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FREQUENCY-MODULATED MULTIPLE-TONE DISTORTION PRODUCT

OTOACOUSTIC EMISSIONS IN YOUNG CHILDREN WITH NORMAL HEARING

A Doctoral Thesis

Presented to

The Graduate College of

Missouri State University

In Partial Fulfillment

Of the Requirements for the Degree

Doctor of Audiology, Communication Sciences and Disorders

By

Kathryn Arielle Vlietstra Baker

May 2021
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FREQUENCY-MODULATED MULTIPLE-TONE DISTORTION PRODUCT

OTOACOUSTIC EMISSIONS IN YOUNG CHILDREN WITH NORMAL HEARING

Communication Sciences and Disorders

Missouri State University, May 2021

Doctor of Audiology

Kathryn Arielle Vlietstra Baker

ABSTRACT

Distortion-product otoacoustic emissions (DPOAEs) are objective tests of the integrity of the outer hair cells of the cochlea in response to a single-tone pair stimulus. Despite advances in DPOAEs test protocols and technology, there is little research about the use of frequency modulated tones to improve response characteristics. This study evaluates the efficacy of a new frequency modulated stimulus with multiple-tone pair DPOAEs (mDPOAEs) compared to the standard stimulus protocol for mDPOAEs to determine whether frequency modulation (FM) will achieve more robust and faster results. Normative data for this novel test protocol were obtained in 11 healthy normal-hearing children aged 3-6. Amplitude, signal-to-noise ratio, and testing time of mDPOAEs with and without FM were measured and compared. Results of repeated-measures ANOVA indicate that mDPOAEs frequency modulated responses show no significant differences in amplitude or testing time from standard mDPOAEs without FM. The mean signal-to-noise response (SNR) of mDPOAEs without FM is greater than the SNR of mDPOAEs with FM. However, results suggest that mDPOAEs with FM are less variable overall than standard mDPOAEs, which indicates that mDPOAE responses obtained with FM may be more reliable than standard mDPOAEs. This suggests that FM may reduce the influence of DPOAE fine structure variations on the detection of the presence of a DPOAE response, which may be beneficial in a clinical setting. Findings are affected by the small number of participants because of halting data collection due to COVID-19; more research is necessary to evaluate the application of frequency modulated mDPOAEs in children.

KEYWORDS: frequency-modulated, distortion product otoacoustic emissions, normal hearing, children, fine structure, amplitude, signal-to-noise ratio
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May 2021

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In the interest of academic freedom and the principle of free speech, approval of this thesis indicates the format is acceptable and meets the academic criteria for the discipline as determined by the faculty that constitute the thesis committee. The content and views expressed in this thesis are those of the student-scholar and are not endorsed by Missouri State University, its Graduate College, or its employees.
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I dedicate this thesis to my beloved husband, Nathan James Baker.
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INTRODUCTION

Since the hearing of infants and young children are categorically difficult to test behaviorally, the employment of accurate objective tests is essential. Otoacoustic emission testing (OAE) has been used for screening and diagnosing hearing loss for decades, ever since Dr. David Kemp’s classic work revealed the capacity to record otoacoustic emissions in 1978 (Kemp, 1978). OAE tests allow for an evaluation of the peripheral auditory function up to the level of the outer hair cells within the cochlea. Presence of OAE with normal response amplitude reflects normal outer hair cell and cochlear amplifier function and is highly correlated with behavioral hearing sensitivity thresholds (Gorga, Neely, Dorn & Hoover, 2003; Janssen, 2013; Suri, Gupta, Kotwal & Kotwal, 2018). Distortion product otoacoustic emission (DPOAE) testing is one of the OAE measures that provide frequency-specific responses, thereby revealing important tonotopic information about the function of the peripheral auditory system via objective measurements.

Applications and Limitations of DPOAEs

DPOAE testing provides a quick, noninvasive, frequency-specific test of cochlear function that does not require a behavioral response (Abdala & Visser-Dumont, 2001). Therefore, clinicians use DPOAE tests as a part of test batteries for a variety of purposes. These test battery purposes range from newborn hearing screening protocols to diagnostic testing in pediatrics and other special populations, nonorganic hearing loss, ototoxicity monitoring, and auditory neuropathy (Reavis, McMillan, Austin, Gallun, Fausti, Gordon, Helt & Konrad-Martin,
DPOAEs are commonly used clinically to complement auditory brainstem response (ABR) screening procedures with newborn hearing screenings, since ABR testing has been shown to have fewer false positive results than OAE testing for newborn hearing screening (Llanes & Chiong, 2004). Llanes and Chiong (2004) have reported that accuracy with newborn hearing screening testing is improved with a combination of DPOAEs and ABR testing. Conversely, DPOAEs can be completed faster and involve less preparation and fewer supplies than an ABR, and they are frequency-specific tests that can be performed quickly (Campbell, 2007). It is not always possible to obtain behavioral responses on hearing tests, especially from newborns or children with behavioral or developmental disorders or suffering from conditions requiring ototoxic regimens that have been determined medically necessary e.g. chemotherapy, which means that objective test measures like OAEs are an important tool for monitoring hearing in these patients.

Conventional DPOAE testing is performed by presenting a pair of two primary pure tone signals—f1 and f2—simultaneously to the ear and recording the emission response that is received back from the cochlea as a result (Abdala & Visser-Dumont, 2001). The most commonly used combination of tones used to evoke the distortion product response is 2f1-f2, where the ratio of f2/f1 is 1.22 (Torre, Cruickshanks, Nondahl & Wiley, 2003; Dhar & Hall, 2012). DPOAE testing is clinically significant for revealing frequency-specific information about cochlear function, although variability of DPOAE response levels has been shown to increase
with increased behavioral thresholds, thereby decreasing reliability of present and absent responses (Garner, Neely & Gorga, 2008).

Sensitivity and specificity results of standard DPOAE testing, using two primary tones stimuli, can vary considerably depending on the frequencies tested, patient population, amount of hearing loss and type of hearing loss (Torre et al., 2003; Llanes & Chiong, 2004; Robinette & Glattke, 2007). One study of children with hearing acuity ranging from normal to profound hearing loss found that sensitivity and specificity of DPOAEs on average were 77.9% and 80.6%, respectively, however this same study found variations in sensitivity and specificity dependent on whether the child had hearing loss, and if so, how much (Llanes & Chiong, 2004). Another study in older adults found that DPOAE sensitivity and specificity will vary depending on frequency as well as response characteristics such as amplitude and signal-to-noise ratio (SNR), with sensitivity ranging from 60% to 89%, and specificity ranging from 59% to 85% (Torre et al., 2003).

Noisy testing environments are a particular concern with standard DPOAE testing; it is not known to be effective in the detection of hearing loss in conditions with high levels of noise or when the primary tones are in the low frequencies (500 Hz – 1000 Hz), since the SNR tends to be reduced in low frequencies as a result of elevation in the noise floor (Abdala & Dumont, 2001; Robinette & Glattke, 1996). Gorga et al. (2003) found that DPOAEs may have poor sensitivity and specificity at 500 Hz, with the most accuracy found at 4000 Hz. Regardless of the acknowledged clinical benefits of DPOAEs, the results of these investigations reveal the need for better testing techniques to improve response amplitude, increase sensitivity and specificity, and
shorten testing time in order to combat the particularly time-sensitive needs of identifying and diagnosing hearing loss in young children.

**Advancements in DPOAE Test Protocols**

**Multiple-tone Distortion Product Otoacoustic Emissions.** One method that researchers have developed to help improve clinical use of standard DPOAEs is simultaneous presentations of multiple pairs of primary tones in order to perform more than one DPOAE evaluation at a given time, also known as multiple DPOAEs (mDPOAEs). Researchers have found that, while some differences exist, a strong correlation between responses was obtained using conventional single-pair tones DPOAEs stimuli and simultaneous mDPOAEs. These findings support the possibility of performing mDPOAE tests with the goal of reducing the total time necessary to test across the frequencies, since reproducible responses were obtained while performing two or more DPOAE tests simultaneously (Schairer, Clukey, & Gould, 2000; Beattie, 2003; Smurzynski & Janssen, 2015). Research has also shown that using mDPOAEs has successfully reduced the amount of time required to complete DPOAE testing in adults by one-third to one-half of the test time as compared to the length of time required for standard DPOAE test protocols (Kim, Sun, Jung & Leonard, 1997; Beattie, 2003).

