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**CONTRALATERAL SUPPRESSION OF DISTORTION PRODUCT
OTOACOUSTIC EMISSIONS IN CHILDREN WITH AND WITHOUT
AUDITORY PROCESSING DISORDERS**

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CONTRALATERAL SUPPRESSION OF DISTORTION PRODUCT OTOACOUSTIC
EMISSIONS IN CHILDREN WITH AND WITHOUT AUDITORY PROCESSING
DISORDERS

(Spine Title: Suppression of DPOAEs in children with and without APD)
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by

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Graduate Program
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ABSTRACT

This manuscript provides data on contralateral suppression of distortion product otoacoustic emissions in normal hearing children and children with Auditory Processing Disorders. Listeners included children 8 to 13 years-old. DPOAEs were elicited at three test frequencies around a narrow test ratio of $f_2/f_1 = 1.1$ along with the traditional $f_2/f_1 = 1.22$. Results suggest a frequency effect with suppression decreasing as f_2 frequency increased, and a ratio effect with greater suppression at the narrow ratio. Additionally, no significant differences existed between normal children and previously obtained adult norms for measures of maximum suppression, mean suppression and maximum/mean suppression ratio. The APD group however, showed greater variance in these measures than normal children, reaching significance for maximum suppression at $f_2 = 3$ kHz and $f_2/f_1 = 1.22$. The large variance of the APD population may be of clinical interest pending a better understanding of the deficits underlying the disorder.

KEYWORDS

Auditory Processing Disorder, Children, Fine Structure, Otoacoustic Emission, Distortion Product

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LIST OF ABBREVIATIONS

ABR	Auditory Brainstem Response
APD	Auditory Processing Disorder
CAS	Contralateral Acoustic Stimulation
dB	Decibel
DPOAE	Distortion Product Otoacoustic Emission
HL	Hearing Level
Hz	Hertz
kHz	Kilohertz
MANOVA	Multivariate Analysis of Variance
MEMR	Middle Ear Muscle Reflex
MOC	Medial Olivocochlear
MOCB	Medial Olivocochlear Bundle
ms	Millisecond
OAE	Otoacoustic Emission
OC	Olivocochlear
OCB	Olivocochlear Bundle
SL	Sensation Level
SNR	Signal-to-Noise Ratio
SPL	Sound Pressure Level
TEOAE	Transiently Evoked Otoacoustic Emission
VNT	Vestibular Neurotomy

I. INTRODUCTION

Contralateral Suppression of Distortion Products

The cochlear amplifier is an active mechanism responsible for enhanced sensitivity, superb temporal processing and the fine tuning of the basilar membrane. A byproduct of outer hair cell (OHC) electromotility and stereociliary mechanical nonlinearities that exist within this mechanism is the generation of vibrations that propagate to the external auditory meatus where they can be measured as otoacoustic emissions (OAEs). There are four basic categories of OAEs; the first to be recorded occurred spontaneously without an acoustic stimulus ([SOAEs] Kemp, 1979), however, other varieties may be evoked using auditory stimuli. Transient evoked otoacoustic emissions (TEOAEs) occur in response to a click or tone burst stimulus that elicits a broadband response from a wide region of the basilar membrane. The stimulus frequency OAE gives a more narrowband response that is elicited by a puretone, but because the response occurs at the frequency of stimulation it is technically challenging to record and has not been adopted for clinical use. Distortion product otoacoustic emissions (DPOAEs) also elicit a relatively narrowband response, utilizing a stimulus comprised of two puretones with traveling waves that interact along the basilar membrane (See DPOAE spectrogram, Appendix A). DPOAEs are ideal for clinical testing because they provide an inexpensive, rapid, and objective measure that can be used to examine difficult-to-test patients. It is for these reasons that DPOAE measurements are in wide use in such programs as the Ontario Infant Hearing Program.

Distortion product otoacoustic are elicited in the human ear by the presentation of two puretones, commonly denoted f_1 and f_2 , that differ in frequency by a given ratio

(Kemp, 1979). Although a number of distortion products may be elicited, the most commonly observed and the one of interest in the present study occurs at a frequency of $2f_1 - f_2$ and is referred to as the cubic difference tone. A large-scale study of DPOAEs identified that 95% of normal listeners exhibit emissions greater than -15 dB SPL at $f_2 = 2$ kHz and $f_2 = 3$ kHz, and -10 dB SPL at $f_2 = 4$ kHz (Gorga et al., 1997). Because the expected emission values are relatively small, an effort must be made to minimize background noise levels to optimize the signal-to-noise ratio (SNR).

The presence of contralateral acoustic stimulation has been shown to activate the medial olivocochlear (MOC) efferent system in human listeners, which elicits changes in outer hair cell function. These changes can be observed as alterations in distortion product otoacoustic emission (DPOAE) amplitude in a manner that is typically suppressive (Chery-Croze, Moulin, & Collet, 1993; Moulin, Collet, & Duclaux, 1993), but in some cases enhancement has been observed (Bassim, Miller, Buss, & Smith, 2003; Lisowska, Smurzynski, Morawski, Namyslowski, & Probst, 2002). Although the change resulting from contralateral acoustic stimulation can be either suppressive or enhancing, for simplicity, the absolute change in emission magnitude will be referred to as suppression in this paper as the change is most often of a suppressive nature. These changes are of clinical interest because they demonstrate a functioning efferent system in the auditory brainstem. Unfortunately, a great deal of inter-subject variability exists that makes the establishment of normal values quite difficult. Although it has been shown that DPOAEs resulting from lower level stimulus tones (~ 45 dB SPL) may be more easily suppressed (Williams & Brown, 1995), it is suggested that testing closer to the

DPOAE response plateau of 65-70 dB SPL may be the best compromise to elicit OAEs from the majority of individuals (Bassim et al., 2003).

When eliciting a DPOAE, the level of the emission peaks at the onset of the f_1 and f_2 stimulus tones, before falling to its steady-state value in a biphasic manner (Bassim et al., 2003). This initial adaptation involves a steep decrease in emission amplitude, followed by a slower decrease until steady-state values are obtained. The amplitude of the emission can be perturbed from this steady-state value by the addition of contralateral acoustic stimulation, and this suppression follows a similar biphasic time course both in animal models and human listeners. In human listeners, the amplitude of this effect has been shown to be smaller than in animal models (Bassim et al., 2003), but occurs on a similar time course to the initial adaptation described above (Kim, Dorn, Neely, & Gorga, 2001). Additionally, in the guinea pig, this effect has been shown to be simulated or blocked by intracochlear injection of the neurotransmitter acetylcholine or a cholinergic antagonist, respectively (Kujawa & Liberman, 2001).

Other studies have further evaluated effects of contralateral stimulation on the latency and timing of the DPOAE. Silva and Ysunza (1998) hypothesized that the introduction of acoustic stimulation would have an effect on the steady-state latency of DPOAEs, however their studies using a phase gradient model to calculate latencies based on wave periods showed otherwise. It was determined that a 35 dB HL broadband noise signal did not significantly alter the emission latency at any of the twelve stimulus tone pairs presented. Some studies have employed a real-time analyzer to evaluate both amplitude and time course of the suppressive effect. James, Harrison, Pienkowski, Dajani and Mount (2005) determined that contralateral stimuli as short as 5 ms can elicit the

suppressive effect in chinchilla models. The effect lasts for a minimum of 40 ms, indicating that some sort of temporal integration function may be involved.

Contrary to animal models, ipsilateral suppressor tones close to the f_2 stimulus tone frequency and contralateral stimulation have been shown to have a similar suppressive effect in humans. This effect is seemingly due to the equal number of crossed and uncrossed medial olivocochlear fibers in the human MOC bundle, responsible for the ipsilateral and contralateral reflex arcs, respectively (Guinan, 2006). However, the contralateral signal has been shown to alter the tuning curve of an ipsilateral suppressor, attenuating its peak and elevating its tails (Williams, & Brown, 1995).

Although contralateral broadband noise signals have repeatedly been shown to have an overall suppressive effect on DPOAEs (Bassim et al., 2003; Jacobson, Kim, Romney, Zhu, & Frisina, 2003; James et al., 2005; Williams & Brown, 1997; Zhang, Boettcher, & Sun, 2007), the same cannot be said for tone pairs or narrowband noise signals (Lisowska et al., 2002). Therefore the clinical utility of observing changes in DPOAE level with contralateral acoustic stimulation might be best pursued using broadband noise.

DPOAE Fine Structure

The decrease in amplitude with contralateral stimulation has been found to be most pronounced within the fine structure of the amplitude function. Unfortunately the meaning of the term fine structure is not concrete; for the purpose of this paper, fine structure will be defined as the way the DPOAE emission changes as the frequency of f_1 is swept across a frequency band surrounding one of two f_2/f_1 frequency ratios used. Williams and Brown (1997) found that most of their subjects' traces displayed

pronounced fine structure, where peak-to-trough height was diminished in the presence of contralateral acoustic stimulation. When the data were collapsed across all measurements and subjects, they found that maximal DPOAE amplitude occurred at an f_2/f_1 ratio of 1.184 for the $2f_1-f_2$ distortion product, with a lower ratio eliciting the greatest distortion product amplitude at higher f_2 frequencies and vice versa. Furthermore, it has been noted that major bipolar changes in the effect of contralateral stimulation occur, as a result of small shifts in stimulus tone level, at these particular frequencies where DPOAE fine structure exhibits pronounced dips (Müller, Janssen, Heppelmann & Wagner, 2005). By locating these notched regions of the DPOAE input/output functions, and then stepping the level of the f_1 stimulus tone over a small level range, the contralateral stimulation can elicit DPOAE adaptation magnitude changes far greater than those previously reported for steady-state DPOAE changes with contralateral suppression. The method used by Müller et al. (2005) compared the stimulus tone combination eliciting the greatest enhancement of the distortion product to the combination producing the greatest suppression in each individual in order to calculate the overall level difference, the mean value of which was found to be over 14 dB in human listeners. By employing a larger matrix of stimulus frequencies and levels, Wagner, Heppelmann, Müller, Janssen and Zenner (2007) were able to locate fine structure dips and consequent bipolar changes in suppression due to contralateral stimulation in 100% of their test subjects; once again large bipolar level difference effects were reported, however mean absolute level difference was shown to be 2.17 dB across all listeners. The highest incidence of fine structure dips was found in the frequency range below 4.2 kHz. Fine structure dips occur when the two DPOAE sources interfere with similar magnitudes and different phase

polarities. Thus, the contralateral acoustic stimulation having more of an effect on one distortion source than another would explain the observed changes surrounding these dips (Wagner et al., 2007). It was therefore determined that the largest MOC reflex is found at frequencies where DPOAE fine structure dips are exhibited. Similar results were also obtained in adult listeners using the ramped stimuli model employed by the present study. By eliciting DPOAEs around the traditional measurement ratio of $f_2/f_1=1.22$ as well as a more narrow ratio of $f_2/f_1=1.1$, Purcell, Butler, Saunders and Allen (in press) were able to locate fine structure in the majority of test subjects, obtaining maximum suppression levels of 3.22 dB, 3.92 dB, and 2.83 dB, at $f_2=2$ kHz, $f_2=3$ kHz, and $f_2=4$ kHz respectively. However, opposing results have been recently reported. When stimulus frequencies are swept at up to 17 points per octave, it has been found that the points labeled as peaks in the DP Gram exhibited greater suppression due to contralateral stimulation than those labeled dips (Zhang et al., 2007).

