuli onactive cochlear micro-mechanical properties in human subjects. Hearing Research, 43, 251–262.

Cooper, N. P., Pickles, J., and Manley, G. (2008). "Traveling waves, second filters, and physiological vulnerability: A short history of the discovery of active processes in hearing", Springer Handbook of Auditory Research.

de Boer, J., Thornton, A. R., and Krumbholz, K. (2012). What is the role of the medial olivocochlear system in speech-in-noise processing? Journal of Neurophysiology, 107, 1301-1312.

Deeter, R., Abel, R., Calandruccio, L., and Dhar, S. (2009). Contralateral acoustic stimulation alters the magnitude and phase of distortion product otoacoustic emissions. Journal of the Acoustical Society of America 126, 2413-24.

Dewson, J. H. (1967). Efferent olivocochlear bundle: Some relationships to noise masking and to stimulus attenuation. Journal of Neurophysiology, 30, 817-832.

Dewson, J.H., (1968). Efferent olivocochlear bundle: Some relationships to stimulus discrimination in noise. Journal of Neurophysiology, 31,122-130.

Dhar, S., Long, G., Talmadge, C., and Tubis, A. (2005). The effect of stimulus-frequency ratio on distortion product otoacoustic emission components. Journal of the Acoustical Society of America, 117, 3766–3776.

Dolan, D., Guo, M., and Nuttal, A. (1997). Frequency-dependant enhancement of basilar membrane velocity during olivocochlear bundle stimulation. Journal of the Acoustical Society of America, 102, 3587-3596.

Dolan. D. and Nuttal, A. (1987). Masked cochlear whole-nerve response intensity functions altered by electrical stimulation of the crossed olivocochlearbundle.Journal of the Acoustical Society of America, 83, 1081-1086.

Francis, N. and Guinan, J. (2011). The dependence of medial olivocochlear feedback on signal-to-noise ratio during auditory intensity discrimination[Abstract]. *Abstracts of the Midwinter Research Meeting/Association for Research in Otolaryngology, 34,* 180.

Froehlich, P, Collet, L., &Morgon, A. (1993). Transiently evoked otoacoustic emission amplitudes change with changes of directed attention. Physiology & Behavior, 53, 679–682.

Ferber-Viart, C., Duclaux, R., Collet. L., &Guyonnard, F. (1995). Influence of auditory stimulation and visual attention on otoacousticemissions.Physiology& Behavior, 57, 1075-1079.

Garinis, A. Werner, L. and Abdala, C. (2011). The relationship between MOC reflex and masked threshold. Hearing Research., 282, 128-137.

Gelfand, S. A., Schwander, T. and Silman, S. (1990). Acoustic reflex thresholds in normal and cochlear-impaired ears: Effects of no-response rates on 90th percentiles in a large sample. Journal of Speech and Hearing Disorders, 55, 198-205.

Giard, M., Collet, L, Bouchet, P. and Pernier, J. (1994). Auditory selective attention in the human cochlea. Brain Research, 633, 353-356.

Giraud, A. L., Garnier, S., Micheyl, C., Lina, G., Chays, A. and Chery-Croze, S. (1997). Auditory efferents involved in speech-in-noise intelligibility. Neuroreport, 8, 1779–1783.

Goodman, S., & Keefe, D. (2006). Simultaneous measurement of noise-activated middle-ear muscle reflex and stimulus frequency otoacoustic emissions. Journal of the Association for Research in Otolaryngology, 7, 125-139.

Guinan, J. J., Jr. (2006). Olivocochleareferents: Anatomy, physiology, function, and measurement of efferent effects in humans. Ear and Hearing, 27, 589-607.

Guinan, J.J., Jr. (2011). Physiology of the Medial and Lateral Olivocochlear Systems. In: D.K. Ryugo, A.N. Popper and R.R. Fay (Eds). Auditory and Vestibular Efferents (pp. 39-81). New York: Springer Science+Business Media.

Guinan, J. J., Jr., Backus, B., Lilaonitkul, W. and Aharonson, V. (2003). Medial olivocochlear

efferent reflex in humans: Otoacousticmmission (OAE) measurement issues and the advantages of stimulus frequency OAEs. Journal of the Association for Research in Otolaryngology, 4, 521-540.