**Frequency-modulated Distortion Product Otoacoustic Emissions.** A more recent advancement in technology for performing DPOAEs is the use of frequency modulation in the presentation of the DPOAE pure tone stimuli, or FMDPOAEs. This proprietary technique changes the frequency of the primary tones slightly over time, within a range of approximately 100 Hz at a rate of approximately 1.5 Hz (Janssen, 2015). The purpose of this is to change the
phase of the pure tone stimuli, reducing interference from the secondary source of DPOAEs – the reflection otoacoustic emissions created at the 2f1-f2 site (Robinette & Glattke, 2007; Dhar & Hall, 2012; Janssen, 2015; Lodwig, 2016).

This interference tends to create peaks and valleys in the fine structure of the DPOAE response and researchers have posited that the difficulty in correlating DPOAEs to behavioral thresholds with hearing loss is due to the variation of the amplitude caused by the fine structure (Shaffer, Withnell, Dhar, Lilly, Goodman & Harmon, 2003; Shera, 2004). In addition, interference can lead to a decreased amplitude of DPOAE and potentially a false positive result on the test, causing a normally hearing child to be referred for a diagnostic hearing evaluation or result in a passing DPOAE response with a mild hearing loss (Dhar & Hall, 2012; FMDPOAE, 2019). Dr. Andre Lodwig, the developer of this test protocol, postulates two theories which may explain how frequency modulation results in alleviating the effects of fine structure in DPOAE results: either through obtaining an average of the DPOAE response across the approximate 100 Hz region which is being stimulated or as a result of the stimulation frequencies changing so quickly that the reflection source does not have time to generate a reaction (Lodwig, 2016).

Proponents of FMDPOAEs believe that this testing paradigm may reduce variation in noise level and deep notches in the response, resulting in larger amplitude responses than standard stimuli, allowing for easier detection and recording (Janssen, 2015; Smurzynski, 2018). As shown in Figure 1, Smurzynski (2018) found that the amount of variation in amplitude of both DPOAE response and noise level is reduced with the use of FMDPOAE protocol in young adults, and the number of times that peaks and valleys occur is also decreased. Smurzynski’s study evaluated 30 ears in normally-hearing adults using FMDPOAEs with multiple-tone pairs
Smurzynski found that the total number of fine structure peaks was reduced from 266 peaks without FM to 66 with FM, and fine structure peaks were completely eliminated in four of the ears after applying FMDPOAE testing protocol (2018).

Smurzynski further concluded that FMDPOAEs provide reliable test results that may improve testing time when combined with multiple tone and binaural techniques (2018). Thus, recording DPOAEs using both multiple-tone pairs and using frequency modulation (FM) would allow testing to be completed in a shorter period of time since the passing criteria would be met more quickly, and may possibly be obtained in less-than-optimal conditions due to noise. While Smurzynski’s study on frequency modulated DPOAEs provides only descriptive data, which was presented at the World Congress in 2018 and has not yet been published, it indicates that this

**Figure 1.** Multiple DPOAEs (black trace) showed fine structures with deep notches in the recorded response mainly between 2000 Hz to 3000 Hz. However, these deep notches as well as noise level (grey trace) were significantly reduced with the use of frequency modulation stimuli (FMDPOAE responses shown in red). Data were recorded from 15 young adults with normal hearing. Graph developed and presented by Smurzynski, 2018.
development could prove especially helpful with testing children, who may move and otherwise cause noise during testing.

Marcrum, Hofle, Picou, Steffens, Kummer & Kwok (2020) performed a study of 83 young adults which investigated the use of FMDPOAEs in comparison to standard DPOAE test protocol and found that FMDPOAEs are effective in reducing the effects of fine structure on the DPOAE response without greatly reducing the DPOAE amplitude. Their findings suggest great potential for clinical use for FMDPOAEs for testing both adults and children, although the researchers note that further research into the use of FMDPOAEs with children would be essential in order to generalize these results to a clinical pediatric population (Marcrum et al., 2020).

In addition, using the FMDPOAE testing protocol shown by Smurzynski (2018, unpublished study) resulted in reduction in noise level amplitude. Therefore, it may be possible to detect OAE responses with greater reliability in low frequencies, which would provide better information about hearing sensitivity across a wider frequency range than current DPOAE testing protocols. It is important to note that young children often are not cooperative over a long testing session and may not always tolerate a professional handling their ears for long periods of time; therefore, if FMDPOAE testing can provide a quicker result without sacrificing accuracy, it would be highly desirable. In addition, independent and disinterested research is necessary to evaluate the performance of the FMDPOAE technique in order to understand how effective it is in a clinical setting.

**Hypothesis**

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With only one published study on FMDPOAEs in adults (Marcrum et al., 2020), no research has been published on the response characteristics of FMDPOAEs using multiple-tone pairs in young children. This study seeks to compare the response amplitude, signal-to-noise ratio, and test time for mDPOAEs with and without the use of frequency modulation in children ages three – six years old. We expect that using mDPOAEs with FM stimuli may elicit DPOAE responses with greater amplitudes in a shorter time than mDPOAEs without FM stimulus while obtaining accurate responses and fewer false referrals.
METHODS

Participants

In total, eleven healthy children (6 boys and 5 girls) between the ages of three and six years participated in this study (mean age = 4.27). Participants were recruited from a local preschool affiliated with the university at which this study was performed, as well as through word-of-mouth and email recruitment efforts in the local community (see Appendix A). Participant inclusion criteria included normal middle ear status, hearing within normal limits, and no occluding cerumen in the external auditory canals. Children were excluded from the study if they had hearing impairments, middle ear disorders, or attention, language, cognitive or learning difficulties. Unfortunately, participant recruitment and data collection were unexpectedly halted due to the occurrence of the COVID-19 pandemic, which resulted in fewer participants for this study than the design of the study required to achieve adequate power for generalization of data results.

This research study on children ages three to six with its written consent form was approved on November 22, 2019 by the Institutional Review Board (IRB) committee at Missouri State University (IRB #: FY2020-256 – see Appendix B). The author completed this IRB submission under the name of Kathryn Vlietstra; the author’s last name has since changed to Baker. Written informed consent were obtained from a parent or guardian of each child to conduct the study procedures (see Appendix C). When possible (dependent on the research participant’s cognitive development stage and writing abilities) the research participant completed the participant assent form in addition to parental consent (see Appendix D). A case
history form was completed by a parent or guardian of each research participant to help screen participants to ensure they met the inclusion criteria (see Appendix E).

**Screening Procedures**

Evaluation of the ear canal, hearing sensitivity, and middle- and inner-ear status was performed bilaterally using otoscopy, pure tone audiometry, tympanometry, and mDPOAEs without FM to ensure participants met the inclusion criteria. Otoscopic examination was performed prior to any testing to determine the condition of the ear canal. Tympanometry was used to rule out any middle ear disorders that could impact DPOAE responses (Kei, Brazel, Crebbin, Richards & Willeston, 2007). Single-frequency tympanometry was performed using a GSI TympStar Middle Ear analyzer with a 226 Hz probe tone, as 226 Hz has been shown to be an appropriate frequency for evaluating middle ear function in children older than nine months of age (Alaerts, Luts, & Wouters, 2007). Silman and Silverman report that normative data studies on static-acoustic middle-ear admittance in children ages three to ten using a conventional low-frequency probe tone showed a range of 0.35 cm³ up to 1.25 cm³ between the 5th and 95th percentiles, whereas Palmu and Rahko’s study, limited to children ages four and five, found a normative range of static acoustic admittance of 0.2 cm³ up to 1.0 cm³ (Silman & Silverman, 1996; Palmu & Rahko, 2003). Therefore, inclusion parameters for tympanometry in this study are classification of Jerger type A tympanogram, with a tympanometric peak pressure (TPP) between -100 and +50 daPa, peak-compensated static admittance between 0.2 and 1.0 cm³, and ear canal volume between 0.2 cc³ and 0.9 cc³ (Hunter & Sanford, 2015; Silman & Silverman, 1996).
Puretone hearing screening to determine hearing sensitivity was performed with a clinical audiometer (GSI 61) and insert earphones. Testing was performed in a sound-treated booth. Children were screened at 20 dB HL at 500 Hz, 1000 Hz, 2000 Hz, 4000, and 8000 Hz. 20 dB HL was determined to be the intensity level for screening based on the American Academy of Audiology (AAA) Clinical Practice Guidelines for screening children (Childhood Hearing Screening Task Force, 2011), as well as for consistency in normative data, since many studies of DPOAEs in children use 20 dB HL as the limit for determining normal hearing sensitivity (Owens, McCoy, Lonsbury-Martin & Martin, 1993; Konrad-Martin, Knight, McMillan, Dreisbach, Nelson & Dille, 2017; Feder, Michaud, McNamee, Fitzpatrick, Ramage-Morin & Beauregard, 2017; Lyons, Kei & Driscoll, 2004). If a child failed to respond to the screening intensity level at any frequency more than once out of three presentations, the child was excluded from the study due to the potential of hearing sensitivity outside of normal limits.