Auditory Processing Disorders

The working definition of auditory processing disorders, as discussed at the 2000 Bruton consensus conference, is a deficit in the processing of information, specific to the auditory modality, despite normal auditory thresholds (Jerger, & Musiek, 2000). This specific deficit is most pronounced in degraded listening environments; individuals typically have trouble listening in the presence of background noise, have trouble deciphering degraded speech signals and have difficulty following verbal directions (Chermak & Musiek, 1997). APD is, in actuality, a complex group of related disorders caused by a deficit in one or more of the processes that may be involved in the generation of auditory evoked potentials. The following abilities may be affected: sound

localization and lateralization, auditory discrimination, pattern recognition, temporal integration, temporal resolution, performance with competing acoustic signals and auditory performance with degraded acoustic signals (American Speech-Language-Hearing Association [ASHA], 2005).

The current audiological test battery used to diagnose APD consists primarily of behavioural tests. Electrophysiological measures, although more objective, are considered more time consuming and more expensive and, as a result, are not in widespread clinical use (Chermak, 2002). However, because evoked potentials are of use in evaluating auditory system integrity and otoacoustic emissions can evaluate cochlear function, it is recommended that such measures be taken as a part of the basic evaluation protocol where possible. Although APD may appear in isolation, it is suggested that it may be associated with other common developmental deficits including dyslexia, specific language impairments, attention deficit disorder, and the related attention deficit hyperactivity disorder (Vanniasagaram, Cohen, & Rose, 2004). This is not unexpected, as all auditory tasks, from puretone perception to language processing are likely influenced by non-modality-specific factors such as attention, learning, motivation and decision processing. This causes difficulty in diagnosis, as it can be difficult to distinguish the linguistic aspects of the disorder from the more general perceptual deficits. This has led to the suggestion that the diagnosis of APD may currently be inappropriate or impossible in cases where APD is comorbid with language development disorders, due to overlapping phenotype (Vanniasagaram et al., 2004).

If the site of neural dysfunction underlying the deficits present in Auditory Processing Disorders could be located, an evaluation of that area could be beneficial as a

more objective correlate of disease. The functional roles of auditory efferents are not completely understood, but they have been electrophysiologically linked to reductions in compound action potential and auditory nerve firing rates. This is indicative of an inhibitory, and thus protective function of the olivocochlear bundle (OCB). It has also been noted that this inhibitory function could lead to an improvement in coding of signals embedded in noise, suggesting that they may be involved in release from masking (Lieberman, 1988).

In the contralateral medial OCB reflex, upward-bound auditory information, carried by auditory nerve fibers, crosses the brainstem at the level of the trapezoid body and is projected to the contralateral ear by uncrossed medial OCB fibers (Guinan, 2006). It is this pathway that is of particular interest when discussing the concept of contralateral suppression. By altering outer hair cell stiffness, the OCB efferents are, in effect, changing the responsiveness of the outer hair cells and subsequently altering their amplification pattern. This is important to consider because it is the energy caused by the reflection and distortion mechanisms of the basilar membrane that is sent backward through the middle ear to form OAEs. Thus, by decreasing the gain of the cochlear amplifier, the OCB efferents are inhibiting cochlear responses and altering the OAEs produced, which is the basis of contralateral suppression (Guinan, 2006).

In order to detect a possible link in humans, Micheyl, Morlet, Giraud, Collet and Morgon (1995) examined the correlation between the OCB activity induced by the contralateral suppression of evoked OAEs and detection performance of 1 and 2 kHz tone pips in the presence of 50 dB contralateral broadband noise. Their data suggested that subjects' ability to detect tone pips in noise tended, on the whole, to worsen upon

contralateral stimulation in those subjects showing no or only slight OAE suppression to CAS, and to improve in those subjects whose OAEs could be significantly suppressed (Micheyl & Collet 1996). They determined that the shift in auditory nerve fiber rate-level function produced by the contralateral stimulation affected the coding of changes in stimulation level because depressed auditory nerve firing rates at low stimulation levels would restore the sensitivity of the neural fibers to changes in stimulation level. Thus, increased efferent activity would result in greater sensitivity to change in background noise due to reduced auditory nerve activity. It is important to note that this is only true if the interfering noise is presented contralaterally or binaurally, lending further evidence to the involvement of the medial olivocochlear bundle.

In addition to puretone detection thresholds, efferent sectioning in monkeys was shown to alter the ability to discriminate vowels in noise, suggesting that efferents are involved in the detection of more complex sounds in noise (Giraud et al., 1997). Giraud et al. (1997) sought to extrapolate the concept of complex auditory stimuli detection to humans. Using patients with unilateral vestibular neurectomy (VNT, a model for human OC sectioning) they found that an improvement in phoneme recognition rate in the presence of contralateral noise was present on the healthy side, but absent on the de-efferented side. Additionally, they found that stronger medial OC feedback was correlated with greater phoneme recognition improvement in the presence of contralateral noise (Giraud et al., 1997). Thus, studies in both monkeys and humans suggest that the firing rates of the contralateral auditory nerve fibers, which are being saturated by the continuous noise, are decreased by OC activation, such that they can regain some sensitivity to transient signals. However, a conclusive demonstration of the role of

olivocochlear efferents on ability to discriminate sounds in noise remains to be shown. Wagner, Frey, Heppelmann, Plonte and Zenner (2008) found that, when comparing scores on a speech-in-noise intelligibility task with the strength of MOC efferent activity through contralateral suppression of DPOAEs, no significant correlation existed. Moreover they found that no relationship existed using both a standard suppressive protocol and when exploiting fine-structure dips in the output function (Wagner et al., 2008).

Recent studies have shown reduced functioning of the medial olivocochlear bundle in children diagnosed with APD. Due to complications inherent to working with the APD population, a method of quickly and reliably evaluating brainstem integrity in the absence of subjective behavioural responses would be beneficial. Moreover, early detection is desirable in order to reduce delays in language development. Muchnik et al. (2004) investigated medial OCB function using the suppression of transient-evoked OAEs in APD children. Children were diagnosed as APD using a diagnostic battery of behavioural and objective measurements including: a competing sentences test, speech-in-noise test, masking-level differences, gap detection, ABR, TEOAEs, immittance testing and acoustic reflex testing. They used a 74 dB SPL click as the stimulus signal, and delivered a 40 dB SL white noise signal to the contralateral ear. They found a significantly reduced suppressive effect of TEOAEs in children with APD as compared to children in the control group, indicating a correlation between reduced medial OCB activity and the presence of APD. Additionally, they observed higher TEOAE levels in subjects with APD, which may be due to an inherent reduced medial OCB strength onto the outer hair cells (Muchnik et al., 2004). Because of the wide variety of deficits

contributing to a diagnosis of an auditory processing disorder and the individuality of symptomology, the APD population is considered very heterogeneous; consequently, predicting outcomes within this population can be difficult. Because both suppression and enhancement of the OAE output function are considered the result of efferent activity, we expect that there will be differences between the APD and control groups, however the nature of these differences remains to be seen.

Purpose of the Study

The exploitation of fine structure to improve measures of contralateral suppression of distortion products has yet to be documented in children. Additionally, there is currently no literature regarding the suppression of DPOAEs in children with auditory processing disorders. Muchnik et al. (2004) found that transient evoked OAEs in children with APD showed less mean suppression in the presence of contralateral stimulation than those of normal hearing children. It is, however, worthwhile repeating these measures using distortion products as the differences in source characteristics and more narrowband response may yield different results. Additionally, the suppression of distortion products at a narrow f_2/f_1 ratio may show a greater fine structure-based inter-group difference and may thus be a more effective diagnostic tool.

II. METHODS

Participants

Eight normal hearing children (8-13 years of age; Mean = 10.78 +/- 1.35) and eight children with Auditory Processing Disorders (8-13 years of age; Mean = 11.33 +/- 1.92) participated in this study. Participants were gender matched with three females and

five males in each group. Participants in the APD group were chosen based on previous diagnosis by the University of Western Ontario Child Hearing Research Laboratory. Traditional behavioral measures of central auditory processing used in the diagnostic battery included the Staggered Spondaic Word Test (SSW) (Katz, 1998), the Auditory Fusion Test-Revised (AFT-R) (McCroskey & Keith, 1996), Words in Ipsilateral Competition (WIC) (Ivey, 1969), the Pitch Pattern Sequence Test (PPS) (Pinheiro, 1977) and Filtered Speech (FS) (Willeford, 1976) (see Appendix B for full battery). Diagnosis of APD was made when performance fell greater than two standard deviations below the mean on one of these tests, or one standard deviation below the mean on two tests. Children deemed suitable for this study were contacted by telephone and requested to participate. Normal hearing children were recruited from the community through word of mouth. Parents were required to read and sign the Letter of Information and Consent Form (Appendix C) and after verbal explanation of what the study would entail, child participants were also asked to sign the Consent Form.

All testing was conducted at the participants' convenience at the Electrophysiology Laboratory in the National Centre for Audiology at the University of Western Ontario. Children were given school supplies or a small toy for participating. All participants had to demonstrate normal hearing sensitivity (≤ 20 dB HL at all octave frequencies from 500 Hz through 4 kHz) and middle ear function (ASHA 1994) prior to entry into the study. Additionally, participants were required to have distortion product otoacoustic emission levels exceeding the lower 5th percentile of normal as defined by Gorga et al. (1997) at the frequencies used in the contralateral suppression task (2, 3 and

4 kHz) and were required to display acoustic reflex thresholds to broadband noise of no less than 75 dB SPL. There was no penalty for withdrawing from the study.

Stimuli

Auditory stimuli were generated using a measurement system developed by Purcell, Van Roon, John, and Picton (2006). The system is based on National Instruments hardware and is controlled by software written in the LabVIEW programming language. Stimulus tones were delivered by an Etymotic ER-10B+ otoacoustic emissions probe connected to a pair of Etymotic ER2 transducers, each delivering one tone to minimize distortion in the stimulus production. The probe was secured in each subject's ear, which was chosen at random, with a plastic tip chosen to best fit their ear canal size. The contralateral signal was a 60 dB broadband noise signal delivered via an Etymotic ER3A transducer. The tip of this transducer was sealed to the ear opposite the emission probe using a compressible soft foam tip.

The DPOAE was elicited using a tone pair with individual tones denoted f_1 and f_2 , where $f_1 < f_2$. The frequency of the f_2 tone remained fixed during each measurement while the f_1 tone was swept across a range of approximately 132 to 263 Hz (depending on f_2 frequency). Other studies using swept stimuli have used a fixed ratio, sweeping both f_1 and f_2 stimulus tones (Müller et al., 2005; Wagner et al., 2007), however the present study used a fixed f_2 to maintain a constant distortion product generation place, and to explore a variety of frequency ratios. Measurements were taken with f_2 fixed at 2, 3 and 4 kHz, representing frequencies important within the speech spectrum that have been proven to be useful for DPOAE measurement. Measurements were also obtained surrounding two different f_2/f_1 ratios. To obtain f_2 dominant emissions, f_2/f_1 was swept

about a ratio of 1.22 and to obtain mixed source emissions, f_2/f_1 was swept about a ratio of 1.1. The levels of the stimulus tones were fixed at $L_1=60$ dB and $L_2=55$ dB SPL.

