Distortion product otoacoustic emissions and clinical significance of primary stimulus levels

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Otoacoustic emissions are emitted acoustic energies from the cochlea to the external ear canal which can be recorded by a sensitive microphone. It has been observed that this acoustic energy stems from the micromechanical activity of the outer hair cells. Distortion product otoacoustic emissions can be detected in all normally hearing subjects by presenting two different frequencies and evoking a third different frequency. After a brief review about otoacoustic emissions, a study was presented which performed in 20 healthy subjects concerning different primary stimulus levels to elicit maximum distortion product otoacoustic emissions. [Journal of Turgut Özal Medical Center 2(1):22-27, 1995]
***Key Words** : Otoacoustic emission, distortion product otoacoustic emission*

Distorsiyon prodakt otoakustik emisyonlar ve primer stimulus seviyelerinin klinik önemi

Belirli şartlar altında kokleadan dış kulak yoluna doğru yayılan akustik enerjiye otoakustik emisyon denir ve hassas bir mikrofonla kaydedilebilir. Bu akustik enerjinin koklea dış saç hücrelerinin mikromekanik aktivitesinden kaynaklandığı tespit edilmiştir. Distorsiyon prodakt otoakustik emisyonlar işitmesi normal olanların tamamında elde edilebilen bir uyarılmış otoakustik emisyon çeşididir. İki farklı frekansta primer stimulusun simultane olarak kokleaya ulaştırılması ve kokleanın bu uyarıya stimuluslardan farklı frekansta verdiği cevaptır. Otoakustik emisyonlar hakkında genel bir bilgi ile beraber 20 sağlıklı kişide maksimum distorsiyon prodakt otoakustik emisyon oluşturan farklı primer stimulus seviyelerini araştırdığımız çalışmamız literatürdeki diğer çalışmalarla tartışılarak sunulmuştur. [Turgut Özal Tıp Merkezi Dergisi 2(1):22-27, 1995]
***Anahtar Kelimeler** : Otoakustik emisyon, distorsiyon prodakt otoakustik emisyon*

Under certain stimulus conditions, the cochlea emits acoustic energy that is measurable in the ear canal. This phenomenon is referred to as an otoacoustic emission (OAE)[1]. Recent observations suggest that OAEs are produced by the motile activity of the outer hair cells[2]. Mechanical energy from basilar membrane motion leads to depolarization of the outer hair cells, which, in turn, become motile, due to contractile proteins (actin, myosin, tropomyosin) they comprise. The motility increases basilar membrane motion. This basilar motion is transmitted in a retrograde fashion through the stapes footplate and middle ear and vibrates the tympanic membrane and causes emitted sounds in the external ear canal where they are picked up by a sensitive microphone. OAEs provide evidence that the cochlea is not only a passive organ due to Bekesy's traveling wave theory for hearing, but is also an active participant in the processing of acoustic signals. Movements of outer hair cells probably act to enhance the sensitivity and frequency tuning of the vibration of the cochlear partition, as a cochlear amplifier which sharpens the peak of the traveling wave.

The presence of an OAE in the absence of external acoustic stimulation is referred to as a spontaneous otoacoustic emission which can be detected in about 50% of normally hearing humans. Three forms of evoked OAEs are recognized on the basis of the types of stimuli needed to elicit them. Evoked emissions occur in response to the deliberate application of acoustic stimulation. The evoked

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emissions are distinguished by the particular type of stimulation that elicits them. The transiently evoked otoacoustic emissions are elicited by clicks or other brief stimuli. The stimulus-frequency otoacoustic emissions are evoked by a continuous, low-level pure tone. If the stimulus consists of two simultaneous tones of different frequencies (f_1 and f_2), the emitted acoustic energy occurs at a third frequency different from the original two stimulus frequencies. This phenomenon is known as a distortion product otoacoustic emission (DPOAE) which can be recorded in all normally hearing humans.