In addition, children were required to have normal mDPOAEs response amplitude to participate in this study. They were tested at approximately 1000 Hz, 2000 Hz, 3000 Hz, 4000 Hz, 5000 Hz and 6000 Hz using mDPOAEs without frequency modulation (see procedural details below). mDPOAEs measurements were performed using the Sentiero Path Medical Otoacoustic device (version: 2.0.1.7957). The child was considered eligible for participation in the study if the mDPOAE response was present at least 6 dB SPL at four out of six tested frequencies (Konrad-Martin et al., 2017; Dhar & Hall, 2012). Children were excluded from the study if either ear was outside of these normal limits on the day of testing based on the screening results of both ears, including present mDPOAEs. Experimental testing was not performed even if the response in one ear was still within normal, due to the concern that any disorder that
affected mDPOAE response in one ear could potentially be affecting the other. Calibration for all equipment was performed according to the manufacturer's instructions. Calibration of the probe for the mDPOAE tests was performed automatically prior to every testing procedure.

**Experimental Procedures Using mDPOAEs with and without FM**

Using the Sentiero Path Medical Otoacoustic device, mDPOAE primary tones of f2 were presented simultaneously and randomly at frequencies at least one octave apart, to avoid interference from the multiple traveling waves (Smurzynski & Janssen, 2015). Each of the multiple tones, f1 and f2 with f2 > f1, were presented at a fixed f2/f1 ratio of 1.22, with f2 intensity level (L2) at a set intensity of 40 dB SPL and f1 intensity level (L1) intensity level automatically optimized for the greatest response for DPOAEs of 2f1-f2 frequency using the Sentiero Path Medical proprietary software (Brown & Kemp, 1984; Lodwig, 2016). mDPOAEs were recorded between 1000 Hz to 6000 Hz using five frequencies per octave; testing of each frequency was completed non-sequentially to avoid testing frequencies closer than one octave at the same time (Dhar & Hall, 2012). Testing was not recorded at 8000 Hz due to reduced reliability at this frequency (Gorga et al., 2003). At each of the tested f2 frequencies, 32 averages were obtained from data that were lower than the artifact reject criterion (10 dB SPL based on the ambient noise level at the beginning of the test) (Torre et al., 2003). The set of averages at the first test frequency was rejected if the noise level was more than 10 dB SPL greater than the ambient noise level. Recording automatically stopped after it ran through the protocol when these response criteria are reached: SNR ≥ 6 dB SPL and distortion product amplitude ≥ -10 dB SPL (Smurzynski, 2018).
In the same testing session, mDPOAE procedures were completed with the frequency modulation feature turned on. To randomize the order of testing and avoid any confounding factors due to test order, mDPOAEs without FM were performed followed by mDPOAEs with FM on approximately half of the participants. The test order was reversed (mDPOAEs with FM followed by DPOAEs without FM) for the other half of the participants. mDPOAE procedures with and without FM were recorded twice to ensure reliability of the response (Dhar & Hall, 2012).

Children were seated comfortably inside a sound booth and were instructed to remain as quiet as possible during testing, to avoid any confounding factors due to body position (Atcherson & Mattheis, 2011). Appropriate probe seal and depth was ensured before testing and maintained throughout the test session (Dhar & Hall, 2012). Testing was conducted on the right ears of the children in order to avoid possible confounding factors due to ear differences (Keogh, Kei, Driscoll, Smyth, 2001; McFadden, Martin, Stagner & Maloney, 2009).

**Statistical Analysis**

Data from eleven children (eleven right ears) were analyzed. Averaged mDPOAE responses were computed from the two recorded responses from each participant for each mDPOAE procedure. The mean averaged response was plotted in the form of DP-grams of the mDPOAEs to display both the response amplitude and the SNR across frequencies (Dhar & Hall, 2012). Responses to f2 tones at 1000 Hz, 2000 Hz, 3084 Hz, 4000 Hz, 5187 Hz, and 6169 Hz were analyzed in this study. For each participant, test duration was recorded in seconds and the two runs of mDPOAEs with FM and the two runs of mDPOAEs without FM, respectively, were
averaged. Frequency-specific mDPOAE measurements were excluded from analysis if the absolute response amplitude was < -10 dB SPL or if SNR was ≥ 6 dB SPL.

This study uses a within-subject design with two mDPOAEs stimulus conditions (mDPOAEs with FM vs. mDPOAEs without FM) as the within-subject independent variable, and three measured within-subject dependent variables (DPOAEs amplitude, SNR, and recording time) for each of the tested six f2 frequencies over a frequency range of 1000 to 6169 Hz. Gender is analyzed as the between-subject factor to evaluate possible ear differences due to gender (Keogh et al., 2001). For mDPOAE amplitude and SNR, descriptive statistics are provided by frequency. A series of Pearson zero-order correlations were performed on the averaged amplitudes and SNR for mDPOAEs with and without FM to determine the linear relationship between the two measures at each of the six f2 frequencies measured (see Appendix F).

Statistical analysis was then conducted using 2 (stimulus: with FM and without FM) x 6 (f2 frequencies) repeated measures analysis of variance (ANOVA) for each of the six f2 frequencies assessed in this study to determine whether there were statistically significant differences in response amplitude and SNR between mDPOAEs with and without FM. If a significant difference was found, a post hoc analysis of measures with and without FM was performed for each of the frequencies using paired-sample t-test to further investigate the differences between stimuli. For test duration, descriptive statistics were provided, and Pearson’s correlation analysis and a paired-sample t-test were used to evaluate whether there are statistically different test time lengths for mDPOAEs with and without FM. Statistical analysis
was performed using Jeffreys’s Amazing Statistics Program (JASP) 0.14 and graphs were created using JASP and Microsoft Office Suite.
RESULTS

Amplitude Response with and without FM

The amplitude of each mDPOAE measurement was recorded in dB SPL. Figure 2 shows an example of the amplitude of one participant’s mDPOAE test results with and without FM.

Figure 2. Example recording of mDPOAEs with FM (top) and without FM (bottom) obtained from a single ear. In general, noise floor levels and DPOAE response amplitudes for both test results correspond closely, however, the mDPOAE recording with FM is slightly flatter.
The mean and standard deviations of the averaged mDPOAE amplitude with and without FM for each frequency are reported in Table 1. The mean amplitude of mDPOAEs with FM ranges from 7 dB SPL to 14.4 dB SPL and the amplitude of mDPOAEs without FM ranges from 7.6 dB SPL to 15.6 dB SPL.