Procedure

For each tone pair, twenty-one sweeps of the stimulus were collected, each sweep containing the full range of f_1 both in the presence and absence of the contralateral broadband noise signal of 60 dB SPL (see illustration, Appendix D). The order of presentation of the two f_2/f_1 ratios was randomized to reduce any order effects associated with changes in emission response over the course of the experiment. Because each f_2 frequency elicits a distortion product from a different area of the basilar membrane, randomization of f_2 frequency was deemed unnecessary. All measurements were performed in a sound-attenuated booth where participants sat comfortably in a reclined easy chair. Due to the importance of silence to the collection of quality measurements, a monitor was placed inside the booth and participants were shown a silent animated film to focus their attention and reduce movement. Measurement time was approximately 32 minutes (6 conditions x 21 repetitions x 15.36 s/repetition). Because this proved to be too long a time for many participants to remain still and quiet, the measurement period was often broken up into shorter segments to allow participants sufficient breaks in order to ensure that they were able to complete the study as required. With the exception of one participant, the probe was never removed during these breaks, reducing the possibility of probe placement shifting over the course of the experiment.

Analysis

The microphone records for each measurement condition were synchronously averaged in the time domain after a noise rejection algorithm was employed according to the technique developed by Purcell, John, Schneider and Picton (2004). This rejection technique used a two-fold approach whereby any epoch in which noise exceeded an absolute threshold value of -5dB was discarded along with the noisiest 2.5% of epochs collected. The latter criterion was achieved by calculating the mean noise level in each epoch, referred to as the noise metric, and then discarding any epoch that exceeds the mean noise metric for a given sweep by two standard deviations. The absolute threshold was disregarded in some measurements where the noise distribution was such that the inclusion of this criterion caused a loss in excess of 20% of the collected data for that measurement. This did not cause a significant detriment to the integrity of the data as only those epochs in which the signal to noise ratio exceeded 6 dB were used in the final analysis. DPOAE magnitude and phase were then extracted by a Fourier analyzer, which can analyze a specific frequency at an instant in time (Purcell et al., 2004). This was necessary, as the changing emission frequency with time makes extraction with standard Fourier analysis, which analyzes the entire time window at once, impossible. An F-ratio test was used to determine whether responses were significantly different from the background noise at frequencies below the response frequency. Finally, the first four epochs of the first sweep of each measurement were discarded to allow steady-state values to be achieved following the onset of the DPOAE stimulus and contralateral noise.

Mean and maximum suppression were calculated for each set of parameters as the difference in magnitude between the average DPOAE with and without the contralateral noise and the greatest difference between the two, respectively.

III. RESULTS

Comparison of Normal Hearing Children to Existing Adult Data

One primary focus of this study was to compare the contralateral suppression of DPOAEs in normal hearing children with results from normal hearing adults previously obtained with the same experimental apparatus (Purcell et al., in press). Table 1 provides the measures of mean and maximum suppression, as well as the maximum/mean suppression ratios for both populations at each of the f_2 frequencies and f_2/f_1 ratios employed in both studies. Although direct comparisons can be made, the difference in population size between the two studies warrants some consideration; Purcell et al. (in press) obtained a sample size of $N=22$ while the control population of the current study was comprised of 8 children.

Figure 1 shows the averages and standard deviations of the mean suppression in the control child population as compared to the adult data of Purcell et al. (in press). There are no significant differences between the group means across all measurements, and the two populations display homogeneity of variance. Although there appears to be a trend in the data whereby the control child population shows slightly larger maximum suppression (Figure 2) and consequently larger maximum/mean suppression ratios at each of the testing paradigms employed, the difference in these measures fails to reach

Table 1. Suppression data (mean \pm SD) for the control population and APD population from the present study along with adult data from Purcell et al. (2008).

Frequency & Ratio	Group	Mean Suppression	Max Suppression	Max/Mean Suppression
2 kHz Narrow	Adult	1.063 \pm 0.5681	3.170 \pm 1.4652	3.269 \pm 1.4620
	Control Kids	0.983 \pm 0.5345	4.100 \pm 1.7332	4.916 \pm 2.8105
	APD Kids	1.043 \pm 0.4614	4.500 \pm 0.7165	4.840 \pm 1.6687
3 kHz Narrow	Adult	1.177 \pm 0.5343	3.926 \pm 2.0822	3.516 \pm 1.2662
	Control Kids	0.983 \pm 0.4309	4.217 \pm 2.3353	4.096 \pm 0.9512
	APD Kids	1.329 \pm 1.0012	5.457 \pm 3.9021	4.197 \pm 1.7016
4 kHz Narrow	Adult	0.870 \pm 0.4665	2.395 \pm 1.6765	2.747 \pm 0.8858
	Control Kids	0.883 \pm 0.4535	3.683 \pm 2.4020	3.858 \pm 1.4013
	APD Kids	1.000 \pm 0.4509	3.414 \pm 2.4505	3.201 \pm 1.1423
2 kHz Wide	Adult	0.903 \pm 0.5020	2.508 \pm 1.7696	2.761 \pm 0.9082
	Control Kids	0.800 \pm 0.4517	3.700 \pm 1.5937	6.574 \pm 6.4909
	APD Kids	1.043 \pm 0.3207	4.057 \pm 1.2947	3.961 \pm 0.9490
3 kHz Wide	Adult	0.798 \pm 0.3288	2.676 \pm 1.6322	3.199 \pm 0.7571
	Control Kids	0.933 \pm 0.3386	2.833 \pm 0.9352	3.131 \pm 0.9284
	APD Kids	0.771 \pm 0.5499	3.071 \pm 1.7481	8.324 \pm 13.5666
4 kHz Wide	Adult	0.430 \pm 0.2880	1.072 \pm 0.7925	2.566 \pm 0.6148
	Control Kids	0.467 \pm 0.2066	1.683 \pm 0.8353	3.743 \pm 1.5637
	APD Kids	0.357 \pm 0.1512	0.886 \pm 0.4375	2.512 \pm 0.7335

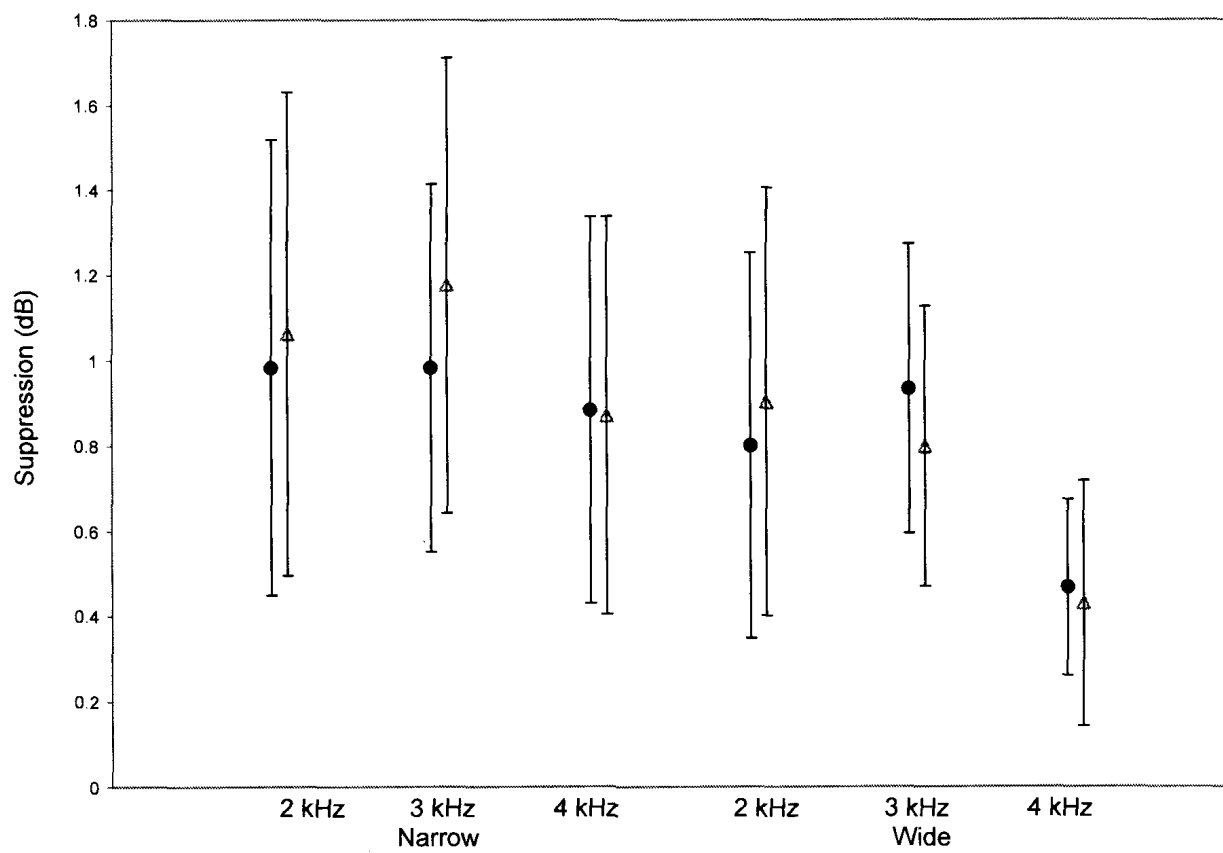


Figure 1. Group average mean suppression levels with standard deviations. Data for the control child and adult populations are represented by solid circles and open triangles, respectively.

