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Automated Assessment of Hearing Threshold in Neonates by Means of Extrapolated DPOAE I/O-Functions

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Content

Abbreviations

ABR	auditory brainstem response
A/D	analogue/digital converter
AP	action potential
CH, MP, MV, NB,NC	subject initials
D/A	digital/analogue converter
DPOAE	distortion product otoacoustic emission
f1, f2	frequencies of the primary tones
HL	hearing level
IHC	inner hair cell
I/O-function	input/output-function
JCIH	Joint Committee on Infant Hearing
Ldp	DPOAE level
L1, L2	primary tone levels
OAE	otoacoustic emission
OHC	outer hair cell
p	probability of error
PC	personal computer
PCA	postconceptional age
pdp	distortion product sound pressure
r^2	correlation coefficient / stability index
s	slope of the DPOAE I/O-function
SNR	signal-to-noise ratio
SPL	sound pressure level
TEOAE	transiently evoked otoacoustic emission
UNHS	Univeral Newborn Hearing Screening
WHO	World Health Organization

1. Introduction

Hearing loss is the most frequently occurring birth defect and influences the development of every child strongly. The far-reaching consequences of a permanent hearing impairment may be underestimated by the general public. If not detected at an early stage it will impede speech, linguistic competence, literacy and cognitive development. The primary cause of hearing impairment is dysfunction of the cochlea, whereas hearing loss due to neural disorders is seen very rarely (Finckh-Krämer et. al, 2000).

At birth the neural pathways are not completely developed. Synaptogenesis depends on acoustic stimulation, otherwise synapses will perish. Just a few months of acoustic stimulus reduction during early infancy leads to irreversible damage. Subsequent use of hearing aids or cochlear implants hardly adjusts this defect. In contrast, early intervention can improve the child's quality of life significantly (Joint Committee on Infant Hearing, 2000). The child's family can also benefit from early intervention, since a hearing handicap is a hard stroke of fate that influences the long-term life planning of the entire family. Therefore, Universal Newborn Hearing Screening (UNHS) is a reasonable measure for neonates. A lot has been done recently to propagate this kind of preventive medical examination, also in German-speaking countries (Welzl-Müller, 2001; Plinkert et al., 2001).

Since hearing impairment in neonates is neither obvious nor easy to diagnose through observation or subjective tests (e.g. response to presented sounds), objective testing methods are necessary. In Europe 0.8 – 2.3 babies in one thousand have a congenital hearing loss (Welzl-Müller, 1998); thus, such measurements are of great interest. Reliable methods for the assessment of possible hearing disorders in newborns are measurement of otoacoustic emissions (OAEs) and auditory brainstem response (ABR). OAEs are sound emissions from the inner ear that are detectable by a very sensitive microphone placed in the outer ear canal. ABRs are neural potentials of the brainstem to sounds presented to the ear; they are deducible through electrodes attached to the surface of the head.

Evoked OAEs can be separated into transiently evoked otoacoustic emissions (TEOAEs) that are evoked by a click stimulus and distortion product otoacoustic emissions (DPOAEs). The latter appear when two tones are delivered to the ear due to the nonlinear sound processing of cochlear micromechanics. The first are more commonly used in clinics, especially in pedaudiology for hearing screening, and they provide a "pass" or a "fail" result. In case of a "fail" result no TEOAEs could be measured and the newborn has to undergo time-consuming and costly audiological testing. The advantage of DPOAE testing is that emissions are

measurable even if the hearing loss reaches 50 dB HL (Boege and Janssen, 2002). In contrast, TEOAEs disappear at a slight hearing loss of 20-30 dB HL (Janssen, 1996).
In this study DPOAEs were measured in neonates to get frequency-specific and quantitative information on hearing loss in the early postnatal period.