**Table 1.** Means and Standard Deviations of mDPOAE Amplitude (in dB SPL) with and without FM by f2 Frequency (N=11)

<table>
<thead>
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<th>f2 Frequency</th>
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<td>Without FM</td>
</tr>
<tr>
<td>1000 Hz</td>
<td>11.741 (4.059)</td>
</tr>
<tr>
<td>2000 Hz</td>
<td>15.632 (5.544)</td>
</tr>
<tr>
<td>3084 Hz</td>
<td>13.950 (7.383)</td>
</tr>
<tr>
<td>4000 Hz</td>
<td>15.314 (5.031)</td>
</tr>
<tr>
<td>5197 Hz</td>
<td>13.580 (4.444)</td>
</tr>
<tr>
<td>6169 Hz</td>
<td>7.560 (8.320)</td>
</tr>
</tbody>
</table>

Figure 3 reveals that mDPOAEs with FM resulted in slightly smaller amplitude between 1000 to 4000 and 6000 Hz compared to that of the standard mDPOAE without FM measure. In contrast, Figure 4 reveals that mDPOAEs responses without FM had a larger standard deviation than mDPOAEs with FM at all frequencies measured. These findings suggest that mDPOAEs with FM may produce slightly smaller yet flatter and less variable response amplitude than mDPOAEs without FM.
Figure 3. Mean mDPOAEs amplitude. Mean mDPOAEs with FM has slightly smaller amplitude as compared to mean mDPOAE amplitude without FM mainly at four f2 frequencies (1000-4000 Hz) out of six f2 frequencies. mDPOAEs with FM has a flatter DP-gram amplitude between 2000 Hz to 5187 Hz than mDPOAEs without FM. Note: Slight shift in f2 frequency for better visualization of the response and error bars. Figure was created with JASP 0.14.

Figure 4. Standard deviation of mean amplitude for mDPOAEs. Standard deviation of FM amplitude is consistently smaller than without FM at all f2 frequencies tested, indicating less variance in response amplitude with FM stimulus.
A 2X6 ANOVA with repeated measures for two factors (stimulus and frequency) was calculated to determine stimulus and frequency effect between the amplitude of mDPOAEs with and without FM measures at each frequency (see Appendix G). There were no significant differences in amplitude between mDPOAEs with and without FM stimulus ($F(1,10) = 3.69, p = .084; \eta^2_p = .27$). Although not statistically significant, the effect size of the partial eta-squared ($\eta^2_p$) provides evidence that 27% of the differences in amplitude can be attributed to the type of stimulus employed. However, there were significant differences in amplitude between frequencies ($F(5,50) = 6.011, p < .001; \eta^2_p = .38$). The eta-squared ($\eta^2 = .38$) indicates that 38% of the difference in response amplitude can be attributed to differences in f2 frequency. There was no significant stimulus and frequency interaction ($F(5,50) = .513, p = .765, \eta^2_p = .05$).

Between subjects effect testing revealed no significant gender effect on mDPOAE amplitude ($F(1,9) = .651, p = .440, \eta^2_p = .067$). Figure 5 displays the results of Pearson zero-order correlations of the averaged mDPOAE amplitudes with and without FM at each of the six frequencies analyzed. Results show a strong positive correlation for mDPOAEs both with and without FM at all f2 frequencies measured.

To assess the differences in mDPOAEs amplitude between frequencies two one-way repeated measures ANOVAs were calculated, one for each of the stimulus conditions (with FM and without FM). As expected, there were significant differences in amplitude as function of frequency for both FM ($F(5,50) = 5.657, p = .001, \eta^2_p = .36$) and without FM ($F(5,50) = 5.657, p < .001, \eta^2_p = .36$); see Figure 2. A series of post hoc t-test were calculated to assess differences between frequencies for the DPOAE with FM and without FM measures. For the FM measure, it was observed that frequency 6169 Hz had significantly smaller amplitude than that of 5187 Hz,
Figure 5. Pearson correlations of amplitude of mDPOAEs with and without FM stimuli. A series of Pearson correlations between mDPOAEs amplitude with and without FM. Results show that amplitudes of mDPOAEs with and without FM are strongly to moderately correlated across all six frequencies analyzed.
4000 Hz, and 3084 Hz (p < .05). The trend in frequency differences for mDPOAEs without FM measure was similar to that of the mDPOAEs with FM measure, however given the correction no significant frequency differences resulted. Results show a strong positive correlation for mDPOAEs both with and without FM at all f2 frequencies measured.

**Signal-to-Noise Ratio with and without FM**

For each mDPOAE measurement, the calculated SNR in dB SPL were averaged for each frequency. The mean and standard deviations are reported in Table 2. The mean SNR of mDPOAEs with FM ranges from 15.4 dB SPL to 19.1 dB SPL and the SNR of mDPOAEs without FM ranges from 15.7 dB SPL to 19.5 dB SPL.

<table>
<thead>
<tr>
<th>f2 Frequency</th>
<th>Mean (SD) mDPOAEs Without FM</th>
<th>Mean (SD) mDPOAEs With FM</th>
</tr>
</thead>
<tbody>
<tr>
<td>1000 Hz</td>
<td>16.805 (2.399)</td>
<td>16.314 (2.214)</td>
</tr>
<tr>
<td>2000 Hz</td>
<td>19.345 (2.635)</td>
<td>17.809 (2.389)</td>
</tr>
<tr>
<td>3084 Hz</td>
<td>18.432 (3.773)</td>
<td>18.168 (3.453)</td>
</tr>
<tr>
<td>4000 Hz</td>
<td>19.505 (2.127)</td>
<td>18.009 (2.055)</td>
</tr>
<tr>
<td>5197 Hz</td>
<td>19.073 (1.790)</td>
<td>19.127 (1.811)</td>
</tr>
<tr>
<td>6169 Hz</td>
<td>15.677 (4.390)</td>
<td>15.409 (3.914)</td>
</tr>
</tbody>
</table>

In general, the mDPOAEs with FM stimuli resulted in smaller SNRs compared to that of the standard mDPOAEs without FM, as can be seen in Figure 6. This indicates that better SNRs were observed with DPOAEs without FM. However, Figure 7 shows that mDPOAEs without
Figure 6. Mean mDPOAEs SNR with FM is smaller yet flatter than the mean mDPOAEs SNR without FM at all $f_2$ frequencies, mainly at 2000 Hz and 5187. Note: slight shift in $f_2$ frequency for better visualization of the response and error bars. Figure was created with JASP 0.14.

Figure 7. Standard Deviation of Mean for mDPOAE SNR by $f_2$ Frequency. Standard deviation of mean SNR for mDPOAEs with FM is slightly smaller than without FM at five out of six $f_2$ frequencies, indicating less variance in SNR (mainly at 3084 Hz and 6169 Hz).
FM had a larger standard deviation than mDPOAEs with FM at all frequencies measured. This suggests that mDPOAEs with FM have less variability for SNRs than mDPOAEs without FM.

A series of Pearson zero-order correlations were performed on the averaged amplitudes for mDPOAEs with and without FM to determine the linear relationship between the two measures at each of the six f2 frequencies (see Appendix F). Figure 8 shows a strong positive correlation ($r = .704 - .948$) between mDPOAEs SNR with and without FM at all tested f2 frequencies. A 2X6 ANOVA with repeated measures for two factors (stimulus and frequency) was also performed on SNR data (see Appendix G). A significant statistical SNR effect was observed for stimulus ($F(1,10) = 12.05, p = .006, \eta^2_p = .55$) and frequency ($F(1,50) = 4.721, p = .001, \eta^2_p = .32$). These differences are due to smaller SNR mDPOAEs with FM measured at 2000 Hz ($t(10) = -2.620, p = .026$) and 4000 Hz ($t(10) = -3.765, p = .004$), as shown in Table 4. The magnitude of the partial eta-squared ($\eta^2_p$) indicates that 55% of the differences in SNR can be attributed to differences in stimulus, which suggests that this could be a clinically important result.

As can be seen in Figure 7, the FM stimulus consistently resulted in a smaller SNR compared to that of the mDPOAE stimulus without FM. A series of paired sample t-tests were calculated to further assess differences between each frequency for mDPOAE SNR responses with and without FM. A statistically significant difference was noted at 2000 Hz ($t(10) = -2.620, p = .026$) and 4000 Hz ($t(10) = -3.765, p = .004$), indicating that there are significant differences between types of stimulus at those frequencies (Table 3). No other significant differences were observed at other f2 frequencies. There was no significant stimulus and frequency interaction
Figure 8. Pearson Correlations of SNR of mDPOAEs with and without FM. A series of Pearson correlations which shows that SNR of mDPOAEs with and without FM are strongly correlated across all six frequencies analyzed.
Between subjects effect testing revealed no significant effect of gender on SNR ($F(1,9) = .566, p=.471, \eta_p^2=0.059$).