Guinan, J. J., Jr., Warr, W. and Norris, B. (1983). Differential olivocochlear projections from lateral versus medial zones of the superior olivary complex. The Journal of Comparative Neurology, 221, 358-370.

Guinan, J. J., Jr., Warr, W. and Norris, B (1984). Topographic organization of the olivocochlear projections from the lateral and medial zones of the superior olivary complex. The Journal of Comparative Neurology, 226, 21-27.

Harkrider, A. and Smith, S. (2005). Acceptable noise level, phoneme recognition in noise, and measures of auditory efferent activity. Journal of the American Academy of Audiology, 16, 530-545.

He, N.J., and Schmiedt, R. A. (1993). Fine structure of the 2*f* 1-*f* 2 acoustic distortion product: Changes with primary level. Journal of the Acoustical Society of America, 94, 2659-2669.

Heitmann, J., Waldmann, B., Schnitzler, H.P., Plinkert, P.K., and Zenner, H.P. (1998). Suppression of distortion product otoacoustic emissions (DPOAE) near 2f1-f2 removes DP-gram fine structure - Evidence for a second generator. Journal of the Acoustical Society of America, 103, 1527-1531.

Henin, S. and Long, G. (2012). Effect of middle-ear-muscle reflex on measures of efferent-induced suppression of distortion product otoacoustic emissions [Abstract]. *Abstracts of the Midwinter Research Meeting/Association for Research in Otolaryngology*, *35*, 102.

Henin, S., Thompson, S., Abdelrazeq, S., and Long, G. (2011). Changes in amplitude and phase of distortion-product otoacoustic emission fine-structure and separated components during efferent activation. Journal of the Acoustical Society of America, 129, 2068-2079.

Hienz, H., Stiles, P., and May, B. (1998). Effects of bilateral olivocochlear lesions on vowel formant discrimination in cats. Hearing Research, 116, 10-20.

Hirsh, I.J., Davis, H., Silverman, S.R., Reynolds, E.G., Eldert, E. and Benson, R.W. (1952). Development of materials for speech audiometry.Journal of Speech and Hearing Disorders, 17, 321-337.

James A.L., Harrison R.V., Pienkowski M., Dajani H.R. & Mount R.J. (2005). Dynamics of real time DPOAE contralateral suppression in chinchillas and humans. International Journal of Audiology, 44, 118-129.

Jerger, J., and Musiek, F. (2000). Report of the consensus conference on the diagnosis of auditory processing disorders in school-aged children.Journal of the American Academy of Audiology, 11, 467-474.

Johnson, T., Neely, S., Kopun, J. and Gorga, M. (2006). Reducing reflected contributions to ear-canal distortion product otoacoustic emissions in humans. Journal of the Acoustical Society of America, 119, 3896-3907.

Joseph, M., Guinan, J., Fullerton, B., Norris, B. and Kiang, N. (1985).Number and distribution of stapedius motoneurons in cats. Journal of Comparative Neurology, 232, 43-54.

Kalluri, R. and Shera, C. A. (2001). Distortion-product source unmixing: a test of the two-mechanism model for DPOAE generation. Journal of the Acoustical Society of America, 109, 622-637.

Kalluri, R. and Shera, C. A. (2007). Near equivalence of human click-evoked and stimulus-frequency otoacoustic emissions. Journal of the Acoustical Society of America, 121, 2097-110.

Katz, J. (1992). Classification of auditory processing disorders. In J. Katz, N. Stecker, D. Henderson (Eds.), *Central Auditory Processing: A Transdisciplinary View* (p. 81-92). Chicago: Mosby Yearbook.

Katz, J. (2007). APD Evaluation to Therapy: The Buffalo Model. *Audiology online*. Retrieved August 08, 2012, from http://www.audiologyonline.com/articles/ article_detail.asp?article_id=1803.

Kawase, T., Delgutte, B. and Liberman, M. C. (1993). Antimasking effects of the olivocochlear reflex, II: Enhancement of auditory-nerve response to masked tones. Journal of Neurophysiology, 70, 2533-2549.