1.1. Origin and physiological aspects of distortion product otoacoustic emissions (DPOAEs)

Sound to the inner ear has to pass the ear canal, ear drum and ossicular chain before reaching the oval window, which provides access to the two and a half times winded cochlea. Three canals containing lymph (Fig. 1.1) are stacked on top of each other: scala vestibuli, scala media and scala tympani. Scala vestibuli and tympani are connected at the cochlear apex. The scala media contains the Organ of Corti and has a potential of +85 mV in relation to the extracellular space. Its lymph has a high K+-concentration, whereas the lymph of the scala tympani and vestibuli has a high Na+-concentration. The different concentrations are maintained through active ionic transport and passive diffusion. The Organ of Corti (Fig. 1.2) lies upon the basilar membrane; it has three rows of outer hair cells (OHCs) and one of inner hair cells (IHCs), each with stereocilia. The section shown in Fig. 1.2 could appear up to 3200 times in the cochlear duct. Only the stereocilia of the OHCs (up to 150 per cell, arranged like a “w”) are linked with the tectorial membrane. The voltage inside the OHC is –70 mV in contrast to –45 mV in the IHC; therefore, in comparison to endolymph, a voltage difference of 155 mV and 130 mV, respectively, exists. This difference is important for sensory transduction.

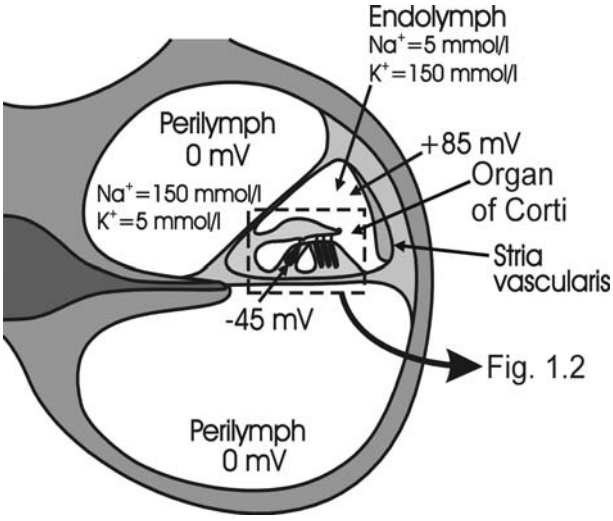

Figure 1.1. *Section of the basal turn of the cochlea (schematic).*
Shown are the different ionic concentrations of the perilymph in the scala vestibuli/tympani and the endolymph in the scala media. Between IHCs (-45 mV) and endolymph (+85 mV) exists a potential of 130 mV (from Janssen, 2000a).

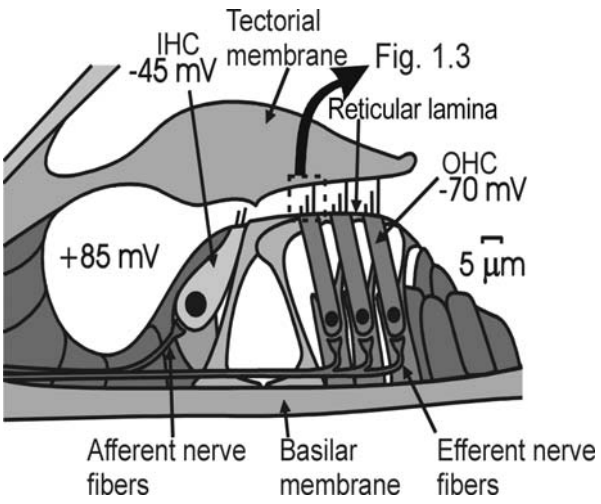

Figure 1.2. *Section of the Organ of Corti of the basal cochlear duct (schematic).*
The Organ of Corti with the inner and OHCs lies upon the basilar membrane. Both hair cell types have stereocilia but only those of the OHCs are linked with the tectorial membrane. The different potentials of IHC, OHC and endolymph are important for the sensory transduction (from Janssen, 2000a).

The basilar membrane and the Organ of Corti are important for sound processing in the cochlea. The sound pressure generates through the tympanic membrane and the stapes a pressure gradient along the basilar membrane resulting in a traveling wave. Its wavelength decreases towards the apical region of the cochlea due to decreasing stiffness of the basilar membrane. The position of maximum displacement of the basilar membrane depends on frequency. High frequencies have their maximum displacement in the basal region, low frequencies in the apical region. The higher the sound level, the higher the displacement, and the more hair cells and nerve fibres are stimulated. These mechanisms are responsible for the sensation of loudness.