**Table 3.** Paired Sample $t$-test Series of mDPOAE Signal-to-Noise Ratios With and Without FM by $f_2$ Frequency (N=11)

<table>
<thead>
<tr>
<th>$f_2$ Frequency</th>
<th>$t$</th>
<th>df</th>
<th>P</th>
<th>Mean Difference</th>
<th>SE</th>
<th>Cohen’s d</th>
</tr>
</thead>
<tbody>
<tr>
<td>1000 Hz</td>
<td>-1.314</td>
<td>10</td>
<td>0.218</td>
<td>-0.491</td>
<td>0.373</td>
<td>-0.396</td>
</tr>
<tr>
<td>2000 Hz</td>
<td>-2.620</td>
<td>10</td>
<td>0.026</td>
<td>-1.536</td>
<td>0.586</td>
<td>-0.790</td>
</tr>
<tr>
<td>3084 Hz</td>
<td>-0.723</td>
<td>10</td>
<td>0.486</td>
<td>-0.264</td>
<td>0.365</td>
<td>-0.218</td>
</tr>
<tr>
<td>4000 Hz</td>
<td>-3.765</td>
<td>10</td>
<td>0.004</td>
<td>-1.495</td>
<td>0.397</td>
<td>-1.135</td>
</tr>
<tr>
<td>5187 Hz</td>
<td>0.178</td>
<td>10</td>
<td>0.863</td>
<td>0.055</td>
<td>0.307</td>
<td>0.054</td>
</tr>
<tr>
<td>6169 Hz</td>
<td>-0.435</td>
<td>10</td>
<td>0.673</td>
<td>-0.268</td>
<td>0.617</td>
<td>-0.131</td>
</tr>
</tbody>
</table>

**Test Duration with and without FM**

A paired samples $t$-test was conducted to compare the amount of time in seconds that mDPOAE testing takes to be completed with and without FM. No significant differences in the test duration for mDPOAE without FM ($M = 60.68 \text{ sec}, SD = 17.20$) and mDPOAE with FM ($M = 60.22 \text{ sec}, SD =7.20$) ($t(10) = -0.104, p = .919$). However, mDPOAE without FM had a larger standard deviation than mDPOAEs with FM at all frequencies measured, and this increased variability is seen in Figure 9. This suggests that mDPOAE with FM may be less variable for test duration than mDPOAEs without FM. A Pearson’s correlation was performed, and a moderate positive correlation was demonstrated between mDPOAE test duration with and without FM ($r(10) = .55, p = .079$), as seen in Figure 10.
Figure 9. Test duration range and distribution for mDPOAEs with and without FM. A boxplot displays the minimum, medium, interquartile range, and maximum of the test duration data for mDPOAEs with and without FM. The mDPOAEs without FM had much greater variability than those with FM.

Figure 10. mDPOAEs Test Duration With and Without FM Stimulus. A Pearson correlation shows that test duration of mDPOAEs with and without FM are strongly correlated.
DISCUSSION

DPOAEs measure have a variety of use for both clinicians and hearing scientists as an objective indicator of the integrity of the cochlea OHCs. DPOAEs are generated in the cochlea in response to two tones or multiple-pair tones of a given frequency and sound pressure level presented in the ear canal. There is scarcity of research on the use of frequency modulation of mDPOAEs with children. This pilot study investigates mDPOAEs response characteristics with and without FM stimulus in children. The researcher hypothesized that recording mDPOAEs with FM will elicit DPOAE responses with greater amplitudes in a shorter time than mDPOAEs without FM.

The overall results of this study do not support the rejection of the null hypothesis; however, it is notable that comparison of standard deviation across frequency and measure suggests that frequency modulated mDPOAEs may be less variable than standard mDPOAEs. This indicates that frequency modulation of DPOAEs may provide greater stability in responses and therefore more reliable test results when found to be present or absent.

A gender effect on the DPOAE SNR in children ages five – seven years old was found in a study by Keogh et al. (2001). The researchers found that the mean SNR of girls was higher than the mean SNR of boys at high frequencies. A between-subject effects analysis was therefore performed with both the amplitude and SNR data to determine whether there was a confounding gender effect present in this study, however, no significant effect between genders was found for either of these variables (see Appendix H). Despite the small sample size, findings cannot be attributed to gender effect in the present study.
mDPOAEs Amplitude with and without FM

Marcum et al. (2020) studied methods to reduce fine structure of DPOAEs in 83 normal-hearing young adults. They compared conventional DPOAEs with FMDPOAEs and DPOAEs with a suppressor tone at F2 levels increasing in 10 dB steps ranging from 25 dB SPL to 65 dB SPL. They found that DPOAE amplitude is not substantially reduced when using FM stimuli as opposed to conventional DPOAE stimuli when testing adult males and females in either the right or left ear. They found that the amplitude of DPOAEs with and without FM were not significantly different at 1000, 4000, and 6000 Hz, although the FMDPOAEs were smaller in amplitude at 2000 and 3000 Hz (Marcum et al., 2020). Similar findings were noted in this study when recording mDPOAEs in children. Results showed slightly smaller mDPOAEs amplitudes with FM than without FM at all tested six f2 frequencies except at 5187 Hz. There was also no significant interaction between the stimulus and frequency for amplitude. It may be that the small sample size, which resulted in low statistical power, could account for the failure to reach statistical significance with the 2 X 6 repeated measures ANOVA.

What is perhaps more noteworthy is that the amplitude of mDPOAE without FM responses reveal a notched DP-gram and a greater standard deviation at all six f2 frequencies, as seen in Figures 2 & 3 and Table 1. In contrast, mDPOAEs with FM consistently showed a flatter DP-gram between 2000 Hz and 5187 Hz and a smaller standard deviation from the mean, which indicates less variability in amplitude responses all six frequencies. Although these amplitude differences are not statistically significant, results suggest that FM stimulus reduce some of the variability in responses and peaks and valleys that is attributed to fine structure, and therefore provide more reliable responses, easier detection, and better confidence in the recorded response,
mainly between 2000 Hz and 5000 Hz. These findings are consistent with previous results that reveal slight frequency modulation over time of the primary tones within a range of approximately 100 Hz at a rate of approximately 1.5 Hz (Janssen, 2015) has been shown to reduce noise level and peaks and valleys in the response (Janssen, 2015; Smurzynski, 2018; Marcum et al., 2020).

Poling, Siegel, Lee, Lee & Dhar (2013) studied the features of fine structure of DPOAEs in male and females ages 10 to 65 years of age and found that fine structure may cause variation in maxima and minima of DPOAE response by as much as 7 dB, with fine structure peaks increasing in height and spacing in conjunction with increases in frequency. In light of the prevalence and potential impact of DPOAE fine structure phenomena on the interpretation of the presence or absence of DPOAE frequency responses for individuals of all ages, particularly in the higher frequencies, it is apparent that the ability to obtain more reliable DPOAE amplitude responses through frequency modulation of primary tones would be beneficial in the clinical setting.

Marcum et al. (2020) tested the effect of level of stimuli presentation on the amplitude of DPOAEs with and without FM, presenting L2 at levels ranging from 25 dB SPL to 65 dB SPL in 10 dB SPL steps, in contrast to the current study, which used L2 set at 40 dB SPL. Additionally, Marcum et al. only tested adults and they did not use mDPOAE stimuli, which this study used with and without FM in testing children. However, their study is relevant as it is the only published research using FMDPOAEs to examine the effect on fine structure of which this researcher is aware to date. They found that the level of presentation has an impact on the amplitude of DPOAEs with and without FM. They report that as the level of presentation was
increased, the level of response amplitude for both conventional DPOAE test protocol and DPOAEs with FM test protocols became correspondingly higher, which was as expected. Marcum et. al (2020) did not find any significant interaction between method of stimulus (i.e. conventional DPOAE protocol vs FMDPOAE protocol) and level of presentation. In this study, a set level of 40 dB SPL was used for all L2 presentations in order to assess the effect of FM on fine structure, as it has been found that the presence of fine structure is reduced with increased stimulus presentation level (Marcrum et al., 2020). The use of a 40 dB SLP stimulus level for L2 could have resulted in reduced DPOAE amplitudes overall, as opposed to using a higher level of presentation for L2 such as 55 dB SPL (Gorga, Nelson, Davis, Dorn & Neely, 2000).