The frequency domain within which DPOAEs can be reliably detected ranges between 0.5 and 8 kHz. The crucial generation and measurement devices include two insert ear phones (Etymotic Research, ER-2), that have reasonably flat response properties, from 200 Hz to about 10 kHz, and a low noise, sensitive, miniature-microphone system (Etymotic Research, ER-10), specially designed to record otoacoustic emissions from the human ear canal. The sound probe is introduced in adults and children without any pain in the external auditory canal. The most prominent DPOAE in mammals is the distortion product emission that occurs at the frequency $2f_1$-f_2 for primary stimulus frequencies of f_1 and f_2, with $f_1<f_2$. The relative levels of the tones corresponding to f_1 and f_2, L_1 and L_2 respectively, set either equal to each other or with L_2 slightly less than L_1 (Figure 1). It is assumed that the generation of the $2f_1$-f_2 DPOAE occurs primarily at the frequency place along the cochlear partition where the f_1 and f_2 forward traveling waves maximally overlap. This particular frequency region is represented conveniently as the geometric mean frequency of the two primaries $[(f_1xf_2)^{0.5}]$. There is evidence that the f_2/f_1 ratio producing maximal DPOAE amplitude varies substantially from one subject to the other, and also as a function of the stimulus intensity levels (L_1 and L_2) and the frequency region that is evaluated[3]. DPOAEs are much lower in amplitude than the levels of the eliciting primary tones, typically 30 dB lower in small mammals and 60 dB lower in humans.

Compared to other classes of OAEs, DPOAEs are highly frequency - specific and easily controllable by varying stimulus conditions. The relation of DPOAE activity to hearing impairment is that DPOAE thresholds provide reasonably good estimates of hearing loss in cases where primary damage to outer hair cells can be safely assumed[1]. DPOAEs can be detected in persons with up to 35-50 dB behavioral threshold levels. Therefore, they are of clinical interest as a means by which cochlear activity at specific sites along the basilar membrane may be monitored.

There are two main test approaches for DPOAE. With one approach, intensity level is held constant and DPOAE data are recorded for different frequency region (usually systematically from lower to higher frequencies). This is called DPgram or DPOAE audiogram. With the other approach, frequency is held constant and stimulus intensity is varied from high to low levels. This is referred to as an input/output (I/O) or growth/response function. The DPOAE audiogram can reveal the pure tone thresholds of hearing impaired subjects at different frequency regions[5]. Both types of DPOAE measures, are useful because DPgram furnishes detailed information about the frequency pattern of emission activity, whereas the input/output function provides knowledge about the DPOAEs detection threshold, dynamic range and growth slope[6]. Detection thresholds for DPOAEs depend almost entirely on the noise floor and the sensitivity of the measuring equipment. For DPOAEs between 1 and 8 kHz, Lonsbury-Martin et al[7]. reported detection thresholds, that were 3 dB above the noise floor, at about 35 to 45 dB SPL.

A substantial number of stimulus variables affect the measured amplitude of the DPOAEs. In the process of establishing this kind of measurements as a clinical tool for the exploration of hearing disorders, it is of great importance to know the dependency of amplitude of the DPOAE (L_{DP}) at $2f_1$-f_2 to various measurement parameters. The purpose of this study was to investigate the effect of parametric variations of the relative levels of the primary tones (L_1 and L_2) on L_{DP}. The main concern was to determine the influence of small variations in intensity level in comparison to the condition where the levels of the two probe tones are equal. For this study, the level was set at 65 dB SPL.

MATERIALS AND METHODS

Data were obtained from 20 healthy normal hearing adult volunteers (8 women, 12 men) with pure-tone air conduction thresholds <10 dB HL at standard audiometric frequencies (125 Hz to 8 kHz) bilaterally. The mean age was 27 years, with a range from 21 to 37 years. All subjects had normal middle ear function based on tympanometric results and otoscopic findings. Each subject reported a negative history of ear infections, noise exposure or ototoxic

