Clinical Observations with Evoked Otoacoustic Emissions at Mayo Clinic

Martin S. Robinette

Abstract
Clinical applications of transient evoked otoacoustic emission (TEOAE) measures began in 1989 at Mayo Clinic Rochester. Normative data indicates: a) greater TEOAE level for women and right ears beginning in the teen years, b) mean TEOAE levels remain relatively stable through the first seven decades of life, c) between subject EOAE level variability for normal hearing adults is high (up to about 30 dB) while within subject variability is low (about 4 dB), suggesting EOAEs should not be used to estimate pure-tone thresholds but are valuable in monitoring hearing status. Good frequency specificity of TEOAEs is demonstrated across high frequency hearing loss. Examples of TEOAEs in differential diagnosis are provided for cases of sudden hearing loss, auditory neuropathy and eighth nerve tumors including pre and post operative testing assessing changes in auditory function related to surgical procedures. Finally, our experience with TEOAEs in newborn hearing screening is described.

Key Words: Otoacoustic emissions, transient otoacoustic emissions, auditory neuropathy, sudden hearing loss, gender

Abbreviations: Evoked otoacoustic emission (EOAE); Transient evoked otoacoustic emission (TEOAE); Distortion product otoacoustic emission (DPOAE); Auditory brainstem response (ABR); Automated auditory brainstem response (AABR); Multiple sclerosis (MS); Neonatal intensive care unit (NICU)

Sumario:
El uso clínico de las emisiones otoacústicas evocadas por transientes empezó en 1989 en la Clínica Mayo, Rochester. La información normativa indica: a) mayor amplitud en las TEOAE en mujeres y oídos derechos, empezando en los años de la adolescencia, b) las amplitudes medias en las TEOAE se mantienen relativamente estables durantes las primeras siete décadas de vida, c) la variabilidad de la amplitud en EOAE entre sujetos adultos normooyentes es alta (hasta de 30 dB), aunque la variabilidad en el mismo sujeto es baja (alrededor de 4 dB), sugiriendo que las EOAE no deben ser utilizadas para estimar umbrales, pero son valiosas para monitorizar la condición auditiva. Una buena especificidad frecuencial en las TEOAE se demuestra en la hipoacusias para las altas frecuencias. Se muestran ejemplos de TEOAE en el diagnóstico diferencial para casos de sordera súbita, neuropatía auditiva y para tumores del octavo par, incluyendo evaluaciones pre y post-operatorias, evaluando los cambios en la función auditiva relacionados con los procedimientos quirúrgicos. Finalmente, se describe nuestra experiencia con las TEOAE en el tamizaje auditivo en recién nacidos.

Palabras Clave: emisiones otoacústicas, emisiones otoacústicas por transientes, neuropatía auditiva, sordera súbita, género.
While several articles on clinical applications of evoked otoacoustic emissions (EOAEs) were published in the 1980's, a first meaningful exposure to the potential clinical benefits of EOAEs for many audiologists was provided at the first meeting of the American Academy of Audiology in April 1989, at Kiawah Island SC, when David T. Kemp who discovered, and first reported the phenomenon (Kemp, 1978) lectured on emissions and demonstrated transient evoked otoacoustic emissions (TEOAEs). It was apparent that if normal middle ear and cochlear function could be assessed by frequency specific acoustic stimulation in a matter of a few seconds or minutes by a noninvasive objective method, the impact on infant hearing screening could be profound. Also apparent was the differential diagnostic value of separating sensorineural hearing loss into objective measurements of both “sensory” and “neural” components.

Although there was no commercial distribution of EOAE systems in the United States at that time, arrangements were made to purchase an Otodynamics Ltd. ILO88 Otoacoustic Emission System (Version 1.0) directly from Dr. Kemp in London by mid 1989. With it Mayo Clinic had its first institutionally supported TEOAE system to evaluate this emerging technology and its potential for improved patient care.

Findings from early studies

Following a pilot investigation using audiology section employees, a single-stimulus setting of 80 dB peSPL with the differential nonlinear test paradigm of the ILO88 was chosen for patient testing. Stimulus specifications per test were the default settings of 2080, clicks (260 subsets of four stimuli for each A and B buffer) presented at 50/s and elicited by 80µs electrical pulses.