Research comparing the use of single-tone pair DPOAEs with mDPOAEs has revealed a common configuration of maxima of mDPOAE amplitude at approximately 1500 Hz and 4000 Hz (Atcherson & Mattheis, 2011; Kim et al., 1997; Schairer et al., 2000). The present study found a similar outline of elevated amplitude at 2000 Hz and 4000 Hz, which may reflect a pattern for mDPOAEs without FM. One caution with the use of mDPOAE tests in general is that interference between mDPOAE stimuli may occur if the concurrently tested f2 frequencies are located too closely on basilar membrane, as it is known that the level of the DPOAE response depends strongly on the tonotopic relationship between the primary tones (Robinette & and Glattke, 2007; Dhar & Hall, 2012; Janssen, 2015). In addition, some researchers have found that the levels of noise increase with increases in frequency when performing simultaneous testing of paired pure tones, which adversely affect the detection of OAE activity and thus cause difficulty in obtaining accurate results (Schairer et al., 2000; Beattie, 2003; Smurzynski & Janssen, 2015).
Given these risks for accuracy, it is essential that more research be performed to analyze the clinical application of mDPOAEs.

**mDPOAEs Signal-to-Noise Ratio with and without FM**

When analyzing the SNR of mDPOAEs between the two stimuli (with and without FM), this study found that SNR was smaller when using an FM stimulus as compared to mDPOAEs without FM across all f2 frequencies analyzed. However, a statistically significant difference in SNR between types of stimulus was found at 2000 Hz and 4000 Hz, with no further significant differences found in the remaining f2 frequencies. It may be that there is a significant difference at these two frequencies due to the effect of distortion product interaction which may occur with mDPOAEs, evidenced by a pattern of maxima of mDPOAE amplitudes at these frequencies as discussed above, which are resulting in a greater SNR at 2000 and 4000 Hz in the tests without FM, resulting in a statistically significant difference at those two frequencies.

While the mean SNR was found to be more robust for mDPOAEs without FM overall, it is noteworthy that again, there was less variability in general for mDPOAEs with FM, as there were smaller standard deviations from the mean for SNR of FMDPOAEs at each frequency except 5187 Hz. Similarly, these findings indicate that FM stimulus reduces noise and fine structure peaks and valleys, resulting in a slightly smaller yet cleaner response. Torre et al. (2003) report that both amplitude and SNR may be used for determining the presence or absence of a DPOAE. However, they point out that SNR is a more clinically useful response characteristic, since only a single SNR value (e.g. +9 dB) could be used to determine whether a response was present or absent, as opposed to using amplitude to determine the presence of
DPOAEs, since the response criteria for amplitude vary by frequency, ranging from -6 dB SPL at 2000 Hz to -22 dB SPL at 8000 Hz. Therefore, the potential to obtain a more reliable SNR response via FMDPOAEs is clinically relevant and advantageous.

**Test Duration with and without FM**

Another factor which this study investigated is the length of time that it took to complete testing using mDPOAEs with and without FM. Kim et al. (1997) found a decrease in test time ranging from one-third to one-half (11 to 25 seconds for mDPOAEs as opposed to 40 to 80 seconds for DPOAEs) by using mDPOAEs with three tone-pairs as compared to conventional DPOAE single pair protocols when testing 1500 to 8000 Hz in adults. Other researchers have also found a significant reduction in test time as result of using mDPOAEs as compared to standard DPOAES (Beattie, 2003; Atcherson & Matthies, 2011). Beattie (2003) studied mDPOAEs at 1000 through 4000 Hz in adults with normal hearing and mild hearing loss and found that mDPOAEs resulted in less than half the test time as compared to conventional DPOAE test time in both populations. He found that the mean DPOAE test time was 37 seconds in normal hearing participants and 160 seconds in the participants with mild hearing loss, while mDPOAEs were obtained in 25 seconds and 51 seconds for the same groups, respectively (Beattie, 2003).

This study found no significant difference in the mDPOAEs test duration between the two stimuli; however, the mean test time for mDPOAEs with FM was slightly lower than the mean test time for mDPOAEs without FM (60.9 seconds for mDPOAEs with FM vs 60.2 seconds for mDPOAEs without FM). This suggests that frequency modulation per se may not
play an important role in decreasing overall test time for measuring mDPOAEs, compared to using standard DPOAEs. It is also possible that the inclusion of testing frequencies below 1500 Hz increased the test time, as there is often an increase in noise floor level at low frequencies (Atcherson & Mattheis, 2011). However, while the present study did not find a significant decrease in test time for mDPOAEs with FM as compared to mDPOAEs without FM, it is remarkable that the test length of FMDPOAEs was much less variable (see Figure 8). This suggests that the test time for FMDPOAEs is comparable to and possibly more consistent than test time for standard mDPOAEs. It is possible that the moderate level of correlation seen in Figure 10 may be due to the amount of variability in duration that was demonstrated in tests between mDPOAEs with and without FM.

Limitations

The findings of this study must be seen in the light of limitations. Children in this age group are particularly susceptible to middle ear disorders, which limited the number of eligible participants available to the researchers. The time of year in which data collection was obtained was in the early spring, which increased the likelihood of ear infections and the presence of negative pressure or middle ear fluid as a result. In addition, unforeseen circumstances related to the COVID-19 global pandemic resulted in premature termination of data collection, which severely limited the power of the study and prevented this researcher from testing the number of participants which was originally planned during the design of the study. Obtaining more data on children utilizing mDPOAEs both with and without FM is essential to better understand the potential to improve DPOAE testing and response characteristics in this population and allow for
greater generalization of findings. It would be advisable to conduct research on individuals of all ages with hearing loss to determine the sensitivity and specificity for FMDPOAE testing protocol in conjunction with DPOAE response characteristics across frequency. It is also recommended that research be done examining the performance of DPOAEs with and without FM that do not employ simultaneous multiple tones, in order to avoid any confounding factors due to possible interference from the use of simultaneous pure tones.

**Conclusion**

The purpose of this study was to gather data on children ages three to six using mDPOAEs with and without FM. The researcher looked at mDPOAE amplitude, SNR, and test duration in both conditions. Although the results of this study did not support the hypothesis that frequency modulation of mDPOAEs would provide more robust amplitudes and SNR as well as reduce test time, it is apparent that mDPOAEs with FM are generally comparable to mDPOAEs without FM, and their use may be clinically useful due to less variance in their results. A primary limitation of this study is the curtailed data collection as a result of the COVID-19 pandemic, resulting in fewer participants than necessary for a high powered study. Therefore, more research with FMDPOAEs in the pediatric population is recommended to further evaluate their clinical utility.
REFERENCES


Appendix A. Participant Recruitment Flyer

RESEARCH PARTICIPANTS NEEDED!

IS YOUR CHILD BETWEEN 3 TO 6 YEARS OLD? WE HAVE A HEARING RESEARCH OPPORTUNITY AVAILABLE!

An Investigation of Increased Reliability and Decreased Test Time using Multiple Frequency Modulated Distortion Product Otoacoustic Emissions in Young Children with Normal Hearing

We are looking for children with normal hearing between 3 to 6 years old to be part of our study on comparing test time and responses with different testing protocols for performing objective testing for normal auditory function in children. This research may help to improve the ability of clinicians to identify hearing loss in children more easily and allow for faster intervention.

All testing will take place in the Professional Building on the Missouri State University campus. Address is listed below:

609 E Cherry St, Springfield, MO 65806

Looking for male and female participants between the ages of 3-6 years

Total testing time: About 90 minutes

Benefits of participating:
Free hearing test!