Kawase, T., Hidaka, H.andTakasaka T. (1997). Frequency summation observed in the human acoustic reflex.Hearing Research, 108, 37-45.

Kawase, T. and Liberman, M. C. (1993). Antimasking effects of the olivocochlear reflex, I. Enhancement of compound action potentials to masked tones. Journal of Neurophysiology 70, 2519-2532.

Keith, R. (2009a). SCAN-3:C. Tests for Auditory Processing Disorders for Children, San Antonio, TX: Pearson.

Keith, R. (2009b). SCAN-3:A. Tests for Auditory Processing Disorders in Adolescent and Adults, San Antonio, TX: Pearson.

Kemp, D. T. (1978). Stimulated acoustic emissions from the human auditory system, Journal of the Acoustical Society of America, 64, 3566-3576.

Kumar, U.A. and Vanaja, C.S. (2004). Functioning of olivocochlear bundle and speech perception in noise. Ear and Hearing, 25, 142-146.

Kummer, P., Janssen, T. and Arnold, W. (1998). Level and growth behavior of the 2f1-f2 distortion-product otoacoustic emission and its relation to auditory sensitivity. Journal of the Acoustical Society of America, 103, 3431-3444.

Liberman, M.C. (1980). Efferent synapses in the inner hair cell area of the cat cochlea: an electron microscopic study of serial sections. Hearing research, 3, 189-204.

Liberman MC (1988). Response properties of cochlear efferent neurons: monaural vs. binaural stimulation and the effects of noise. Journal of Neurophysiology, 60, 1779-1798

Liberman, M. C. and Brown, M. C. (1986). Physiology and anatomy of single olivocochlear neurons in the cat. Hearing Research, 24, 17-36.

Liberman, M. and Guinan, J. (1998). Feedback control of the auditory periphery: anti-masking effects of middle ear muscles vs. olivocochlear efferents. Journal of Communication Disorders, 31, 471-482.

Lilaonitkul W. and Guinan, J.J. Jr (2009a). Human medial olivocochlear reflex: effects as functions of contralateral, ipsilateral, and bilateral elicitor bandwidths. Journal of Association Research in Otolaryngology, 10, 459-470.

Lilaonitkul W. and Guinan, J.J. Jr (2009b). Reflex control of the human inner ear: a half-octave offset in medial efferent feedback that is consistent with an efferent role in the control of masking. Journal of Neurophysiology, 101, 1394-1406.

Liliaonitkul, W. and Guinan, J.J., Jr. (2012). Frequency tuning of medial-olivocochlear-efferent acoustic reflexes in humans as functions of probe frequency. Journal of Neurophysiology, 107, 1598-1611.

Long, G.R., Jeung. C., & Talmadge, C.L. (2009). Dependence of Distortion-Product Otoacoustic Emission Components on Primary-Level Ratio. In "Concepts and Challenges in the Biophysics of Hearing" Edited by N.P. Cooper and D.T. Kemp. World Scientific Press, Singapore. pp 203-208.

Long, G. R. and Talmadge, C.L. (1997). Spontaneous otoacoustic emission frequency is modulated by heartbeat. Journal of the Acoustical Society of America, 102, 2831-2848.

Long, G.R., Talmadge, C.L. and Lee, J. (2008) Measuring distortion product otoacoustic emissions (DPOAE) using continuously sweeping primaries. Journal of the Acoustical Society of America, 124, 1613-1626.

Maison, S., Micheyl, C., & Collet, L. (2001). Influence of focused auditory attention on cochlear activity in humans. Psychophysiology, 38, 35-40.

Mauermann, M. and Kollmeier, B. (2004). Distortion product otoacoustic emission (DPOAE) input/output functions and the influence of the second DPOAE source. Journal of Acoustical Society of America, 116, 2199–2212.

Mauermann, M., Uppenkamp, S., van Hengel, P. W., and Kollmeier, B. (1999a). Evidence for the distortion product frequency place as a source of distortion product otoacoustic emission (DPOAE) fine structure in humans. I. Fine structure and higher order DPOAE as a function of ratio. Journal of the Acoustical Society of America, 106, 3473-3483.