To determine the optimal testing environment TEOAEs were measured in the presence of several levels of white noise introduced into the test suite. With secure probe fit in the ear canal, TEOAE response levels were not altered unless the ambient noise was greater than 45 dBA. The lack of standard TEOAE probes was addressed by having the Engineering Section at Mayo Clinic punch larger holes in various sized Amplaid Immitance probe tips. This modification allowed these probe tips to fit the ILO88 probe housing, thereby providing a snug canal fit for most patient ears (Robinette, 1992a).

Over the following 12 months approximately 2,000 patients participated in TEOAE evaluations following pure-tone audiometry and immittance measures. Patients were informed that they would hear a popping sound about the level of a telephone dial-tone, and we would measure “echoes” from their ear canals. Test time generally was 45–75 s/ear. Response data were printed and placed in the patient file for future evaluation. Unitary, single stimulus level recordings were conducted for each ear. While the mean and median stimulus levels were near the selected 80 dB peSPL, due to variance in canal size the range of stimulus levels was from 75 to 93 dB peSPL. Software version 1.0 did not automatically adjust stimulus level in the canal to the desired 80 dB peSPL.

From this emerging data base, TEOAE results were placed in three categories: a) patients with normal hearing (≤ 25 HL 500 – 6000 Hz), b) patients with sensorineural hearing loss and agreement between pure-tone sensitivity and TEOAE results, and c) patients with sensorineural hearing loss and lack of agreement between pure-tone sensitivity and TEOAE results. Initial evaluation of TEOAEs from normally hearing ears showed TEOAEs present for all 265 normally hearing adult ears. Moreover, from this relatively large sample, TEOAE levels were reported for the first time as significantly larger for females vs. males and for right ears vs. left ears (Robinette, 1990a, 1992a).

Abreviaturas: EOAE = emisiones otoacústicas evocadas; TEOAE = emisiones otoacústicas evocadas por transientes; DEPOAE = emisiones otoacústicas por productos de distorsión; ABR = respuestas auditivas del tallo cerebral; AABR = respuesta auditiva automática de tallo cerebral; MS = esclerosis múltiple; NICU = unidad de cuidado intensivo neonatal.
Patients with normal hearing

Figure 1 shows means and standard deviations (SDs) for TEOAE levels for two groups of normal ears across gender and ears. The age range was 20-80 yr. The four bars on the left half of Figure 1 represent 178 highly sensitive ears with pure-tone thresholds ≤ 10 dB HL for the frequency range of 500 through 6000 Hz. The bars represent mean level in dB SPL and the vertical lines above the bars represent the SDs. The mean level for female right ears was the largest at 12.7 dB SPL whereas the male left ear TEOAEs were the smallest at 7.5 dB SPL for persons with hearing sensitivity ≤ 10 dB HL at 500 – 6000 Hz. The four bars on the right half of Figure 1 display the same level differences by gender and ears for a larger group (n = 484) of subjects with a more common definition of normal hearing (i.e., pure-tone thresholds ≤ 25 dB HL for the frequency range of 500 through 6000 Hz). As expected TEOAE levels are smaller, from 10.8 dB SPL for female right ears to 6.9 dB SPL for male left ears, but the pattern of larger TEOAE levels for females and right ears remains. Statistical analysis (ANOVA), for this group (n=484) showed that the 1.2 to 1.5 dB level difference between right and left ears was significant (f = 6.44, p = 0.018), as was the larger difference by gender of 2.4 to 2.7 dB (f = 23.29, p = 0.0001).

Such observed gender and ear differences may be related to the higher prevalence of spontaneous otoacoustic emissions (SOAEs) in female and in right ears of normal hearing subjects (Bilger et al, 1990; Martin et al, 1990; Penner et al, 1993). When present, SOAEs sum with TEOAEs resulting in more robust TEOAE levels (Kulawiec and Orlando, 1995; Prieve and Falter, 1995). The TEOAE response across frequency is not uniform for the normally hearing ears. The percentage of frequency components decreases as frequency increases. For the 178 ears with thresholds ≤ 10 dB HL, the distribution of number of responses by frequency was: 1 kHz, 100%; 2 kHz, 98%; 3 kHz, 95%; and 4 kHz, 88%. For the 484 ears with thresholds ≤ 25 dB HL, the distribution of number of responses by frequency was: 1 kHz, 96%; 2 kHz, 94%; 3 kHz, 89%; and 4 kHz, 76%. The predominance of energy was in the 1 to 2-kHz range, and absence of TEOAEs in the high frequencies does not necessarily imply high-frequency sensorineural hearing loss.