INTERESTED?
PLEASE CONTACT:

Kathryn Vlietstra, B.S.
kathryn1996@live.missouristate.edu
(920) 946-8365

Taylor Proske, B.S.
proiske113@live.missouristate.edu
(314) 341-7595

or

use this link to sign up:
https://forms.gle/H3ATwn8yPJwhLCZf8

PRINCIPAL INVESTIGATOR OF THE STUDY:

Wafaa Kaf, M.D., Ph.D.
Email: wafaakaf@missouristate.edu
Phone: (417) 836-4456
IRB approval #FY2020-256
Appendix B. Human Subjects IRB Approval

To:
Wafaa Kaf
Communication Sciences & Disorders

RE: Notice of IRB Approval
Submission Type: Initial
Study #: IRB-FY2020-256
Study Title: Normative Values for Frequency Modulated Distortion Product Otoacoustic Emissions in Healthy Young Children with Normal Hearing
Decision: Approved

Approval Date: November 22, 2019

This submission has been approved by the Missouri State University Institutional Review Board (IRB). You are required to obtain IRB approval for any changes to any aspect of this study before they can be implemented. Should any adverse event or unanticipated problem involving risks to subjects or others occur it must be reported immediately to the IRB.

This study was reviewed in accordance with federal regulations governing human subjects research, including those found at 45 CFR 46 (Common Rule), 45 CFR 164 (HIPAA), 21 CFR 50 & 56 (FDA), and 40 CFR 26 (EPA), where applicable.

Researchers Associated with this Project:
PI: Wafaa Kaf
Co-PI:
Primary Contact: Taylor Proske
Other Investigators: Kathryn Vlietstra, Emily Beeman
Appendix C. Informed Consent Form

Missouri State University

INFORMED CONSENT FORM

Consent to Participate in a Research Study
Missouri State University
College of Health and Human Services

Normative Frequency Modulated Distortion-Product Otoacoustic Emissions in Healthy Young Children with Normal Hearing

Principal Investigator: Dr. Wafaa Kaf (417-836-4456; wafaakaf@missouristate.edu)
Investigators: Taylor Proske, B.S. (314-341-7595; proske113@live.missouristate.edu) and Kathryn Vlietstra, B.S. (920-946-8365; kathryn1996@live.missouristate.edu)

Introduction

We are asking for your permission for your child to participate in a doctoral research study that is part of the requirement for a Doctorate degree in Audiology for Taylor Proske and Kathryn Vlietstra. Before you agree for your child to participate in this study, it is important that you read about and understand the study and the procedures it involves. The investigators will also explain the project to you in detail. If you have any questions about the study or your role in it, be sure to ask the investigators. If you have more questions at a later time, Dr. Kaf, Taylor Proske and Kathryn Vlietstra will be happy to answer them for you. You may contact the investigators.

You will need to sign this form giving us your permission for your child to be involved in the study. Taking part in this study is entirely your choice. If you decide for your child to take part, but later change your mind, you may stop at any time. If you decide to stop, you do not have to give a reason and there will be no negative consequences for ending your participation.
**Purpose of this Study**
Distortion-Product Otoacoustic Emissions (DPOAEs) are used as an objective measure of hearing sensitivity, but the standard protocol may not result in the best possible responses for early detection of hearing loss in newborns. The use of Frequency Modulated DPOAE (FM-DPOAE) signal may result in better detection of a response. The reason for this study is to test the efficacy of using FM-DPOAEs as a part of the audiological test battery and obtain better responses than with the standard DPOAE testing protocol for objective hearing testing.

**Description of Procedures**
If you decide to allow your child to take part in this study, you will also be asked a series of questions about your child’s medical and birth history, and your child will undergo a hearing screening. These include examination of the ear canal using an otoscope, middle ear status using a tympanometry, hearing screening using pure tone audiometry, and inner ear status using standard DPOAE protocol. Your child has to pass these screening assessments to participate in the experimental FM-DPOAE protocols. All testing will be performed on one session, lasting approximately 1.5 hours. Any information about your child will be kept confidential. To protect your child’s privacy, your child will be assigned a coded number and your child’s name or any other identifying information will not appear on any of the data.

**What are the risks?**
We estimate that the potential risks of this study are minimal. All screening procedures are standard, non-invasive clinical procedures that involve no risk. Participants may get bored during the 1 ½ hour testing.

**What are the benefits?**
Benefits to participants include a free audiological evaluation including hearing and middle ear and inner ear function measurement. We will give you a copy of the screening findings. The overall results from all 20 children who will complete this study, will be disseminated at professional conferences and published. These results will provide audiologists and researchers with a possibly better protocol for DPOAE testing, and therefore facilitate/improve the use of DPOAEs for objective hearing screening in infants and difficult to test populations.

**How will my child’s privacy be protected?**
Information about your child will be coded by number and will be saved on a secure server. Your child’s name will not appear on the data collected. The information gathered will be accessible only by the investigators and it will be kept in a locked facility at Dr. Kaf’s office. Your child will not be identified by name in any publications that result from this research and findings will be presented using the average data from all 20 children. All information from this study will be
destroyed five years after the study ends or after publication of the findings at a professional journal, whichever occurs first.

**Consent to Participate**

If you want your child to participate in this study, *Normative values for Frequency Modulated Distortion Product Otoacoustic Emissions in three to six year-old children*, you are required to sign below as an indication of your willingness for your child to participate:

I have read and understand the information in this form. I have been encouraged to ask questions and all of my questions have been answered to my satisfaction. I have also been informed that I can withdraw from the study at any time. By signing this form, I voluntarily agree for my child to participate in this study. I have received a copy of this form for my own records.

______________________________   ____________________________
Printed Name of Participant   Date

______________________________   ____________________________
Signature of Participant’s Parent/Legal Guardian   Date

______________________________   ____________________________
Signature of Witness (investigator)   Date
Appendix D. Participant Assent Form.

PARTICIPANT ASSENT FORM

TITLE: Normative Values for Frequency Modulated Distortion Product Otoacoustic Emissions in Healthy Young Children with Normal Hearing

The study doctor has told you about a research study they are inviting you to be in. They also read you a paper that tells you all about the study and what will happen to you during the study if you take part in it. You were told you can ask questions about the study any time you want. Your parent(s) or your guardian(s) was/were present for this.

You were told you don’t have to do this if you don’t want.

You were also told you could stop being in the study any time that you want to quit, and that it is okay. No one will be upset with you if you don’t want to be in the study or if you stop wanting to be in the study.

You were told that the study doctor might write a report about this study. You were told your name would not be used in the report.

You, ____________________________ (participant), want to be in the study.

______________________________ ______________________
Participant’s Signature (if capable) Date

______________________________ ______________________
Parent/Guardian’s Signature Date

______________________________ ______________________
Signature of Investigator Date
Appendix E. Participant Case History

Audiology Research Project Case History

Participant ID____________________

Child’s birthday ____/____/______ Child’s gender Male/Female

As far as I am aware, my child has normal hearing Yes/No

My child has a history of ear infections Yes/No

If yes, when was the most recent ear infection? __________________________

Was the ear infection treated? Yes/No

If yes, how?

____________________________________________________________________

Did your child pass their newborn hearing screening? Yes/No

Has anyone in your child’s family been diagnosed with hearing loss before 30 years of age? Yes/No

If yes, who and at what age? ____________________________________________

____________________________________________________________________

Was any of the following present in your child’s life? Please check all that apply:

□ Measles □ Infections at birth or in utero (e.g. CMV, herpes, rubella, syphilis, toxoplasmosis)

□ Meningitis □ Postnatal infections associated with hearing loss (e.g. herpes, meningitis)

□ Mumps □ Syndromes associated with hearing loss (e.g. neurofibromatosis, Usher syndrome, Waardenburg)

□ Allergies □ Neonatal intensive care for more than 5 days

□ Hyperbilirubinemia (jaundice) □ Anoxia (oxygen deprivation)

□ Ototoxic medications (e.g. gentamycin, aminoglycoside, loop diuretics)
Is there anything about your child (health history or otherwise) that you feel would be helpful for us to know prior to testing?