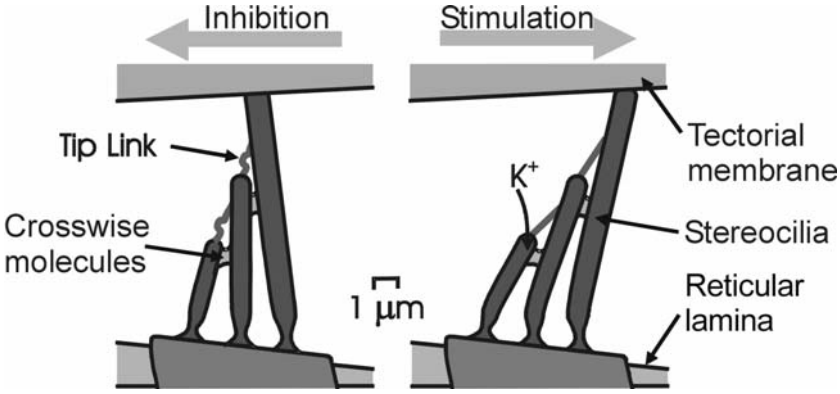

Figure 1.3. *Postulated stereocilia movement and opening of the ionic canals by acoustical stimulation.*
An acoustic stimulus causes a pressure gradient along the basilar membrane resulting in a traveling wave. Through this traveling wave the stereocilia are bent between the tectorial membrane and the reticular lamina. The result is a strain on the tip links that causes the ionic canals to open at the tips of the stereocilia (stimulation). During inhibition the stereocilia are deflected in the opposite direction, and the ionic canals are closed (from Janssen, 2000a).

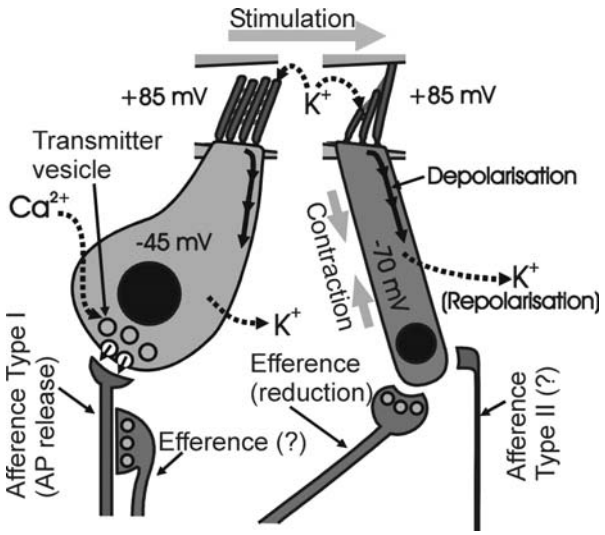

Figure 1.4. *Sensory transduction.*
Acoustic stimulation leads (after the processes described before) to an influx of potassium ions into the cytoplasm of the hair cell. This causes membrane depolarization to occur, which leads to a stream of calcium ions from the perilymph into the IHC. The result is a release of neurotransmitters into the synaptical gap and, finally, an action potential in the afferent nerve fibre. The contraction of the OHC causes an amplified oscillation of the basilar membrane and, therefore, a higher stimulus for the IHC (from Janssen, 2000a).

The two types of hair cells transform sound into electricity when they are bent and deflected between the tectorial membrane and the reticular lamina. Further on, the OHCs are important because they work as traveling wave amplifiers in order to enhance sensitivity and frequency selectivity of cochlear mechanics. Thus, OHCs amplify the stimulation of the IHCs responsible for the afferent transmission. Figures 1.3 and 1.4. explain these processes in detail. In the rarefaction phase of the stimulus, the stereocilia are bent outwards due to the connection with the tectorial membrane. The result is a strain on the tip links that causes the opening of the ionic canals at the tips of the stereocilia (stimulation). In the condensation phase of the stimulus, the stereocilia are deflected in the opposite direction and the ionic canals are closed (inhibition). When the stereocilia are bent outwards (Fig. 1.4) and the ionic canals are open, this leads to an influx of K+-ions from the endolymph into the cytoplasm of the hair cell. The difference in voltage results in a contraction of the OHC leading to an amplified oscillation of the basilar membrane and a higher stimulus for the IHC. The change of potential causes membrane depolarization in the IHC, which leads to a stream of calcium ions emanating from the perilymph into the cell. Due to the calcium trigger, there is a release of neurotransmitters into the synaptical gap. A generator potential is built up, which triggers an action potential in the afferent nerve fibre. Thus, the IHC is a mechanic-electrical transducer.