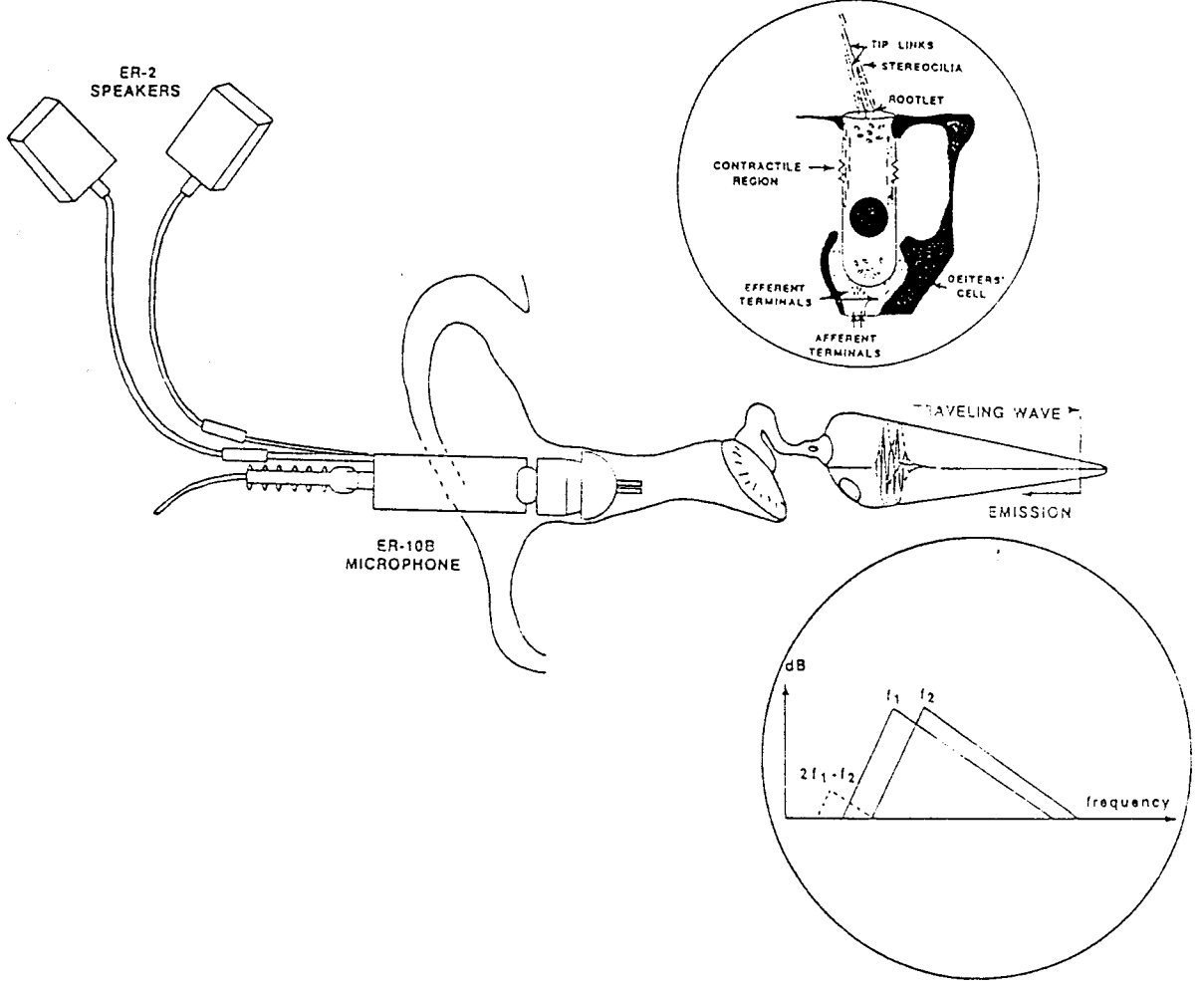

Figure 1. Basic technique for measuring distortion-product emissions. Spectral analysis of the sound field detected in the closed meatus is used to extract the cochlear response, in the form of the emissions, created, in response to acoustic stimulation by a two-tone stimulus complex, by reverse traveling waves. Sound source is in the form of two earspeakers (ER-2), while the sensor is typically a subminiature microphone (ER-10B). Inset (*top*) illustrates the probable basis of otoacoustic-emission generation in the ability of the cell body of the outer hair cell to contract and relax in response to the alterations in the electrical milieu of the cell associated with stimulus-induced deflections of the stereocilia bundle. The motility of the outer hair cell is depicted here as zig-zags along the lateral plasma membrane ("Contractile Region"). Inset (*below*), the general pattern of the traveling waves, associated with the f_1,f_2, and DPOAE, are depicted. The area of the basilar membrane that makes the primary contribution to the generation of the $2f_1$-f_2 DPOAE is in the region of the maximum overlap of the f_1 and f_2 traveling waves, that is, near the geometric mean of the two primaries.

drug administration. The condition of the ears were checked prior to each test session. During OAE measurements the subjects were seated in a comfortable chair placed in a double walled sound-attenuated test booth, and instructed to remain quiet and relaxed and not to move. Since there is a slight OAE difference between right and left ear, only right ears of the subjects were tested. Each test session lasted approximately 25 minutes including otoscopic examination, tympanometry, pure-tone audiometry and DPOAE testing. DPOAEs were measured using the M 1.8 software from the Virtual Otoacoustic Emissions Test Instrument Model 330 which was connected to a Macintosh color classic. The frequencies of the two primary tones were set so that the f_2/f_1 ratio equaled 1.21 and $2f_1$-f_2 occurred at the standard audiometric frequencies from 0.5 kHz to 8 kHz. Pure tone audiometry and tympanometry for these subjects were performed using Virtual 310 device and Amplaid 720, respectively. Four primary stimulus level conditions, condition-A (L_1= 65 dB, L_2= 65 dB), condition-B (L_1= 65 dB, L_2= 60 dB), condition-C (L_1=65 dB, L_2= 55 dB) and condition-D (L_1= 65 dB, L_2= 50 dB) were set by keeping L_1 constant at 65 dB and changing L2 levels to discover the highest amplitude of the emissions (Table I).