__________________________________________________________________________

__________________________________________________________________________

__________________________________________________________________________
### Appendix F. Pearson Correlation Series

#### Pearson’s Correlation Series

**mDPOAE Amplitude with and without FM Measure by Frequency (N=11)**

<table>
<thead>
<tr>
<th>Frequency</th>
<th>Pearson’s r</th>
<th>P</th>
</tr>
</thead>
<tbody>
<tr>
<td>mDPOAE 1000 Hz</td>
<td>0.699*</td>
<td>0.017</td>
</tr>
<tr>
<td>mDPOAE 2000 Hz</td>
<td>0.888***</td>
<td>&lt;.001</td>
</tr>
<tr>
<td>mDPOAE 3084 Hz</td>
<td>0.987***</td>
<td>&lt;.001</td>
</tr>
<tr>
<td>mDPOAE 4000 Hz</td>
<td>0.980***</td>
<td>&lt;.001</td>
</tr>
<tr>
<td>mDPOAE 5187 Hz</td>
<td>0.711*</td>
<td>0.014</td>
</tr>
<tr>
<td>mDPOAE 6169 Hz</td>
<td>0.899***</td>
<td>&lt;.001</td>
</tr>
</tbody>
</table>

*p < .05, ** p < .01, *** p < .001

#### Pearson’s Correlation Series

**mDPOAE SNR with and without FM Measure by Frequency (N=11)**

<table>
<thead>
<tr>
<th>Frequency</th>
<th>Pearson’s r</th>
<th>P</th>
</tr>
</thead>
<tbody>
<tr>
<td>1000 Hz</td>
<td>0.859***</td>
<td>&lt; .001</td>
</tr>
<tr>
<td>2000 Hz</td>
<td>0.704*</td>
<td>0.016</td>
</tr>
<tr>
<td>3084 Hz</td>
<td>0.948***</td>
<td>&lt;.001</td>
</tr>
<tr>
<td>4000 Hz</td>
<td>0.802**</td>
<td>0.003</td>
</tr>
<tr>
<td>5187 Hz</td>
<td>0.840**</td>
<td>0.001</td>
</tr>
<tr>
<td>6169 Hz</td>
<td>0.885***</td>
<td>&lt;.001</td>
</tr>
</tbody>
</table>

*p < .05, ** p < .01, *** p < .001
Appendix G. Two by Six Repeated Measures ANOVA

### 2 (Measure; FM vs without FM) X 6 (Frequency) ANOVA of Amplitude with Repeated Measures on both Factors (An All Within Group Design)

<table>
<thead>
<tr>
<th>Cases</th>
<th>Sum of Squares</th>
<th>df</th>
<th>Mean Square</th>
<th>F</th>
<th>p</th>
<th>η²</th>
</tr>
</thead>
<tbody>
<tr>
<td>Measure (DPOAEs with &amp; without FM)</td>
<td>15.426</td>
<td>1</td>
<td>15.426</td>
<td>3.687</td>
<td>0.084</td>
<td>0.269</td>
</tr>
<tr>
<td>Residuals</td>
<td>41.835</td>
<td>10</td>
<td>4.184</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Frequency</td>
<td>936.617&lt;sup&gt;a&lt;/sup&gt;</td>
<td>5&lt;sup&gt;a&lt;/sup&gt;</td>
<td>187.323&lt;sup&gt;a&lt;/sup&gt;</td>
<td>6.011&lt;sup&gt;a&lt;/sup&gt;</td>
<td>&lt;.001&lt;sup&gt;a&lt;/sup&gt;</td>
<td>0.375&lt;sup&gt;a&lt;/sup&gt;</td>
</tr>
<tr>
<td>Residuals</td>
<td>1558.115</td>
<td>50</td>
<td>31.162</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Measure ★ Frequency</td>
<td>9.088&lt;sup&gt;a&lt;/sup&gt;</td>
<td>5&lt;sup&gt;a&lt;/sup&gt;</td>
<td>1.818&lt;sup&gt;a&lt;/sup&gt;</td>
<td>0.513&lt;sup&gt;a&lt;/sup&gt;</td>
<td>0.765&lt;sup&gt;a&lt;/sup&gt;</td>
<td>0.049&lt;sup&gt;a&lt;/sup&gt;</td>
</tr>
<tr>
<td>Residuals</td>
<td>177.226</td>
<td>50</td>
<td>3.545</td>
<td></td>
<td></td>
<td></td>
</tr>
</tbody>
</table>

*Note.* Type III Sum of Squares  
<sup>a</sup> Mauchly's test of sphericity indicates that the assumption of sphericity is violated (p < .05).

### 2 (Measure; FM vs without FM) X 6 (Frequency) ANOVA of SNR with Repeated Measures on both Factors (An All Within Group Design)

<table>
<thead>
<tr>
<th>Cases</th>
<th>Sum of Squares</th>
<th>df</th>
<th>Mean Square</th>
<th>F</th>
<th>p</th>
<th>η²</th>
</tr>
</thead>
<tbody>
<tr>
<td>Measure</td>
<td>14.667</td>
<td>1</td>
<td>14.667</td>
<td>12.046</td>
<td>0.006</td>
<td>0.546</td>
</tr>
<tr>
<td>Residuals</td>
<td>12.176</td>
<td>10</td>
<td>1.218</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Frequency</td>
<td>222.035&lt;sup&gt;a&lt;/sup&gt;</td>
<td>5&lt;sup&gt;a&lt;/sup&gt;</td>
<td>44.407&lt;sup&gt;a&lt;/sup&gt;</td>
<td>4.634&lt;sup&gt;a&lt;/sup&gt;</td>
<td>0.001&lt;sup&gt;a&lt;/sup&gt;</td>
<td>0.317&lt;sup&gt;a&lt;/sup&gt;</td>
</tr>
<tr>
<td>Residuals</td>
<td>479.100</td>
<td>50</td>
<td>9.582</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Measure ★ Frequency</td>
<td>12.735&lt;sup&gt;a&lt;/sup&gt;</td>
<td>5&lt;sup&gt;a&lt;/sup&gt;</td>
<td>2.547&lt;sup&gt;a&lt;/sup&gt;</td>
<td>2.253&lt;sup&gt;a&lt;/sup&gt;</td>
<td>0.063&lt;sup&gt;a&lt;/sup&gt;</td>
<td>0.184&lt;sup&gt;a&lt;/sup&gt;</td>
</tr>
</tbody>
</table>
2 (Measure; FM vs without FM) X 6 (Frequency) ANOVA of SNR with Repeated Measures on both Factors
(An All Within Group Design)

<table>
<thead>
<tr>
<th>Cases</th>
<th>Sum of Squares</th>
<th>df</th>
<th>Mean Square</th>
<th>F</th>
<th>p</th>
<th>η²_p</th>
</tr>
</thead>
<tbody>
<tr>
<td>Residuals</td>
<td>56.530</td>
<td>50</td>
<td>1.131</td>
<td></td>
<td></td>
<td></td>
</tr>
</tbody>
</table>

*Note.* Type III Sum of Squares

*a* Mauchly's test of sphericity indicates that the assumption of sphericity is violated (p < .05).
### Appendix H. Between Subjects Effects

**Between Subjects Effects**

<table>
<thead>
<tr>
<th>Cases</th>
<th>Sum of Squares</th>
<th>df</th>
<th>Mean Square</th>
<th>F</th>
<th>p</th>
<th>η²</th>
</tr>
</thead>
<tbody>
<tr>
<td>mDPOAE Amplitude with and without FM Measure by Frequency (N=11)</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Gender</td>
<td>138.236</td>
<td>1</td>
<td>138.236</td>
<td>0.651</td>
<td>0.440</td>
<td>0.067</td>
</tr>
<tr>
<td>Residuals</td>
<td>1910.419</td>
<td>9</td>
<td>212.269</td>
<td></td>
<td></td>
<td></td>
</tr>
</tbody>
</table>

*Note.* Type III Sum of Squares

### Between Subjects Effects

<table>
<thead>
<tr>
<th>Cases</th>
<th>Sum of Squares</th>
<th>df</th>
<th>Mean Square</th>
<th>F</th>
<th>p</th>
<th>η²</th>
</tr>
</thead>
<tbody>
<tr>
<td>mDPOAE Signal-to-Noise Ratio with and without FM</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Gender</td>
<td>26.346</td>
<td>1</td>
<td>26.346</td>
<td>0.566</td>
<td>0.471</td>
<td>0.059</td>
</tr>
<tr>
<td>Residuals</td>
<td>418.716</td>
<td>9</td>
<td>46.524</td>
<td></td>
<td></td>
<td></td>
</tr>
</tbody>
</table>

*Note.* Type III Sum of Squares