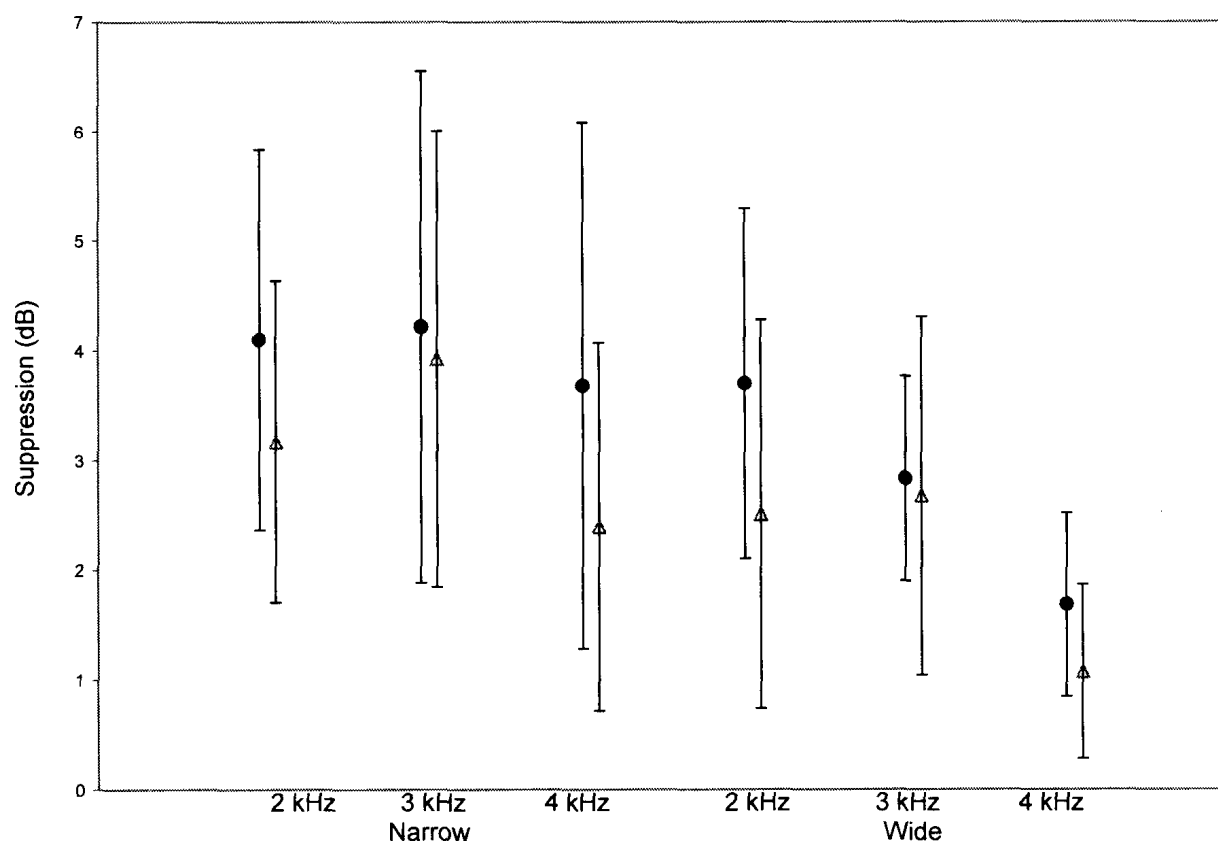


Figure 2. Group average maximum suppression levels with standard deviations. Data for the control child and adult populations are represented by solid circles and open triangles, respectively.

significance due in large part to the large-scale inter-subject variability and relatively small sample sizes.

Notes on Test Effects

One interesting finding surrounds the suppression of DPOAEs at $f_2=2$ kHz, swept about the traditional measurement ratio of $f_2/f_1=1.22$ (hereafter denoted as the 2 kHz wide measure). This particular measurement paradigm was shown to be effective for data collection in the normal adult population (Purcell et al., in press), however produced problematic results in the child population examined in the current study. In four of the eight control children (50%) and seven of the eight APD children tested (87.5%), the noise level in the 2 kHz wide measurement exceeded the absolute cutoff of -5 dB in greater than 20% of recorded epochs, resulting in the rejection of almost 70% of the data in some subjects. The narrow test frequency ratio had a similar effect on four of eight APD children (50%), but did not affect any of the control children. The frequency spectra of these subjects were dominated by low frequency noise such that the noise floor in the sampling area was significantly elevated. The source of this noise was determined to be internal to these subjects and analysis of the input to the OAE probe microphone revealed a rhythmic noise reminiscent of blood flow or respiratory sounds that was resonating in the ear canal. In order to circumvent this loss of data, the absolute noise cutoff was eliminated such that only the noisiest 2.5% of collected epochs were eliminated from the measurement. This allowed for the inclusion of more recordings without jeopardizing the integrity of the measurements as only those data points where the SNR exceeded 6 dB were included in final analysis. However, following the elimination of the absolute noise cutoff, the recordings of some subjects were still

unusable due to a lack of usable data. Thus, the 2 kHz wide measurement paradigm proved to be a less-than-ideal candidate for the suppression of distortion products in children.

A multivariate MANOVA revealed significant effects of the testing parameters on the outcome measures when the data for the control children and APD children from the present study were analyzed along with the adult data from Purcell et al. (in press). Where sphericity was not present in the data, a Greenhouse-Geisser epsilon correction factor was applied, as this was deemed an appropriately conservative estimate based on the limited sample sizes present in the data (Munro, 2005). An overall effect of f_2 frequency was found whereby the suppression at the 2 kHz measurements was equal to the 3 kHz measurements, both of which were significantly larger than the 4 kHz measurements ($p < 0.05$). This effect reached significance for both the mean and maximum suppression measurements, failing to reach significance for the maximum/mean suppression ratio. An overall effect of f_2/f_1 ratio was also observed with the narrow ratio producing a greater suppressive effect than the traditional, wide measurement ratio ($p < 0.05$). This effect of measurement ratio also reached significance for the measures of mean and maximum suppression, falling short of significance for the maximum/mean suppression ratio.

Comparison of Normal Hearing Children and Children with APD

Table 1 shows the values for the mean suppression, maximal suppression and maximum/mean suppression ratio for the population of control children as well as the APD population studied. These results are broken down by f_2 frequency and f_2/f_1 frequency ratio. Figures 3 to 5 show the averages and standard deviations of the mean

suppression, maximum suppression and maximum/mean ratio respectively for the control and APD groups at each of the test frequencies and f_2/f_1 ratios used in this experiment. These figures illustrate that there was no significant difference between the average values for the control and APD populations in any measure, largely due to the large-scale inter-subject variability encountered in these groups. It is, however, interesting to note the heterogeneity of variance that exists between these two experimental populations. When the individual results are plotted against the adult norm values obtained by Purcell et al. (in press) as in Figure 6, it can be seen that there are differences between the groups with respect to how far and how often they fall outside a standard deviation of the mean. The inter-subject variability of the APD group often exceeds that of the control, reaching significance for the measure of maximum suppression at the 3 kHz wide measurement paradigm according to Levene's test of equality of error variances ($p < 0.05$). The difference between the APD and control groups approaches significance for the measures of mean and maximum suppression at the 3 kHz narrow measurement, and the measure of maximum/mean suppression at the 3 kHz wide measurement where the variance in the APD group is greater than the control ($0.05 < p < 0.1$). It also approaches significance at the measure of maximum suppression at the 2 kHz narrow measurement and the measure of maximum/mean suppression at the 2 kHz wide measurement where control variance exceeds that of the APD group ($0.05 < p < 0.1$).

Finally, the present study also examined the strengths of the ipsilateral and contralateral middle ear-muscle reflexes in both the control and APD populations. Figure 7 shows the ipsilateral reflex strengths of both groups. Although the APD group appears to have slightly higher reflexes, appearing more often in the range commonly considered

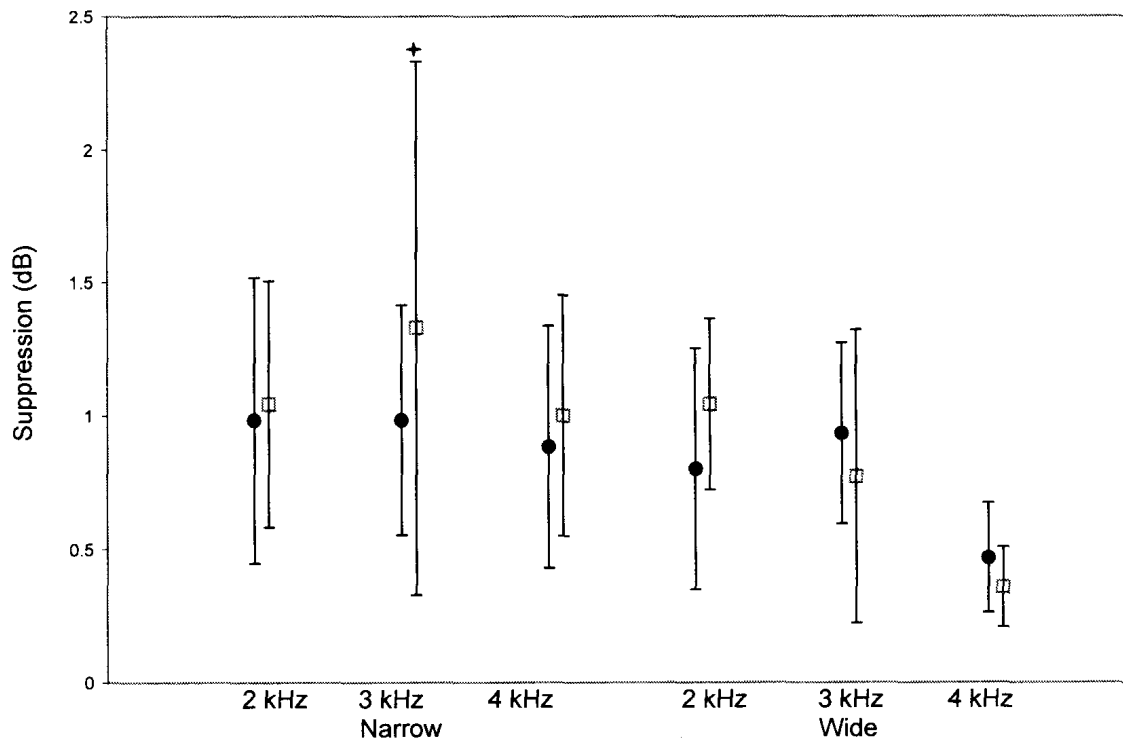


Figure 3. Group average mean suppression levels with standard deviations. Data for the control and APD populations are represented by solid circles and open squares, respectively. A four-point star represents heterogeneity of variance that is approaching significance.

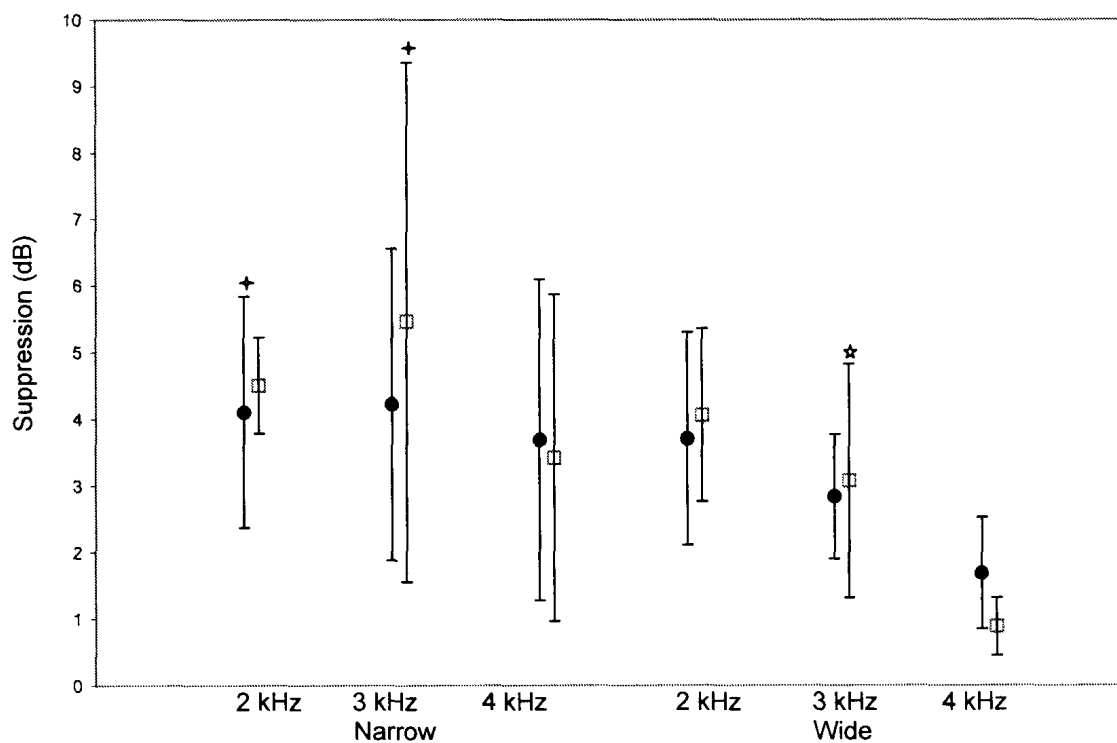


Figure 4. Group average maximum suppression levels with standard deviations. Data for the control and APD populations are represented by solid circles and open squares, respectively. A five-point star represents significant heterogeneity of variance while a four-point star represents heterogeneity of variance that is approaching significance.