With intact OHCs the displacement of the basilar membrane is high and narrow, but with the loss of OHCs, it is flat and wide. At low sound pressure levels a nonlinear growth of the basilar membrane velocity occurs in the intact cochlea (dynamic compression) and leads to a high selectivity. At high sound pressure levels the sound pressure levels and the basilar membrane velocity behave linearly. When OHCs are damaged, a more linear relationship

between the sound pressure level and basilar membrane velocity occurs over the whole level range. As a consequence, hearing forfeits a part of its sensitivity and frequency selectivity (Janssen, 2000a).

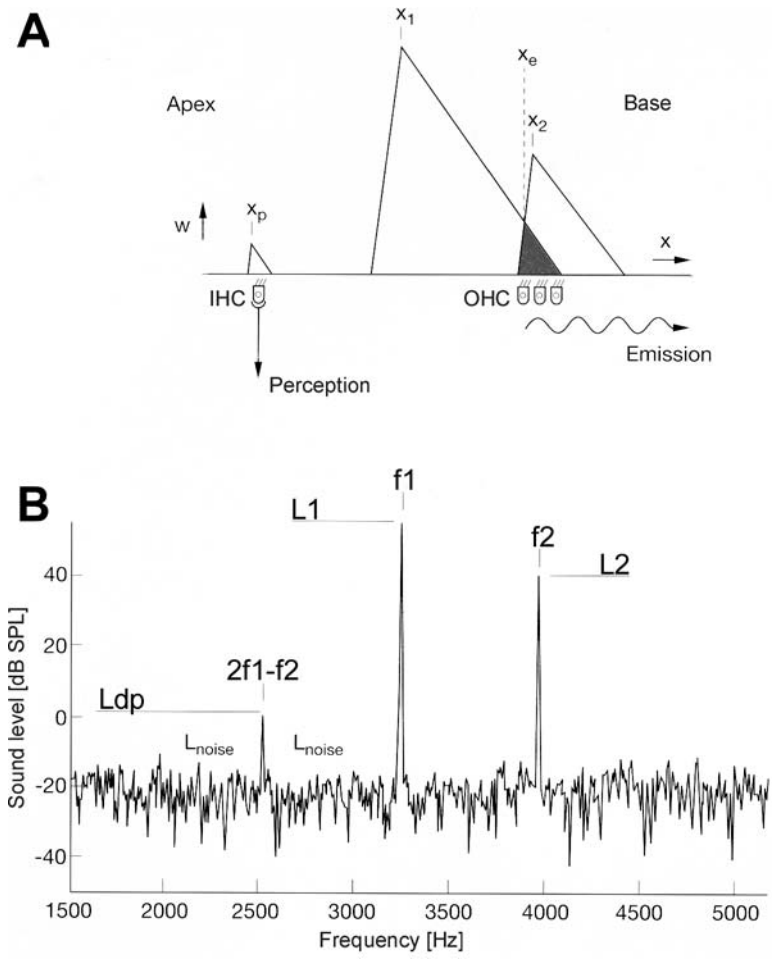

Figure 1.5. *Generation of DPOAEs (from Janssen, 1996).*

(A) The two primary tones of frequencies f1 and f2 and levels L1 and L2 generate traveling waves on the basilar membrane with maxima at x1 and x2. An oscillation with the frequency 2f1 – f2 is elicited in the overlapping region of the primary tone traveling waves (black triangle). This oscillation travels towards the cochlea base and the outer ear, where it can be measured as DPOAE with the frequency 2f1 – f2.

(B) The spectrum shows the primary tones with the levels L1 and L2 as lines at the frequencies f1 and f2, the measured DPOAEs with the sound level Ldp.

Distortion product otoacoustic emissions are evoked by stimulation with two primary tones of frequencies f1 and f2 and levels L1 and L2. They arise from the compressive nonlinearity in cochlear mechanics as described above. The primary tones elicit two traveling waves (Fig. 1.5A) that perform their maximum oscillation at x1 and x2. Due to the steeper slope of the traveling wave towards the cochlear apex, the side of maximum interaction is near f2. Therefore, the OHCs near the f2 place x2 mainly contribute to the generation of DPOAEs. Through the nonlinear mechanisms, an oscillation with the frequency 2f1 – f2 is elicited (Fig.