Figure 2 displays the prevalence of measurable TEOAEs from a randomly selected group of 1200 ears (age 20-80 yr), 488 ears with normal hearing sensitivity and 712 ears with sensorineural hearing loss. All had normal immittance measures (middle ear pressure +/- 100 daPa, and compliance of .3 ml or above) and no known retrocochlear disorders.

Figure 1. TEOAE levels for normally hearing adult ears across gender and ears. The four bars on the left represent 178 ears with pure-tone thresholds ≤ 10 dB HL (500-6000 Hz). The bars represent mean level in dB SPL and the vertical lines above the bars represent the SDs. The left bars (n = 178 ears) represent female right ears (FR), female left ears (FL), male right ears (MR) and male left ears (ML). The four bars on the right display the same level differences by gender and ears for the larger group (n = 484) of normally hearing ears with pure-tone thresholds ≤ 25 dB HL (500 through 6000 Hz).

Figure 2. Prevalence of measurable TEOAEs from a randomly selected group of 1200 ears from patients ranging in age from 20 to 80 years. Of the 178 ears with hearing sensitivity of ≤ 10 dB HL (500-6000 Hz), all had measurable TEOAEs. Of the 488 ears with hearing sensitivity of ≤ 25 dB HL (500-6000 Hz), 484 (99.2%) had measurable TEOAEs. Eleven percent of the 712 ears with hearing loss (i.e., hearing sensitivity ≥ 30dB HL) for all frequencies, had measurable TEOAEs and 8% of ears with hearing loss of ≥ 35 dB HL for all frequencies had measurable TEOAEs. No TEOAEs were recorded for the more than 100 ears with hearing losses ≥ 40 dB HL.
Of the 178 ears with hearing sensitivity of ≤ 10 dB HL (500-6000 Hz), all had measurable TEOAEs. Of the 488 ears with hearing sensitivity of ≤ 25 dB HL (500-6000 Hz), 484 (99.2%) had measurable TEOAEs. Only 11% of ears with hearing loss of ≥ 30 dB HL for all frequencies exhibited TEOAEs and 8% of ears with hearing loss of ≥ 35 dB HL for all frequencies had measurable TEOAEs. No TEOAEs were recorded for the more than 100 ears with hearing losses ≥ 40 dB HL. Interestingly, all ears (8%) with present TEOAEs and hearing loss of ≥ 35 dB HL were right ears, supporting the evidence that TEOAEs are more robust for right ears. While no identified retrocochlear hearing loss was present in the sample of 1200 ears, some of the ears with TEOAEs present in the presence of hearing loss > 30-35 dB HL may have retrocochlear losses that would not be indicated by such outer hair cell (OHC) measures.

Combining these data for adults with data collected by Dr. Theodore Glattke from the University of Arizona for children and young adults age 20 mo through 19 yr yields a data set for 823 normally hearing ears (≤ 20 dB HL (250-4000 Hz) (Glattke et al, 1994). Results are shown in Figures 3, 4 and 5. TEOAE mean
level stability between 9 and 11.5 dB SPL across several decades of life is displayed in Figure 3. There is no clear indication that TEOAEs decrease with age up to 80 years for individuals with pure-tone threshold sensitivity within the normal range. These data support the findings of Stover and Norton (1993), that EOAEs may be expected regardless of age when pure-tone sensitivity is within the normal range. Figure 4 displays mean TEOAE level for the first 7 decades of life across 1000 Hz bandwidths centered at 1000, 2000, 3000, 4000, and 5000 Hz. TEOAE level decreases above 3000 Hz for five of the seven age groups.

From this large sample of normally hearing ears Glattke et al (1994) reported that the TEOAE level difference between male and female ears first is apparent in the teen years (Figure 5), despite the observation by others (Burns et al, 1992) that the higher prevalence of SOAEs for females and right ears is present in infants and children as well as adults.