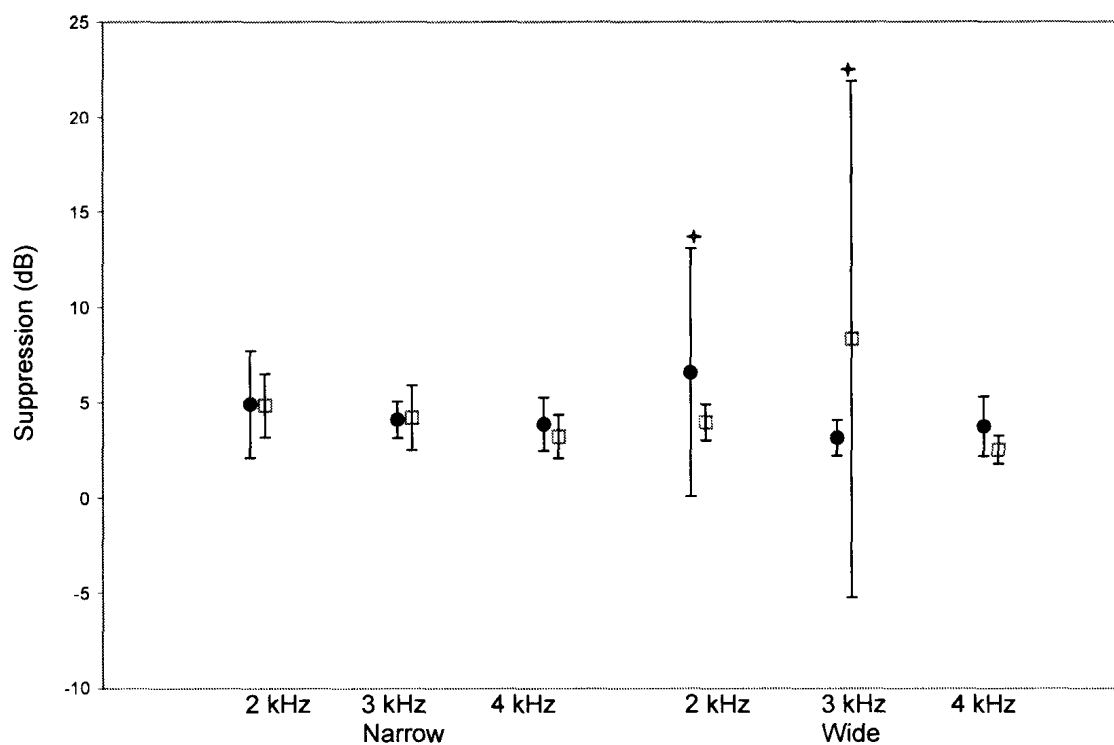


Figure 5. Group average maximum/mean suppression levels with standard deviations. Data for the control and APD populations are represented by solid circles and open squares, respectively. A four-point star represents heterogeneity of variance that is approaching significance.

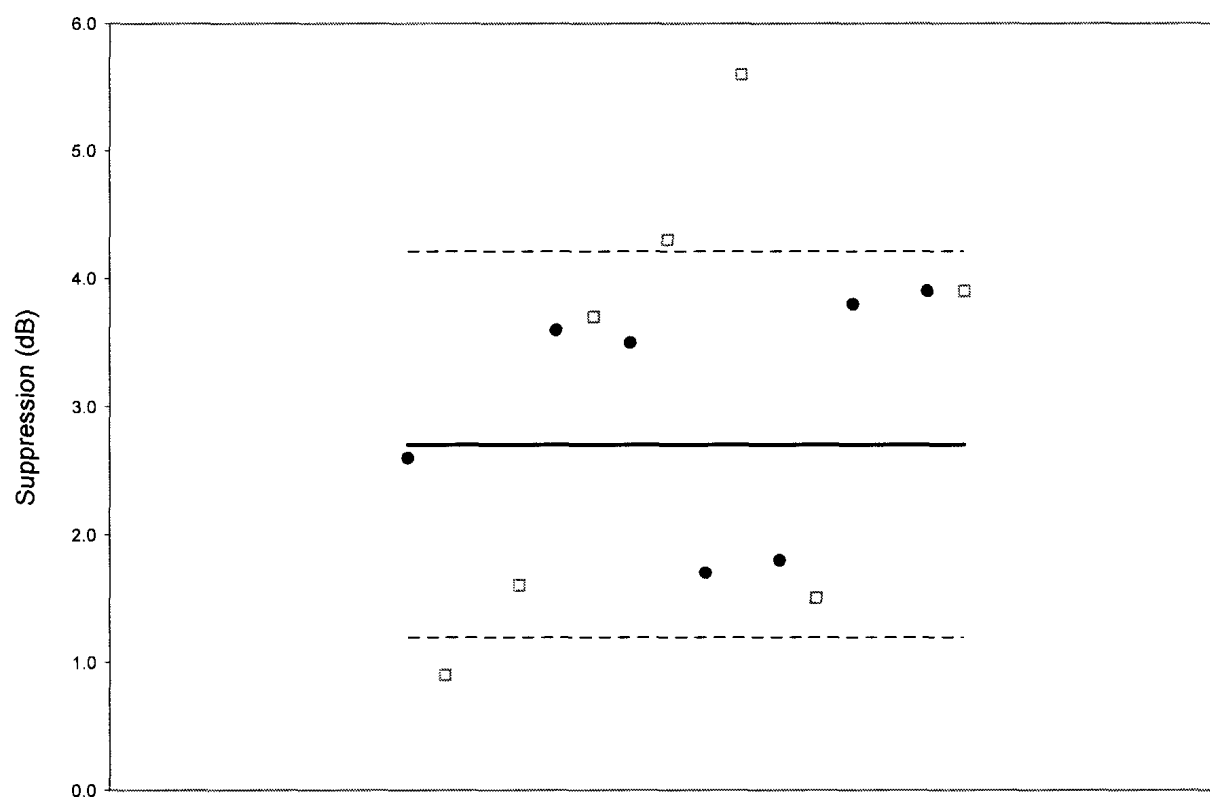


Figure 6. Maximum suppression at the 3 kHz wide measurement. Data for the control and APD populations are represented by solid circles and open squares, respectively. The solid line represents the mean of the adult data for this measurement, while the dashed lines represent one standard deviation from that mean. Data were unavailable for 1 individual in each experimental population, resulting in 7 points per group.

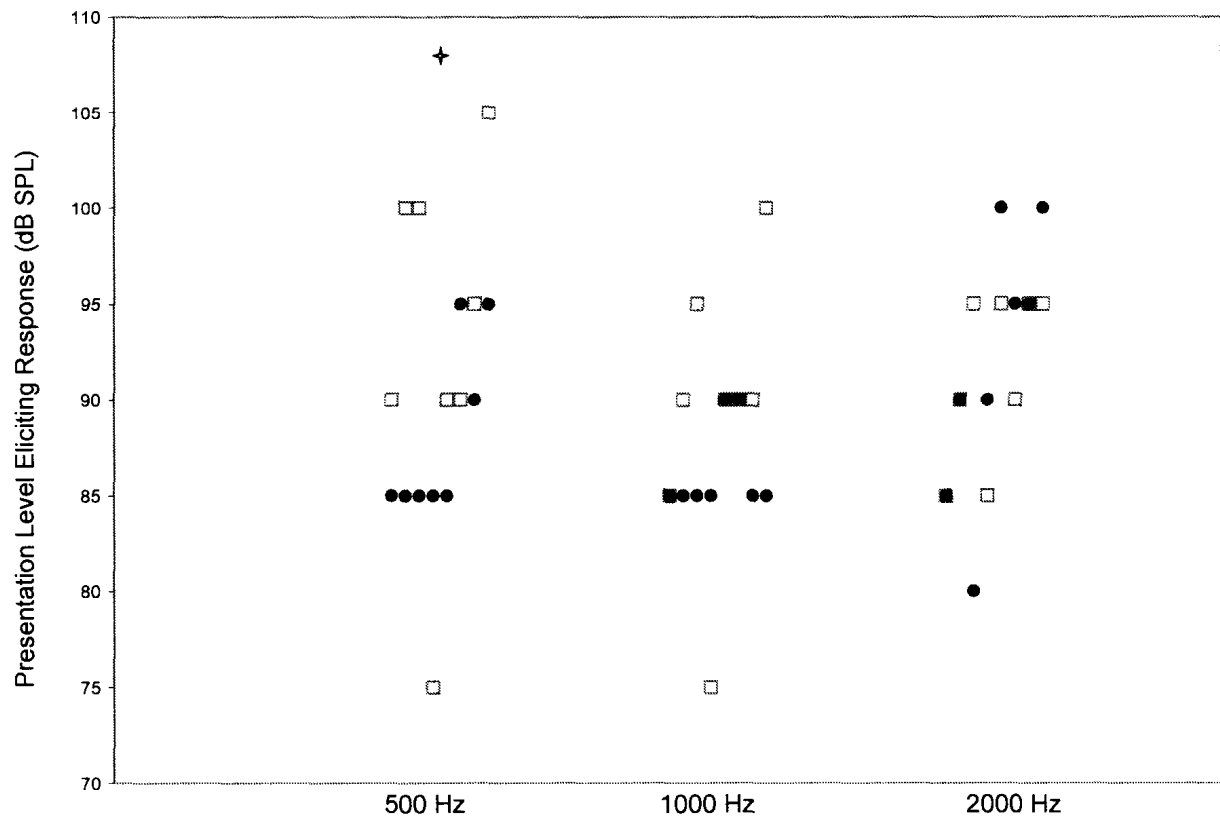


Figure 7. Ipsilateral middle ear muscle reflex (MEMR) strengths. Data for the control and APD populations are represented by solid circles and open squares, respectively. A four-point star represents a difference in means that is approaching significance.

to be elevated, t-tests revealed no significant difference at any test frequency, with the difference in means approaching significance at 500 Hz. Figure 8 shows the contralateral reflex strengths for the control and APD groups. The individuals in the APD group again appear to have elevated reflexes, however t-tests again revealed no significant differences with the difference in means approaching significance in response to broad-band noise.