Mauermann, M., Uppenkamp, S., van Hengel, P. W. J., and Kollmeier, B. (1999b). Evidence for the distortion product frequency place as a source of distortion product otoacoustic emission DPOAE fine structure in humans. II. Fine structure for different shapes of cochlear hearing loss. Journal of the Acoustical Society of.America, 106, 3484-3491.

May, B. and McQuone, S. (1995). Effects of bilateral olivocochlear lesions on pure tone intensity discrimination in cats. Auditory Neuroscience, 385-400.

Micheyl, C. and Collet, L. (1996). Involvement of the olivocochlear bundle in the detection of tones in noise.Journal of the Acoustical Society of America, 99, 1064-1610.

Micheyl, C., Morlet, T., Giraud, A.L., Collet, L. and Morgon, A. (1995). Contralateral suppression of evoked otoacoustic emissions and detection of a multi-tone complex in noise. Acta Oto-Laryngologica, 115, 178-182.

Micheyl, C., Perrot, X. and Collet, L. (1997). Relationship between auditory intensity discrimination in noise and olivocochlear efferent system activity in humans. Behavioral Neuroscience, 111, 801-807.

Moore, D. (2006). Auditory processing disorder: definition, diagnosis, neural basis and intervention. Audiological Medicine, 4, 4-11.

Moore, D. R., Ferguson, M. A., Edmondson-Jones, A. M., Ratib, S. and Riley, A. (2010). Nature of Auditory Processing Disorder in Children.Pediatrics, 126, e382-e390.

Moore, D., Cowan, J., Riley, A., Edmondson-Jones, M. and Ferguson, M. (2011). Development of Auditory Processing in 6- to 11-Yr-Old Children. Ear and Hearing, 32, 269-285.

Moulin, A., Collet, L., &Duclaux, R. (1993). Contralateral auditory stimulation alters acoustic distortion products in humans. Hearing Research, 65, 193-210.

Muchnik, C., Roth, D., Jebara, R., Katz, H., Shabtai, E., and Hildesheimer, M. (2004). Reduced medial olivocochlear bundle and function in children with auditory processing disorders. Audiology and Neurotology, 9, 107-114.

Mukari S.Z. and Mamat W.H. (2008). Medial olivocochlear functioning and speech perception in noise in older adults. Audiology and Neurootology, 13, 328-334.

Mulders, W. H. and Robertson, D. (2002). Inputs from the cochlea and the inferior colliculus converge on olivocochlear neurones. Hearing Research, 167, 206–213.

Murugasu, E., and Russell, L., (1996). The effect of efferent stimulation on basilar membrane displacement in the basal turn of the guinea pig cochlea. The Journal of Neuroscience, 16, 325-332.

MusiekF.E., Bellis T.J. and ChermakG.D. (2005). Nonmodularity of the CANS: Implications for (central) auditory processing disorder. American Journal of Audiology, 14, 128-138.

Nieder, P., and Nieder, I. (1970). Antimasking effect of crossed olivocochlear bundle stimulation with loud clicks in guinea pig. Experimental Neurology, 28, 179-188.

O'Beirne, G. A., McGaffin, A. J., and Rickard, N. A. (2012). Development of an adaptive low-pass filtered speech test for the identification of auditory processing disorders. International Journal of Pediatric Otorhinolaryngology, 76, 777-782.

Perrot, X., Ryvlin, P., Jean Isnard, J., ,Guenot, M., Catenoix, H., Fischer, C., Mauguiere, F. and Lionel Collet, L. (2006). Evidence for corticofugal modulation of peripheral auditory activity in humans. Cerebral Cortex, 16, 941-948.

Relkin, E.M., Sterns, A., Azeredo, W., Prieve, B.A., Woods, C. (2005). Physiological mechanisms of onset adaptation and contralateral suppression of DPOAEs in the rat. Journal of the Association for Research in Otolaryngology 6, 119-135.

Robles, L. and Ruggero, M. A. (2001).Mechanics of the mammalian cochlea. Physiological Reviews, 81, 1305-1352.