Table I. Primary stimuli condition levels

	Primary Stimulus L_1	Primary Stimulus L_2
Condition-A	65 dB	65 dB
Condition-B	65 dB	60 dB
Condition-C	65 dB	55 dB
Condition-D	65 dB	50 dB

RESULTS

The emitted distortion products were discernible above the noise floor for all subjects in all test conditions for frequencies above 0.6 kHz. A dip above the noise floor between 2.5 and 5 kHz was observed (Figure 2). Plots were drawn using Cricket-graph and checked statistically using Statview-2 software package and ANOVA testing. Although there was no statisticaly significant difference among the DPOAE levels due for the 4 stimulus level conditions, condition A (L_1=65 dB, L_2=65 dB) and C (L_1=65 dB, L_2= 55 dB) shoved a tendency to be slightly higher in amplitude than the other two conditions.

DISCUSSION

OAEs may provide unique advantages as a monitor of cochlear function when compared to the pure-tone audiogram. First, an objective response can be measured non-invasively with only passive cooperation of the subjects required. The measurements are time-efficient and straightforward when performed using modern instrumentation. The high sensitivity and specificity of OAE to the status of the cochlea represent an important advantage. There are indications that even subtle changes in cochlear function that do not result in changes in the pure-tone audiogram can show significant changes in OAEs[8].

DPOAEs may have important clinical applications for newborn screening, hearing loss due to ototoxicity, noise and acoustic trauma, and for malingerers. It can be used to detect the recovery from serous otitis media, the improvement of hearing due to middle ear surgery, to detect the temporary decreased thresholds with glycerol administration in Meniere's disease, to distinguish between sensorial and neural hearing loss, to discover the cochlear involvement in retrocochlear diseases, such as acoustic neuroma, and to study efferent cochlear innervation[6].

Hauser and Probst[9] suggested that maximum L_{DP} will occur when the level of f_2 (L_2) is around 10 dB lower than the level of f_1 (L_1). These authors measured the L_{DP} in three frequency regions: 1, 2 and 4 kHz obtained changing f_2/f_1 ratios to 1.25, 1.23 and 1.21 respectively. Gaskill and Brown[10] presented data which suggested that the maximal L_{DP} occurs when L_2 is less than L_1, with a representative value of L_1-L_2 of around 15 dB. As a complicating factor that measurements by Gaskill and Brown were made at a lower overall levels (40-45 dB SPL) than the 65 dB SPL used in the present study.

Rasmussen et al[11]. used L_1 level of 75 dB and either equal and lower L_2 levels to find out highest DPOAE levels. This intensity level is too high to evaluate outer hair cell functions, because it was shown that in experimental animals DPOAEs elicited by stimulation intensities above 66 dB SPL mainly explore passive mechanical properties of the cochlea[12]. Although it remains unclear whether there is a similar distinction between high and low level DPOAEs in humans, recording DPOAEs in response to a 75 dB SPL stimulation intensity used in Rasmussen et al's study may not permit one to investigate active properties within the cochlea.

Since it was certainly shown that negative L_1-L_2 values (L_1<L_2) result in less obvious L_{DP}