1.5B). It has the highest amplitude at xe, which is very close to x2. Thus, the primary tone with the higher frequency is dominating DPOAE generation. The oscillation travels towards the cochlea base and the outer ear, where it can be measured by a very sensitive microphone. The spectrum shows the primary tones with levels L1 and L2 as lines at frequencies f1 and f2. The DPOAEs with the sound level Ldp occur as a line at the frequency 2f1 – f2. The subjective perception of sound comes from the IHC at xp, where the traveling wave generated by the 2f1 – f2 signal reaches its peak (Fig. 1.5A).

By changing the frequencies of the primary tones, different portions of the cochlea can be stimulated. Thus, a frequency-specific assessment of OHC impairment at distinct sides in the cochlea can be achieved. As already mentioned above, the number of OHCs contributing to DPOAE generation depends on the size of the overlapping region. This overlap is determined by the level and the frequency ratio of the primary tones.

1.2. Universal Newborn Hearing Screening (UNHS)

1.2.1. General requirements for screening

"Screening tests sort out apparently well persons who probably have a disease from those who probably do not" (Wilson and Jungner, WHO, 1968). Therefore, the presence or absence of a disease can be detected before it becomes obvious or has any severe consequences. However, there can never be a 100% guarantee that the screening result reflects the reality. In the context of screening for hearing impairment, sensitivity is the proportion of hearing-impaired individuals who fail the test (positive result) and specificity is the proportion of non-diseased subjects with a negative result out of all subjects in the population without the disease. Both parameters should be as high as possible, whereas improving one factor is always at the expense of the other. The false positive rate (i.e., when a well subject tests positive for disease) must be kept down, since it leads to anxiety and uncertainty among those concerned and results in costly follow-up procedures.

Screening should only be performed for diseases that pose an important health problem or that have a significant prevalence. This contributes to a reasonable cost-benefit calculation. The measurement and the data analysis should be performed automatically, so there is no need for expensive training of employees or for qualified personal to apply the method. While it should be obvious that patients benefit from screening, especially in case of a positive test result, screening methods must be acceptable to the population. If the screening involves an elaborate examinination combined with any inconvenience or even pain, compliance will not

be very satisfying. To optimize the benefit of screening, facilities for subsequent treatment should be available and defined in advance. Moreover, the population should have access to intelligible information about the topic. UNHS fulfills all of these criteria.

1.2.2. Realization of UNHS

During the first months of life hearing-impaired children produce infant sounds like well-hearing children, so it takes some time until the suspicion of hearing impairment arises. Statistics show that this period is still too long; in Germany, moderate hearing loss is diagnosed at a mean age of 4.4 years, severe hearing loss at a mean age of 2.5 years, and profound hearing loss at 1.9 years (Finkh-Krämer et al., 1998). As already mentioned, congenital hearing loss occurs in 0.8 - 2.3 babies in one thousand. Children with risk factors like premature birth, perinatal hypoxemia, pre- or postnatal infections, hearing-impaired relatives, etc. have even higher rates. Nevertheless, targeted screening of infants who only have high-risk factors for hearing loss is not advisable (Welzl-Mueller et al., 2001). The cause of the hearing loss often remains unknown.

In cases of neonatal hearing dysfunction, it is recommended that intervention starts before six months of age (JCIH, 2000). This could be achieved by applying UNHS during the early postnatal period, ideally during hospitalization, since most births take place in hospitals and parental compliance is optimally acquired during that period. In case of a failed screening response, a second screening should be performed before discharge, since parents who are asked to schedule a later medical evaluation often forget or ignore the appointment. Besides that, repeated screening helps minimize the false positive rate.

Fortunately, today's screening devices for hearing demonstrate good sensitivity and specificity (Baumann and Schorn, 2001), so a reliable diagnosis can be achieved in most cases.

In the UNHS system, measurement and data analysis are performed automatically, so the test can be done by the attending nurse. Hand-held systems permit bedside use during the early postnatal period. The measurement is noninvasive and can be easily performed while the infant is sleeping.