Russell, I and Murugaso, E. (1997). Medial efferent inhibition suppresses basilar membrane responses to near characteristic frequency tones of moderate to high intensities. Journal of the Acoustical Society of America, 102, 1734-1738.

Sanches, S., and Carvallo, R. (2006). Contralateral suppression of transient evoked otoacoustic emissions in children with (C)APD. Audiology and Neurotology, 11, 366-372.

Selesnick, I. and andHajicek, J. (2010). Weighted averaging for artifact rejection in measurements of OAEs.

Shera, C. A. and Guinan, J. J., Jr. (1999). Evoked otoacoustic emissions arise by two fundamentally different mechanisms: a taxonomy for mammalian OAEs. Journal of the Acoustical Society of America, 105, 782-798.

Shera, C. A., and Guinan, J. J., Jr. (2007). Mechanisms of mammalian otoacoustic emission. In Springer Handbook of Auditory Research Active Processes and Otoacoustic Emissions in Hearing. Edited by Geoffrey A. Manley, Richard R. Fay and Arthur N. Popper. Springer New York.pp 305-342.

Stuart, A. and Butler, A. (2012). Contralateral suppression of transient otoacoustic emissions and sentence recognition in noise in young adults. Journal of the American Academy of Audiology, 23, 686–696.

Sun, X. (2008). Distortion product otoacoustic emission fine structure is responsible for variability of distortion product otoacoustic emission contralateral suppression. Journal of the Acoustical Society of America, 123, 4310-4320.

Talmadge, C. L., Long, G. R., Tubis, A. and Dhar, S. (1999). Experimental confirmation of the two-source interference model for the fine structure of distortion product otoacoustic emissions. Journal of the Acoustical Society of America, 105, 275-292.

Thompson, A. and Thompson, G. (1993). Relationship of descending inferior colliculus projections to olivocochlear neurons. Journal of Comparable Neurology, 335, 402-412..

Vetter, D. E., Saldana, E., &Mugnaini, E. (1993). Inputs from the inferior colliculus to medial olivocochlear neurons in the rat: A double label study with PHA-L and Cholera Toxin. Hearing Research, 70, 173-186.

Veuillet, E., Collet, L., and Duclaux, R. (1991). Effect of contralateral acoustic stimulation on active cochlear micromechanical properties in human subjects: dependence on stimulus variables. Journal of Neurophysiology, 65, 724-735.

Wagner, W, Heppelmann, G., Muller, J., Janssen, T., and Zenner, H.-P (2007). Olivocochlear reflex effect on human distortion product otoacouctic emissions is largest at frequencies with distinct fine structure dips. Hearing Research, 223, 83-92.

Wagner,W., Frey, K., Heppelmann, G., Plontke, S.K. and Hanz-Peter, Z. (2008). Speech-in-noise intelligibility does not correlate with efferent olivocochlear reflex in humans with normal hearing. ActaOto-Laryngologica, 128, 53-60.

Warr, W. and Guinan, J.J., Jr. (1979). Efferent innervation of the organ of corti: two separate systems. Brain Research, 173, 152-155.

Winslow, R. and Sachs, M. (1987). Effect of electrical stimulation of the crossed olivocochlear bundle on auditory nerve response to tones in noise. Journal of Neurophysiology, 57, 1002-1021.

Winslow, R and Sachs, M. (1988). Single-tone intensity discrimination based on auditory-nerve rate responses in backgrounds of quiet, noise, and with stimulation of the crossed olivocochlear bundle. Hearing Research, 15,165-189.

Yalcinkaya, F., Yılmaz, S., and Muluk, N. (2010). Transient evoked otoacoustic emissions and contralateral suppressions in children with auditory listening problems. Auris Nasus Larynx, 37, 47-54.

Yilmaz, S., Sennaroglu, G., Sennaroglu, L. and Kose, S. (2007). Effect of age on speech recognition in noise and on contralateral transient evoked otoacoustic emission suppression. The Journal of Laryngology and Otology, 121, 1029-1034.

Zhang, F., Boettcher, F. A., and Sun, X.-M. (2007). Contralateral suppression of distortion product otoacoustic emissions: Effect of the primary frequency in Dpgrams. International Journal of Audiology, 46, 187-195.