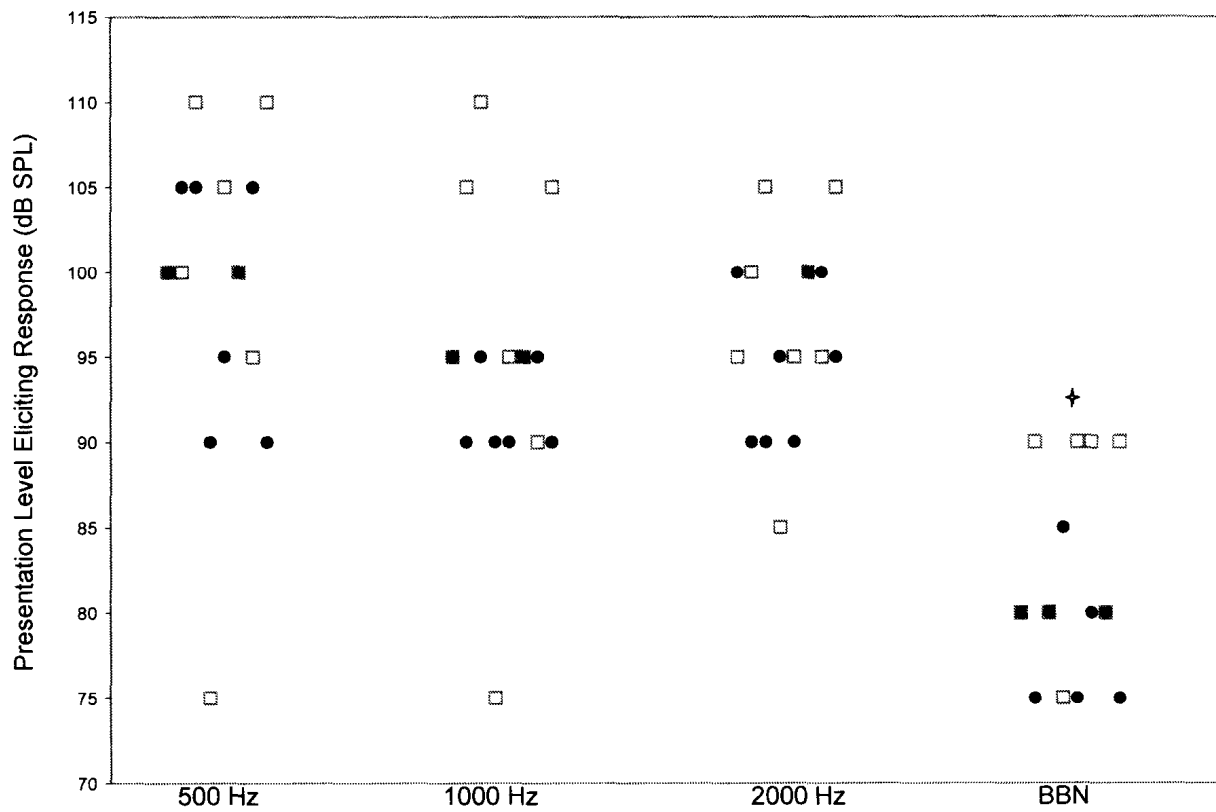


Figure 8. Contralateral middle ear muscle reflex (MEMR) strengths. Data for the control and APD populations are represented by solid circles and open squares, respectively. A four-point star represents a difference in means that is approaching significance.

IV. DISCUSSION

This study demonstrated that the contralateral suppression of distortion products is similar in children to data collected in normal adults. Table 2 summarizes mean DPOAE suppression data from previous studies in normal hearing adult listeners. The reported values for mean suppression range from 0.31 dB to 1.99 dB and are quite similar to the results from the children in the present study. This further confirms that age-related maturity of the auditory system is of no concern when collecting such measures in children as young as seven years of age. The averages of the normal hearing children and the adult data collected by Purcell et al. (in press) were not significantly different and they displayed homogeneity of variance. However, a trend did appear in the data in which the child population in the present study demonstrated slightly higher maximum suppression and maximum/mean suppression ratios than the adults studied by Purcell et al. (in press) for each of the study paradigms employed. This may be coincident with higher overall emission levels often observed in children as compared to adults and is consistent with the trends in the literature showing decreasing emissions and suppressive effects with increasing age in both humans (Kim, Frisina & Frisina, 2002) and animal models (Jacobson et al., 2003). Both the increased emissions and suppression function may reflect differences in neural activity and outer hair cell mechanics between the groups.

Although this difference in maximum suppression is an apparent trend, there is no observable difference in mean suppression between the normal hearing children and adult data. Thus, although the normal hearing children may display transient periods of greater suppression than the adults, the children's traces display greater variability over the

Table 2. Summary of changes in DPOAE level observed in example studies of contralateral acoustic stimulation in humans. Stimulus levels are in dB SPL. In the final column, mean changes with standard deviations (when available) are given in dB. The f_2 stimulus frequency follows in parentheses.

Study	N	DPOAE Stimulus			Contralateral Stimulus		DPOAE Change [mean \pm s.d. dB] (f_2 frequency)
		f_2/f_1 ratio	L1(dB SPL)	L2 (dB SPL)	Level (dB SPL)	Type	
Bassim et al. (2003)	24	1.21	70	65	60	BBN	1.10 (1.8 – 9.7 kHz)
James et al. (2005)	10	1.22	70	65	50-60	BBN	1.14 (4.4 kHz)
Lisowska et al. (2002)	10	1.22	65	55	60	BBN	1.00 (1.5 kHz)
		1.22	55	40	60	BBN	1.50 (2 kHz)
Williams and Brown (1995)	6	1.225	55	40	55	BBN	1.99 \pm 0.69 (2 kHz)
							1.12 \pm 1.00 (3 kHz)
Zhang et al. (2007)	20	1.22	55	40	40	BBN	0.31 (1 – 6 kHz)
		1.22	55	40	60	BBN	1.26 \pm 0.89 (1 – 1.5 kHz)
							1.59 \pm 2.40 (1.5 – 2.5 kHz)
							0.62 \pm 0.61 (3.5 – 4.5 kHz)
		1.22	55	40	70	BBN	1.44 (1 – 6 kHz)

length of the recording, resulting in a mean suppression level equal to that of the adult subjects. Furthermore, because the maximum suppression in normal hearing children is slightly higher than the adults with no observable difference in mean suppression, the maximum/mean suppression ratio is also slightly higher. Although changes in cochlear amplifier function could be attributed to outer hair cell loss with age, Kim et al. (2002) note that differences in the fine structure of the emission alone suggest a metabolic etiology. A high maximum/mean suppression ratio would indicate greater variability of the distortion product output function with changing frequency such that there was a transient point within that recording where suppression was far greater than the average, likely reflecting a dip in the fine structure. Thus a higher maximum suppression, although failing to reach significance, may represent greater likelihood of fine structure dips in recordings from normal hearing children as compared to adults.

The possible activity of the middle ear muscles remains a concern when measuring effects of the MOCB on OAEs. To avoid this confusion, subjects were only admitted if their thresholds for contralateral broadband noise were 75 dB HL or greater, exceeding the level of the contralateral noise used in the present study by a minimum of 15 dB. The contribution of the stapedial reflex to the change in DPOAE levels is believed to be minimal, if any, when the contralateral broadband noise signal is below the acoustic reflex threshold (Sun, 2008). A contralateral noise signal of 60 dB SPL has been used in a number of studies of human OCB function (James, Mount, & Harrison, 2002; James et al., 2005; Lisowska et al., 2002; Müller et al., 2005; Wagner et al., 2007, Zhang et al., 2007) and has been shown to be effective in eliciting changes in the OAE output function. Furthermore, changes due to MOC efferent stimulation such as those observed

in the present study occur on a faster time course, with changes an order of magnitude smaller than changes resulting from the middle ear muscle reflex (MEMR) as observed with real-time analysis (James et al., 2005). Finally, although suppression was the most commonly observed effect following introduction of the contralateral acoustic stimulation, enhancement of the distortion product emission was also seen, an effect which could not stem from middle ear muscle activity and thus supports the fact that the effects of the present study represent MOC efferent effects.

A significant frequency effect was found in the present experiment whereby changes in emission level were smaller at $f_2 = 4$ kHz, with no significant difference between the suppression at $f_2 = 2$ kHz and $f_2 = 3$ kHz. This difference reflects poorer suppression at $f_2 = 4$ kHz by both the control children and APD groups. Thus if a similar setup for the contralateral suppression of DPOAEs is to be used clinically, more robust estimates of MOC efferent activity may be obtained with an f_2 of 2 kHz or 3 kHz. This effect is consistent with prior studies reporting that changes were most observable in the 1 – 3 kHz range (Chery-Croze et al., 1993; Lisowska et al., 2002; Moulin et al., 1993; Williams & Brown, 1997). However, this study presented one effect of frequency that was not present in studies of the adult population using an identical setup (Purcell et al., in press). Some measurements made at $f_2 = 2$ kHz and were dominated by low-frequency noise internal to the test subjects from both the normal hearing child and APD populations. Why this issue presents itself in children and not adults remains to be seen; it may be that differences in ear canal volume and some other unknown factors that change with maturity are causing the noise contamination. Whatever the reason, this increased low-frequency noise is a significant detriment to data collection at this test

frequency and must be given consideration as a longer collection period may be necessary to collect enough epochs to assure the integrity of the measurement. Thus, due to poor suppression levels at $f_2 = 4$ kHz and excessive noise contamination at $f_2 = 2$ kHz, $f_2 = 3$ kHz has proven to be the most effective test frequency in children of those tested in the current experiment. Additionally, this frequency falls within the range of $f_2 < 4.2$ kHz that Wagner et al. (2007) determined to contain the highest incidence of fine structure dips, making it an adequate location to measure maximum/mean suppression ratios.

There was also a significant effect of f_2 ratio observed in this study with the sweep surrounding the narrower frequency ratio of $f_2/f_1 = 1.1$ eliciting greater suppression than that surrounding the traditional measurement ratio of $f_2/f_1 = 1.22$. Although the traditional ratio was selected to maximize the level of the distortion product elicited, the narrower frequency ratio employed in the current study results in a higher frequency emission that is subject to less background noise than a measure made at the same f_2 frequency with the traditional ratio. Thus the impact to the SNR as a result of using the narrow frequency ratio is minimal and, when combined with the greater level of suppression elicited, results in a test paradigm that may prove to be more useful than the traditional ratio for contralateral suppression testing in children. This narrow test ratio was selected to exploit the interaction between the two distortion product source locations, with the anticipation that it would result in a greater number of dips in the fine structure of the output function than the traditional ratio. However, the narrow ratio did not result in a significantly greater number of fine structure dips than the traditional ratio, indicating that the ratio effect is dominated by differences in the fine structure of the tracing rather than major differences in dip occurrence.