Slight changes in audiometric threshold may result in reduction of TEOAE level as illustrated in Figure 6. There is a slight decrement of the TEOAE level with age, so long as no audiometric threshold exceeds 20 dB HL and age is less than 70 years. However the TEOAE level is markedly attenuated for persons who are 70 years or older and whose hearing level is normal (<25 dB HL) but exceeds 10 dB HL at one or more frequencies. Spectral analysis of the TEOAE response indicated that the signal-to-noise ratio remained robust (greater than 7 dB) for 1000 Hz bandwidths centered at 1000, 2000, 3000, and 4000 Hz for all age groups (Glattke et al, 1994; Glattke and Robinette, 1997, 2002).

For normally hearing ears, the between-subject variability of EOAE level is large (up to about 30 dB) while the within-subject variability is small (usually less than ± 4 dB). Figures 7 and 8 illustrate the within-subject and between-subject variability of EOAE levels across frequency for TEOAE and distortion product otoacoustic emission (DPOAE) measures, respectively. Figure 7 represents TEOAE data from 30 adults between the ages of 20-60 yr with hearing sensitivity of 20 dB HL or better for the frequency range of 500-6000 Hz (Robinette and Glattke, 2000). The QuickScreen and low-frequency filter options were employed. Across-subject levels for the half-octaves from 1000 through 4000 Hz ranged from 3 to 37 dB above the noise floor for the 10th to 95th percentiles. It was not uncommon for subjects with thresholds ≤ 10 dB HL to have levels below the 50th percentile and subjects with thresholds ≥ 15 dB HL to have TEOAE levels above the 50th percentile. Consequently, on an individual subject basis, one could not estimate threshold sensitivity based on TEOAE level. Within-subject variability is very small. The shaded area around the 50th percentile represents the test-retest variability (95% confidence interval) of ± 3 dB per half-octave band reported by Marshall and Heller (1996).

Figure 8 summaries the magnitude range and test-retest variability from DPOAE data (Gorga et al, 1996). Between-subject levels for DPOAEs for the half-octaves from 1000 through 8000 Hz ranged from 2 to 34 dB above the noise floor for the 10th to the 95th percentiles. Test-retest variability reported by Franklin et al (1992) is shown in the grey area surrounding the 50th percentile. They reported variability to be lowest between 3000 and 6000 Hz. The test-retest 95% confidence interval was ± 3 dB for 3000 through
The clinical implications of the data represented in Figures 7 and 8 are that one should not predict pure tone thresholds from EOAE level data, but following the establishment of a threshold baseline, EOAE level changes of 4 dB within the same subject provide evidence of changes in cochlear and/or middle ear function.

Figure 9 provides an example of TEOAE frequency specificity for high frequency hearing loss (Robinette, 1990b). The composite audiogram in Figure 9A represents the mean thresholds (circles) and range (shaded area) for 35 ears of adults with normal hearing sensitivity through 3000 Hz and pure-tone thresholds > 25 dB HL for frequencies > 3000 Hz. The audiogram in Figure 9B displays the same data for 76 ears with normal thresholds (i.e., 97%, 98% and 85% of 69 ears for 1000, 1500, and 2000 Hz, respectively). TEOAEs were generally absent for frequencies with hearing loss (i.e., 33%, 21%, 4% and 0% for 2500, 3000, 3500, and 4000 Hz, respectively). Figure 9C (lower left) shows that TEOAEs were present for 36 (80%) of the 45 ears. All 36 ears displayed TEOAEs at 1000 Hz, but diminished rapidly at higher frequencies (i.e., 89%, 30%, 3%, 0% and 3% for 1500, 2000, 2500, 3000, 3500, and 4000 Hz, respectively).

Good frequency specificity of TEOAEs is demonstrated across hearing loss because TEOAEs tend to be present for frequencies corresponding to thresholds within the normal range and absent for frequencies with hearing losses of ≥ 30 dB HL (Bonfils and Uziel, 1989; Harris, 1990; Harris and Probst, 1991; Kemp et al, 1986; Probst et al, 1987). Figure 9 also demonstrates that, when hearing loss is present at some frequencies, the probability of obtaining a measurable TEOAE at any frequency is decreased. No TEOAEs were detected for 6, 9 and 20% of the ears represented by the composite audiograms A, B, and C, respectively. Together these data suggest that TEOAEs are relatively frequency specific in that TEOAEs are generally present for frequencies with normal hearing sensitivity and absent for frequencies with hearing sensitivity below normal. However, the status of the whole cochlea influences TEOAE response measures such that a response at any given frequency region is influenced by contributions distributed over a large portion of the basilar membrane (Avan et al, 1991, 1993).