TEOAE testing is a more widespread screening method since it is quicker to perform and easier to handle than ABR testing. However, only ABR testing can detect defects in the neural pathway in the three different types of hearing loss, i.e., conductive, cochlear and neural. Nonetheless, neural hearing loss is rarely seen and occurs especially in neonates in intensive care units.

In case of a “fail” outcome of hearing screening, an extensive battery of audiologic tests (OAEs, ABRs, tympanometry, stapedius reflex threshold and behavioral responses to sounds) helps confirm the hearing loss and specify its degree and type. The intervention options can comply with these results and facilitate the optimal fitting of a hearing aid. It is important to provide the parents with as much information and supplies as possible so they can better understand and anticipate the infant’s needs.

1.3. Aim of the study

Hearing disorders in infants are a significant problem since subjective testing methods are not possible and most of the affected children do not appear ill. Thus, the far-reaching consequences of hearing loss can be serious, especially when compared with the development of a deaf child in whom diagnosis and intervention were made at an early stage. With the assistance of hearing aids or cochlear implants, social deprivation can be prevented. In particular, it is necessary to avoid the additional damage and escalating costs that result from a delayed diagnosis.

The aim of this study was to examine the feasibility of estimating hearing thresholds in neonates by means of extrapolated DPOAE I/O-functions using a specially developed in-house method (see section 2.3; Boege and Janssen, 2002). Prior to this study, the method was applied to adults only. In comparison with conventional hearing screening methods, the new method provides frequency-specific and quantitative information on hearing capability.

A follow-up study was required to investigate the further question of whether the method is capable of detecting transitory sound conduction disturbances in neonates, since it is known that residual amniotic fluid present during the first days after birth is responsible for false positive screening results.

As the new method is able to assess hearing loss quantitatively, it could fill the gap between conventional hearing screening methods and audiological diagnostic methods.

2. Methods

2.1. Subjects

In this study of a pediatric population, 134 ears (62 left ears, 72 right ears) of 103 neonates (55 females, 48 males) were tested. The age of the subjects varied from 27 hours to 10 days (mean age = 3.2 days). Postconceptional age (PCA) ranged between 35 weeks and 4 days and 41 weeks and 3 days. In the gynecological unit whrere the study was performed, prematurity was defined as birth before 36 weeks of PCA. Therefore, we presumed maturity for the entire neonatal group since only one baby was born three days before the 36-week time point was reached. There were no further selection criteria for participation in the project. The measurement was performed in a quiet room of the neonatal care unit in the gynecological hospital of the Technical University Munich during spontaneous sleep. Agreement of the parents was obtained prior to testing. Thirteen of the 103 neonates were tested again at least four weeks later at home. The measurement was performed after feeding during natural sleep, even if this required a long waiting period. A quiet room was chosen, and the baby was lying in its cradle.

For collecting normative data, 26 ears of 14 adults (7 females, 7 males, mean age = 24.7 years) were tested in a noise insulation cabin while seated in a comfortable recliner. The same measuring device used on the neonates was applied, and the adult subjects were asked to sit quietly during data collection. Prior to testing, it was assured that hearing loss in a subjective hearing test did not exceed 15 dB hearing level (HL) in the audiogram for frequencies ranging from 125 to 8000 Hz. In that test, subjects had to press a button as long as they could perceive tones at different frequencies presented by an audiological assistant.

2.2. Stimulus paradigm and technical aspects

The measurement of DPOAEs was performed using the “DP2000” system (Starkey, USA) on a Windows-based notebook (Pentium 133 MHz). Two primary tones with the frequencies f1 and f2 and the sound pressure levels L1 and L2 were generated by the ear probe and delivered to the inner ear by two speakers (Fig. 2.1). As already described in section 1.1, the sound reaches the inner ear via the tympanic membrane, incus, malleus and stapes. The primary tones elicit two traveling waves on the basilar membrane and produce a contraction of the OHCs. The OHCs produce intermodulation vibrations, which propagate retrograde to the outer ear canal where they can be measured by a very sensitive microphone.