The most interesting finding surrounding the performance of children with auditory processing disorders is that, although their average values for mean, maximum and maximum/mean suppression were not significantly different than those of the control child population, the variance of the APD group often exceeded that of the control. This was not unexpected, as this population is somewhat infamous for their large standard deviations from the mean in a variety of experimental measures. This unpredictability of outcomes is largely due to the multi-faceted nature of auditory processing disorders. Because APD is, by definition, a complex group of related disorders stemming from one or more deficits of the auditory system (ASHA, 2005), expecting all children with an APD diagnosis to perform similarly on one measure would be unrealistic. Thus we cannot expect to glean useful information from average measures; rather, we are able to observe individual performances within a set of group measures to gain some information regarding performance, and possibly consequent functional differences.

This heterogeneity of variance between the control child and APD child groups can be quite easily seen when their data is plotted against the previously recorded adult norms. Figure 6 does so for each group at the 3 kHz wide measurement. From this illustration it can be seen that all of the control subjects fall well within one standard deviation of the adult mean, while 3 of the APD subjects fall outside of this range. Furthermore, the direction of this deviation is non-uniform with one subject displaying less suppression than the normal range, while the other two exceeded normal. Thus, although the average maximum suppression at this measure is similar for the control child and APD populations, this large-scale bidirectional deviation from the mean causes the variance for the APD group to be significantly larger than that of the control. Figure

6 presents an illustration of the measure where the difference in variance reached significance ($p < 0.05$) however, the difference between group variances approached significance for several other measures with the APD group variance exceeding that of the control group in all but two circumstances. In the case of the 3 kHz wide measurement, the APD group variance appeared to exceed that of the control group for the maximum/mean suppression measure at a level that approached significance ($0.05 < p < 0.1$). However, it should be noted that the large standard deviation of the APD group was dominated by one individual who experienced a transient period of intense suppression (3.6 dB), but who maintained a low mean suppression (0.1 dB) resulting in a maximum/mean ratio that greatly skewed the group variance. The control group variance did exceed the APD group at a level that approached significance ($0.05 < p < 0.1$) for the measures of maximum suppression at the 2 kHz narrow measurement paradigm and for the maximum/mean suppression ratio at the 2 kHz wide measurement. This result is somewhat unexpected, however it is interesting that it occurred at the test frequency $f_2 = 2$ kHz as this is the area where ear canal noise became a serious issue in the collection of emission data. As described above, the absolute cutoff employed by the noise rejection paradigm was eliminated for some of the measures at this test frequency to allow for the inclusion of more data. However, because this was necessitated in more cases for the APD group than the control, it must be taken into consideration when evaluating the results at this test frequency.

Changes in contralateral reflex strengths were consistent with the literature, with the majority of subjects showing a decrease of 10-15 dB in the signal required to elicit a response when moving from puretone stimulation to broad-band noise (Gelfand, 2002).

However, it is interesting to note that, although there is no significant difference between the control and APD groups at any of the puretone frequencies tested, the APD group had higher reflex levels in response to broad-band noise at a level that was approaching significance. If subjects in the APD test group were suffering from a neural deficit or minor neural dyssynchrony, one might expect that reflexes would be slightly elevated at different test frequencies. Moreover, if broadband noise were the stimulus used to elicit the MEMR, we might see a compounding of these small variations, due to the tonotopic organization of the auditory system, such that the APD group would begin to separate more significantly from the control population.

Clinical Implications

The ability to alter distortion product otoacoustic emissions in the presence of contralateral acoustic stimulation has been shown to be an important measure of olivocochlear efferent function. Previous studies have shown that a change in emission magnitude can be observed in normal adult listeners at a variety of f_2 frequencies when the f_2/f_1 ratio is set at 1.22 (Bassim et al., 2003; Chery-Croze et al., 1993; Lisowska et al., 2002; Moulin et al., 1993; Williams & Brown, 1995) and more recently when swept about a more narrow ratio of $f_2/f_1 = 1.1$ (Purcell et al., in press). However, to our knowledge the present study is the first to display such results in the child population. The children forming the control population in this study were shown to have mean suppression levels similar to that of normal adults (Purcell et al., in press) and maximum suppression levels that exceed adult norms for each of the measurement paradigms employed. This was also the first study to look at the contralateral suppression of DPOAEs in the APD population, adding to our understanding of brainstem level function

in these children. Although the children with auditory processing disorders were not significantly different than the normal hearing children with respect to their average mean, maximum, and maximum/mean suppression, it is important to note that these children tended to show greater variance in these measures than the normal hearing child population, falling beyond a standard deviation of established adult norms more frequently.

Establishing a relatively noise-free environment continues to be the primary concern surrounding the collection of DPOAE suppression measures. Data must be collected in a sound-attenuated booth as the distortion product levels and the levels of the changes therein are such that any noise contamination could seriously jeopardize the results. Additionally, further consideration to noise originating within the subject is warranted if such measurements are to be made on populations younger than that of the present study. Because a quiet environment is imperative to the integrity of these measurements, it is essential that subjects be able to complete the testing session in a quiet manner. Children in the present study were allowed to watch a silent movie on a monitor placed within the booth which served to focus their attention and reduce subject noise in a manner shown to have no significant effect on the collection of suppression data (De Boer & Thornton, 2007). In younger populations, it may be beneficial to make measurements while the subject sleeps in order to bring noise to a minimum.

Future Directions

Evidence of the ability to suppress distortion product otoacoustic emissions by presenting contralateral acoustic stimulation was extended to the adolescent population in this study. Children in the control population displayed averages for mean, maximum

and maximum/mean suppression ratios that were not significantly different than those of the previously studied adult population. Furthermore, the two groups displayed homogeneity of variance for these measures. Frequency and ratio effects that first presented themselves in a study of the normal adult population (Purcell et al., in press) were observed in the present study with suppression being greater at lower f_2 frequencies and greater surrounding the narrower test frequency ratio of $f_2/f_1 = 1.1$.

The ability of the current test paradigm to show contralateral suppression of DPOAEs was further extended to the population of children with Auditory Processing Disorders. Although the averages for mean, maximum, and maximum/mean suppression ratio of these children were not significantly different than the control child population, the difference in variability approached or reached significance for a number of these measures.

The power of the current study is limited primarily by the small sample size available for testing. In order to improve the measures herein and to make more evident any potential group differences, it is prudent that a similar study be conducted with a greater sample size. This study examined children as young as 7 years of age, however, because the MOCB (Chabert et al., 2006; Gkoritsa et al., 2007) as well as the cochlear amplifier (Abdala, 2001) reach maturity at a very young age, it may be of interest to extend testing to a younger age group, providing the aforementioned potential clinical limitations are overcome. If the differences between the control and APD populations are the result of delayed maturity in the latter group, then earlier testing may be of further benefit as potential differences may be more easily seen before the system is given a chance to catch up to control levels. Additionally, if contralateral suppression is to be

made a part of an electrophysiological test battery for APD, it would be of benefit to be administered as early as possible such that remedial measures can be taken sooner than later.

The major challenge surrounding measures of suppression in APD children, as in many other measures in this population, is that group means are not generally representative of individual performance. This makes the establishment of clinically relevant norms difficult. As mentioned above, the large-scale variance in the APD population is likely a reflection of the multi-faceted nature of the diagnosis. However, as the practice of forming sub-diagnoses within the umbrella of APD proceeds, so too might the usefulness of contralateral suppression as a diagnostic tool. If APD subgroups can be made based upon the proposed source of one's processing disorder or the specific impairments presented, these groups may present with means and deviations different from those of the control group on measures of contralateral suppression. That is to say, if the processing disorders of the subjects in the APD test group all had the same origin or presentation, their performance on the measures of suppression might be more homogeneous, resulting in a mean that differs from the control mean. Further testing in this area is required to determine the actual clinical usefulness of these measures.

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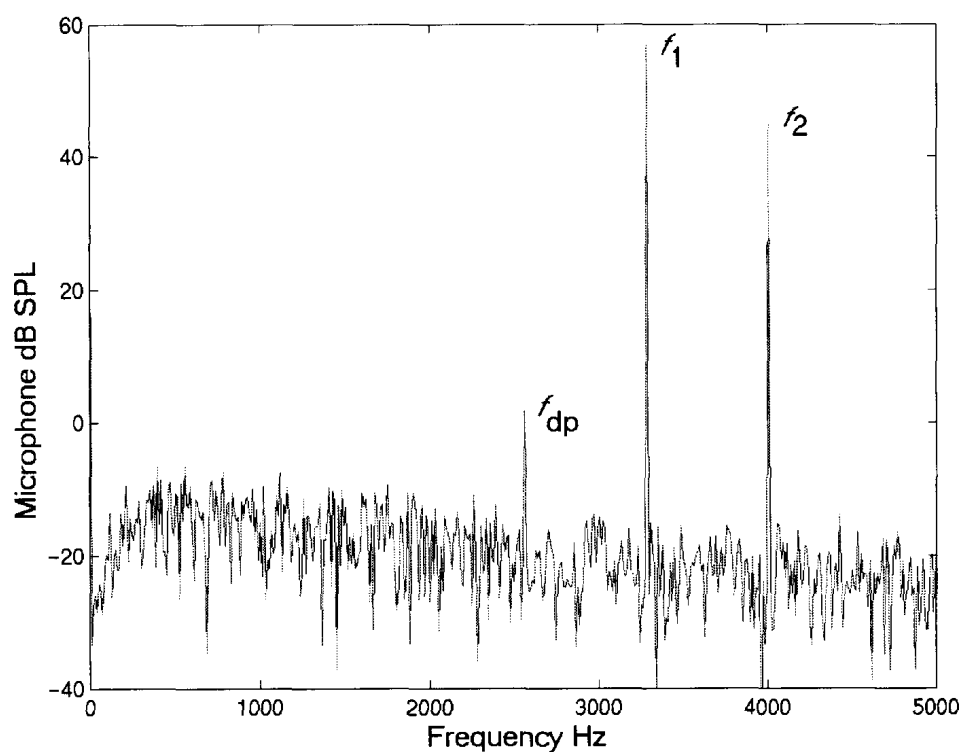
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Appendix A



This diagram shows the frequency spectrum for a DPOAE recorded at $f_2 = 4$ kHz. The stimulus tones f_1 and f_2 are labeled, as is the $2f_1 - f_2$ emission (f_{dp}). Along the Y-axis, the level of the tones are noted as recorded at the microphone in dB SPL. In this example, both the f_1 and f_2 tones are presented at fixed frequencies, and the level of f_1 exceeds f_2 to maximize interactions along the basilar membrane.

Appendix B

APD Test Battery Employed by the Child Hearing Research Laboratory at the University of Western Ontario

The battery of tests used for the evaluation of auditory function includes: audiogram, tympanometry, ipsilateral and contralateral stapedial muscle reflex evaluation, word discrimination scores, filtered speech testing, the standard spondaic word test, evaluation of pitch pattern perception, the auditory fusion test, and competing words test. Electrophysiological testing includes recording of auditory brainstem responses to fast and slow click rates, middle latency responses, late potentials and the p300. Tests of speech, language and phonology include the Peabody picture vocabulary test, evaluation on the oral and written language scales, and a comprehensive test of phonological processing. Cognitive and academic measures include evaluation on the Wechsler abbreviated scales of intelligence, a wide range test of auditory memory and learning, and the test of everyday attention for children. A comprehensive case history was compiled based on information collected from parents and/or teachers. Rating scales employed in the battery include the Screening Instrument for Targeting Educational Risk (SIFTER), the Children's Auditory Processing Performance Scale (CHAPPS), and the Conner's. Tests of psychoacoustics developed by and/or adapted by the CHRL include tests of difference limens (frequency) at 1 kHz, syntax learning (including both visual and auditory stimulation), and sample discrimination.