Analysis of the data of Figure 9C also supports gender and ear laterality differences. The group consisted of 20 females (10 right ears and 10 left ears) and 25 males (12 right ears and 13 left ears). Of the 9 ears
One was a female (left ear), three were male right ears and five were male left ears. Therefore, in this group 100% of female right ears had TEOAEs and only 62% of male left ears had emissions.

Sensorineural hearing loss and aberrant TEOAE findings

Figure 10 is an illustration of the audiometric and TEOAE findings from a report by Robinette and Facer (1991). Though previously published, these findings represent the first patient seen at Mayo for which the results of TEOAE testing changed medical management. The 30 yr old male patient presented with a sudden left ear hearing loss with roaring tinnitus and dizziness. He reported a previous diagnosis of multiple sclerosis (MS) without symptoms of hearing loss. Audiometric results showing a profound left ear sensorineural hearing loss is displayed in Figure 10 (top left). The initial clinical impression was that the sudden hearing loss could be due to one of the following: MS, cochlear dysfunction etiology unknown, perilymph fistula, pseudohypacusis, or a space-occupying retrocochlear lesion. Because sudden profound unilateral hearing loss is not normally associated with MS (Durlovic et al, 1994), it seemed the least likely cause. Negative findings for the pure-tone Stenger test ruled out pseudohypacusis, and negative computerized tomography (CT) results ruled out a space-occupying lesion.

Additionally the findings of normal TEOAEs in the ear with the profound hearing loss ruled out a perilymph fistula or other cochlear cause. On this basis, the hearing loss was diagnosed as being due to an exacerbation of the patients MS condition. The patient was treated with a short course of steroids and 2 wk later experienced complete recovery of hearing in his left ear. Before TEOAE testing ruled out cochlear hearing loss, surgical management for a perilymph fistula was being considered. For this patient, TEOAE measurements influenced diagnosis and medical management.

Prior to the landmark article introducing the term ‘auditory neuropathy’ (Starr, et al, 1996), several reports were published regarding the paradoxical absence of ABRs and the presence of EOAES, and normal radiologic studies (Berlin et al, 1993; Gorga et al, 1995;
Gravel and Stapells 1993; Robinette, 1992b). Figure 11 illustrates the audiometric, TEOAE, and ABR results for a 3 year old male evaluated in 1994 with a severe to profound unilateral sensorineural hearing loss. As shown in figure 11A, play audiometry revealed normal hearing sensitivity for his right ear and a severe to profound hearing loss for his left ear for pure-tone stimuli at 500, 1000 and 2000 Hz. Tympanometry (upper right) was within normal limits for both ears and acoustic reflexes were present with stimuli to his right ear but absent under left ear stimulation. TEOAEs, while present for both ears, were more robust for his left ear (i.e., 17.7 dB SPL for the right ear and 26.3 dB SPL for his left ear). ABR waveforms were measured bilaterally. Results for the right ear were within normal limits, however, as shown in Figure 11B, only waves I and III were identified employing 4-channel recordings from rarefaction click levels of 85 dB nHL. The pattern of findings for his left ear are consistent with what is now labeled auditory neuropathy or auditory dys-synchrony (Berlin, et al, 2001), while right ear findings suggest normal auditory pathway function. From the case history and observation the child appeared to be functioning auditorily in an age appropriate manor.

While both adults and children with symptoms consistent with auditory neuropathy/dysynchrony have been evaluated at Mayo Clinic (Robinette 1992b; Robinette and Durrant, 1997; Robinette and Glattke, 2000; Robinette et al, 2002;), perhaps the most encouraging is the report by Shallop et al (2001) showing the postoperative findings for five children following cochlear implantation, which supported the somewhat unexpected outcome that such treatment was effective in these patients.