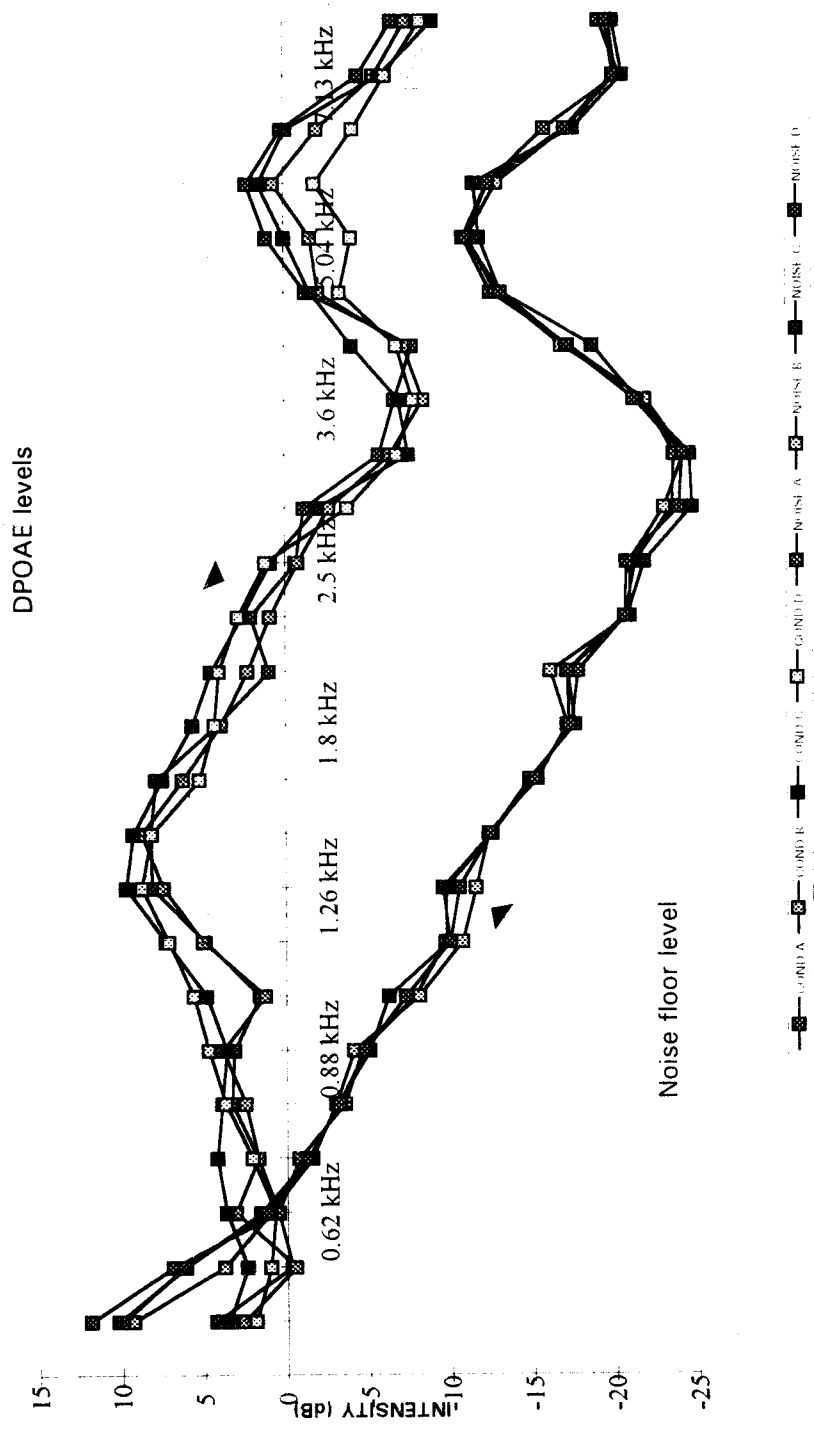

Figure 2. DPOAE and noise floor levels for four different primary stimulus conditions

levels, we used only positive L_1-L_2 values (L_1>L_2) in this study. Gaskill and Brown[10] concluded that the L_{DP} was more dependent on L_1 than on L_2. Rasmussen et al[11]. found that the rate of reduction of L_{DP} in relation to negative values of L_1-L_2 was substantially greater at the higher frequencies. Therefore, if L_2 is greater than L_1, the distortion products in the basal region of the cochlear partition are more prone to be reduced than are those generated in the apical region of the cochlea.

When the potential clinical use of DPOAE measurement is evaluated, not only test parameters are important, but also individual differences. Individual differences in L_{DP} may be associated with patient-related factors such as the circadian rhythms and menstrual cycles[13], anomalies in middle ear function[14] and interaction with other types of OAEs[1].

Lonsbury-Martin et al[6]. reported that many of the ears from their samples displayed a dip of the DPOAE audiogram in the 2-4 kHz region. Our observation for that dip was between 2.5 and 5 kHz frequencies. The dip was not related to any hearing impairment in this region, because emission levels were already above the noise floor in these frequencies. It could be explained on the basis of partial cancellation or enhancement of DPOAE signals arising from multiple sources in the cochlea[15].

Although any statistically significant superiority was not been found among primary stimulus conditions, condition A (L_1=65 dB, L_2=65 dB) and C (L_1=65 dB, L_2=55 dB) appeared to elicit slightly higher DPOAEs. The overall stimulus level used in this study has chosen to be in accordance with physiology of the organ of Corti without allowing mechanical properties of the cochlea to get involved in the responses. We have been using L_1=65 dB and L_2=65 dB and f_2/f_1=1.21 in our daily clinical measurements.

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