Appendix C

Letter of Information for Parents/Guardians**Study: A Comparison of Suppressed DPOAEs in Normal and APD Children**

Primary Investigator: Dr. David Purcell, Ph.D.
Co-Investigators: Dr. Prudence Allen, Ph.D.
Blake Butler, B.M.Sc,

Place of Research: Electrophysiology Laboratory, UWO

Fall, 2007/ Winter, 2008

Dear Parent,

We are conducting a study of hearing and otoacoustic emissions at the National Centre for Audiology located in the University of Western Ontario. Our interest is discovering whether differences exist between normal children and those diagnosed with Auditory Processing Disorders (APD) in terms of our ability to suppress their DPOAEs. We will have approximately 30 children participating in this study. Each child involved in the study will be asked to complete one session of testing lasting no more than 2 hours at the National Centre for Audiology.

During the hearing and electrophysiological testing, your child will sit comfortably in a soundproof room listening to different sounds while wearing earphones. During the hearing testing, your child will be asked to indicate when sounds presented become audible to them. During electrophysiological testing, your child can relax and is not required to do anything. Your child will be allowed breaks between testing blocks, as we are aware that remaining still and quiet for long periods can be difficult.

This study will involve no known risk to your child. The sounds your child will hear are usually as loud as conversational speech and will never be so loud as to be uncomfortable or damaging. At times, long term use of earphones can become uncomfortable, however all attempts have been made to avoid this kind of discomfort. This study is of no direct benefit to your child, but it is our hope that it will be of benefit to children in the future. Your child will receive a small toy or school supplies as a thank you for participating in the study.

Participation in the study is voluntary. You and your child may refuse to participate, refuse to answer any questions, or withdraw from the study at any time.

The information gathered during this study will remain confidential at all times. When your child enters the study, a 4-digit identification code will be assigned and this code is the only identifying information recorded on the test forms. ID codes and corresponding full names of participants will be kept in a journal and locked in a cabinet, or stored on CD-ROM, with password access only. Only the local research team and the UWO HSREB may have access to the cabinet or password. The data will be kept as it is being collected and analyzed. Once the project is completed, all information containing participants' names and ID codes, including backup CD's and journals, will be deleted or destroyed by shredding. No child will be identified in any analysis or publication, however if it is determined that your child may have hearing problems that require further attention, you will be notified of this fact.

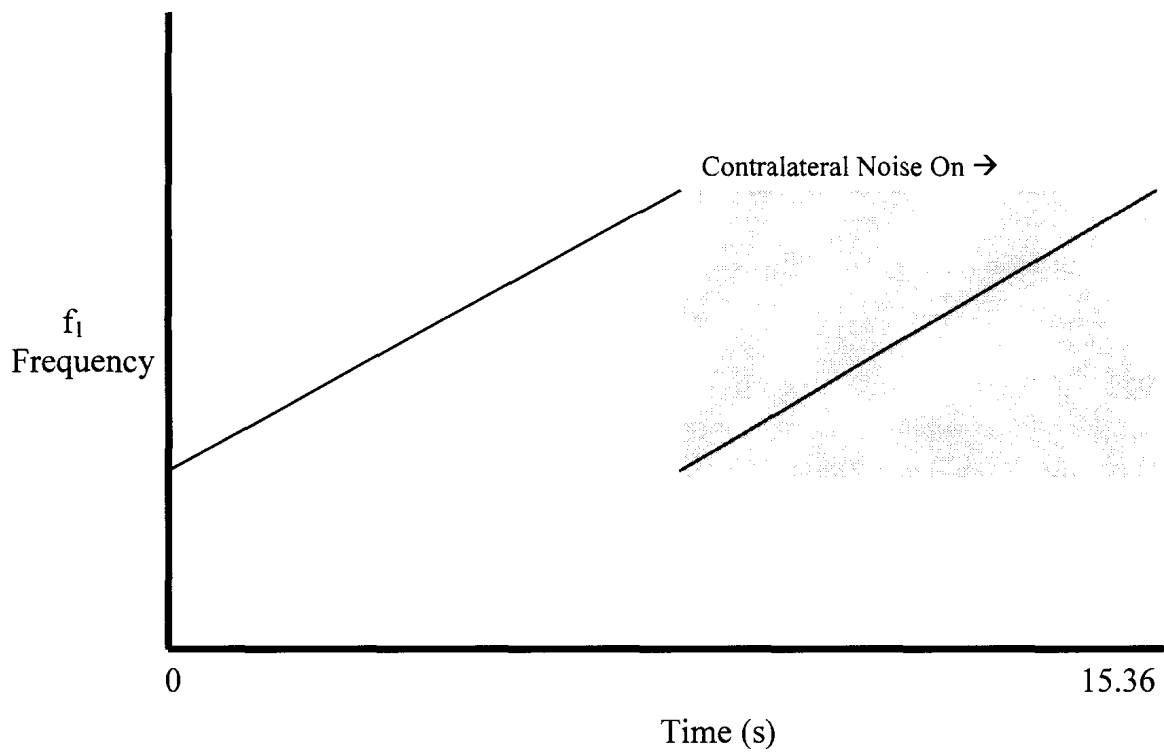
This letter is yours to keep. You will receive a copy of the signed consent form. We would appreciate your permission to allow your child to participate. Please contact Blake Butler in our Child Hearing Research Lab at xxxxxxxx@uwo.ca to arrange an appointment if you do wish to have your child participate in this study. Children will be enrolled in the project on a first-come-first-served basis.

If you have further questions please contact me at the above address or at the following phone number: (xxx) xxx-xxxx extension xxxxx. If you have any questions about the conduct of this study or your rights as a research subject you may contact Susan Hoddinott, Director, Office of Research Ethics, The University of Western Ontario, 519-661-3036 or email at: ethics@uwo.ca. Thank you for your time and consideration.

Sincerely,

Dr. David Purcell
Assistant Professor
National Centre for Audiology
2262 Elborn College, 1201 Western Rd.

Appendix D



While f_2 remained fixed throughout the course of the measurement, f_1 was swept across a range of frequencies (132 to 263 Hz, depending on f_2 frequency) both in the absence and presence of contralateral acoustic stimulation.

Appendix E

Glossary of Terms

Cubic Difference Tone – A distortion product otoacoustic emission occurring at the frequency $2f_1 - f_2$.

Decibel (dB) – One tenth of a bel. The number of dB is equal to ten times the logarithm of the ratio of two intensities or 20 times the logarithm of the ratio of the two pressures.

Epoch – A period of time (1.024 seconds in the present study).

Frequency – The Frequency of a sine wave is the number of periods occurring in one second. The unit is cycles per second, or hertz (Hz).

Hearing Level – A scale of sound amplitude based on the minimal detectable level of a signal in the absence of any external sounds at a particular test frequency in the average normal hearing ear (0 dB HL).

Hertz – The unit of measure for frequency representing cycles per second (1 kHz = 1000 Hz).

Sensation Level – A scale of sound amplitude based on the threshold level for that sound for the individual listener (0 dB SL).

Signal-to-Noise Ratio – The amplitude of a signal, minus the amplitude of the background noise present in the recording.

Sound Pressure Level (SPL) – A measure of sounds pressure expressed in decibels (dB) on a scale in which 0 dB is equal to 20 microPascals.

Stapedial Reflex – A response to intense sound whereby the stapedius muscle of the inner ear contracts to pull the staped away from the oval window of the cochlea to reduce the transmission of potentially harmful signals to the inner ear.

Transient – Occuring over a brief period of time.

Vestibular Neurotomy – deafferentation of the vestibular system commonly used as a treatment of medically refractory vertigo in Menière's disease.

Appendix F



Office of Research Ethics

The University of Western Ontario
 Room 00045 Dental Sciences Building, London, ON, Canada N6A 5C1
 Telephone: (519) 661-3036 Fax: (519) 850-2466 Email: ethics@uwo.ca
 Website: www.uwo.ca/research/ethics

Use of Human Subjects - Ethics Approval Notice

Principal Investigator: Dr. D. Purcell

Review Number: 12610E

Revision Number: 3

Review Date: August 2, 2007

Review Level: Expedited

Protocol Title: Contralateral Suppression of Distortion Product Otoacoustic Emissions

Department and Institution: Communication Sciences & Disorders, University of Western Ontario

Sponsor:

Ethics Approval Date: August 22, 2007

Expiry Date: June 30, 2008

Documents Reviewed and Approved: UWO Protocol, Additional Co-investigators, Letter of Information and Consent (Control)

Documents Received for Information:

This is to notify you that The University of Western Ontario Research Ethics Board for Health Sciences Research Involving Human Subjects (HSREB) which is organized and operates according to the Tri-Council Policy Statement: Ethical Conduct of Research Involving Humans and the Health Canada/ICH Good Clinical Practice Practices: Consolidated Guidelines; and the applicable laws and regulations of Ontario has reviewed and granted approval to the above referenced revision(s) or amendment(s) on the approval date noted above. The membership of this REB also complies with the membership requirements for REB's as defined in Division 5 of the Food and Drug Regulations.

The ethics approval for this study shall remain valid until the expiry date noted above assuming timely and acceptable responses to the HSREB's periodic requests for surveillance and monitoring information. If you require an updated approval notice prior to that time you must request it using the UWO Updated Approval Request Form.

During the course of the research, no deviations from, or changes to, the protocol or consent form may be initiated without prior written approval from the HSREB except when necessary to eliminate immediate hazards to the subject or when the change(s) involve only logistical or administrative aspects of the study (e.g. change of monitor, telephone number). Expedited review of minor change(s) in ongoing studies will be considered. Subjects must receive a copy of the signed information/consent documentation.

Investigators must promptly also report to the HSREB:

- a) changes increasing the risk to the participant(s) and/or affecting significantly the conduct of the study;
- b) all adverse and unexpected experiences or events that are both serious and unexpected;
- c) new information that may adversely affect the safety of the subjects or the conduct of the study.

If these changes/adverse events require a change to the information/consent documentation, and/or recruitment advertisement, the newly revised information/consent documentation, and/or advertisement, must be submitted to this office for approval.

Members of the HSREB who are named as investigators in research studies, or declare a conflict of interest, do not participate in discussion related to, nor vote on, such studies when they are presented to the HSREB.

Chair of HSREB: Dr. John W. McDonald

Deputy Chair: Susan Hoddinott

Ethics Officer to Contact for Further Information		
<input type="checkbox"/> Jennifer McEwen (jmcewen4@uwo.ca)	<input checked="" type="checkbox"/> Denise Grafton (dgrafton@uwo.ca)	<input type="checkbox"/> Grace Kelly (gkelly2@uwo.ca)

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cc: ORE File