**EOAEs and eighth nerve tumors**

Over the past decade we have assessed the value of EOAE measures in the differential diagnosis of eighth nerve tumors and the monitoring of cochlear function to provide preoperative and postoperative information on cochlear reserve for over 150 patients. The diagnostic value of EOAEs in identifying eighth nerve tumors is limited. From a review of seven reports, Robinette and Durrant (1997) found that only 20% of 316 patients with surgically confirmed eighth nerve tumors with mild or greater hearing loss had EOAEs present to support the diagnosis of a retro-
Figure 11. Audiometric, TEOAE and ABR findings for a 3-yr old male. (A) illustrates normal right ear sensitivity and a severe to profound sensorineural hearing loss for his left ear for the test frequencies of 500-2000 Hz (top left). The TEOAE as magnitude spectrum (upper right) and as a waveform (lower portion) is displayed. (B) Four channel ABR waveforms for the patient's left ear from rarefaction click stimuli at 85 dB nHL.
Table 1. Patient groups for whom EOAEs are generally part of the auditory assessment

<table>
<thead>
<tr>
<th>Category</th>
</tr>
</thead>
<tbody>
<tr>
<td>Suspected retrocochlear hearing loss (e.g., whenever ABR testing is employed for neurodiagnostics, EOAEs should be employed for cochlear assessment)</td>
</tr>
<tr>
<td>Sudden idiopathic hearing loss</td>
</tr>
<tr>
<td>Fluctuating sensorineural hearing loss</td>
</tr>
<tr>
<td>Suspected Meniere's disease or autoimmune hearing disorders</td>
</tr>
<tr>
<td>Pre- and post-operative for patients with eighth nerve tumors</td>
</tr>
<tr>
<td>Suspected pseudohypacusis</td>
</tr>
<tr>
<td>Monitoring cochlear status for patients receiving ototoxic treatment</td>
</tr>
<tr>
<td>Cochlear Implant candidates</td>
</tr>
<tr>
<td>Infants and children, with normal/near normal immittance measures</td>
</tr>
<tr>
<td>Difficult to test populations</td>
</tr>
<tr>
<td>Newborn hearing Screening</td>
</tr>
</tbody>
</table>

Cochlear hearing loss. This lack of diagnostic precision may be attributed to cochlear hearing losses that frequently accompany eighth-nerve tumors. The cochlear loss is thought to be due to the restriction of the blood supply to the cochlea related to tumor growth (Levine et al., 1984). The measurement of EOAEs preoperatively and postoperatively, in conjunction with other tests, is helping to define the site of surgical insult when hearing is decreased or not preserved (Robinette and Durrant, 1997; Robinette et al., 1992, 1997). From a group of 11 patients with hearing preservation following acoustic neuroma removal, about half of the patients had poorer hearing postoperatively. Neural function was improved postoperatively for most patients (as measured by ABR), whereas cochlear function was decreased for most patients postoperatively (as measured by EOAEs) (Robinette and Durrant, 1997; Robinette et al., 2002). These data suggest that neural function is often improved when the auditory nerve is preserved following surgery, but subsequent hearing loss may be related more to cochlear damage from vascular compromise during surgery. Such information is helpful in the surgical quest to increase the probability of hearing preservation following surgery.

Newborn hearing screening

Prior to obtaining TEOAE instrumentation, newborns at risk, and those treated in the neonatal intensive care unit (NICU) were screened for hearing loss by diagnostic ABR. Following a local nine-month study during which newborns at risk and those treated in the NICU were tested by both TEOAE and ABR, TEOAE replaced ABR for initial screening in 1994. The selection of TEOAEs as the primary screening procedure was based on shorter test time, less cost, and comparable pass and refer rates (Robinette, 1994, 1998; Robinette and White, 1997, 1998). Due to concerns regarding the risk for auditory neuropathy in the NICU, screening procedures have evolved to a current practice (since 1999) of screening by automated ABR (AABR) in the NICU and EOAEs in the well-baby nursery. AABR testing is also employed prior to hospital discharge on well-baby newborns failing two EOAE screening procedures.

SUMMARY AND CONCLUSIONS

Since our initial experience with developing normative data on TEOAEs in 1989 and 1990, and through collaboration with internal and external colleagues, we have found EOAEs to be an important clinical tool in the evaluation of auditory function. Listed in Table 1 are several patient groups for whom the assessment of outer hair cell function via EOAEs adds valuable information in the evaluation of auditory function.
REFERENCES