Twelve f2-frequencies (1, 1.5, 2, 2.5, 3, 3.5, 4, 4.5, 5, 6, 7 and 8 kHz) were applied. The f2/f1 ratio was constantly held at 1.2. The DPOAE I/O-functions were recorded at ten different primary tone levels. A special setting for the primary tone level was used, which accounts for the difference in compresssion of the two primaries at the DPOAE generation side at f2 (Janssen et al., 1995; Kummer et al., 2000; Boege and Janssen, 2002). Due to the increasing differences among the primary tone levels with decreasing stimulus level (L1 = 0.4L2 + 39 dB SPL), a special paradigm named "Pegelschere" (scissor paradigm) was applied (Fig. 2.2b). DPOAEs were only accepted if the signal-to-noise ratio (SNR) was at least 6 dB. The maximum tone level was 65 dB to avoid artificial distortion produced by the probe.

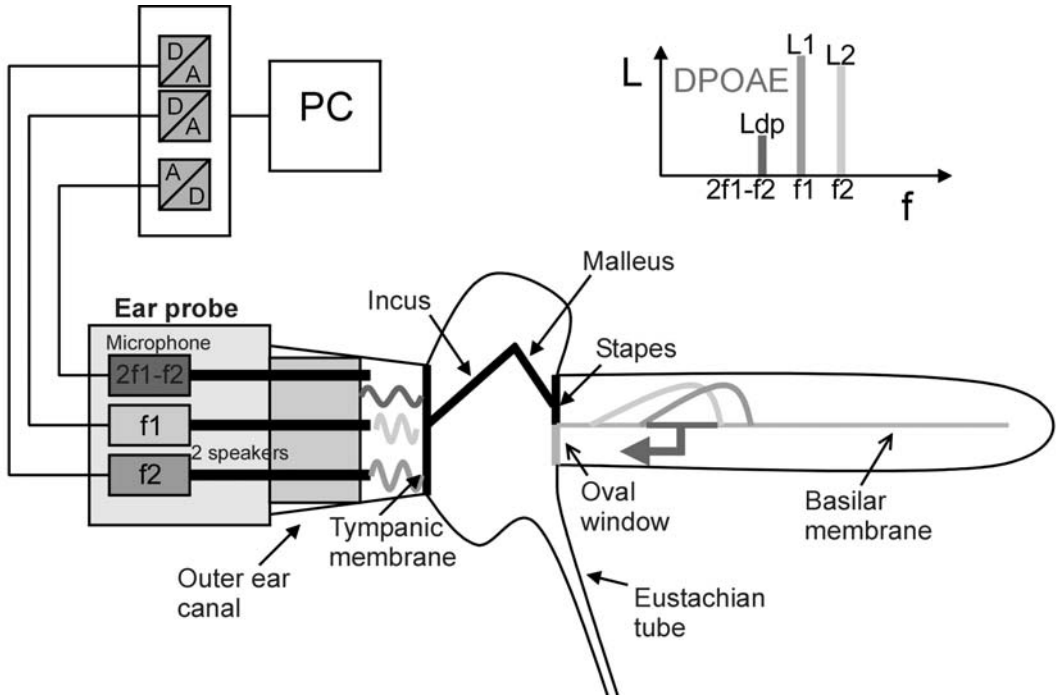

Figure 2.1. *DPOAE measurement system.*
An ear probe generates two primary tones (with frequencies f1 and f2 and sound pressure levels L1 and L2), which are delivered to the inner ear by two speakers. The two traveling waves elicited on the basilar membrane cause an oscillation with the frequency 2f1 – f2 via the OHC. This oscillation travels towards the cochlear base and the outer ear where it can be measured by a very sensitive microphone (from Janssen, personal communication).

The sound pressure in the ear-canal was measured using an Etymotic ER-10C microphone system. For the neonates, the smallest ear tips available (ER-10C-03) were adequate to seal the ear canal in most cases; when these were not sufficient, the larger ER-10C-04 ear tips were used.

Calibration of the sound pressure in the ear canal to ensure proper probe placement was performed automatically. The necessary software was developed in the in-house laboratory.

One DPOAE measurement takes four seconds to obtain, which means eight minutes of measurement are required for twelve frequencies and ten different sound pressure levels.

2.3. Calculation of the slope of the DPOAE I/O-function

In subjects with normal hearing the DPOAE I/O-functions saturate at high primary tone levels, whereas they have a steep run at low primary tone levels. In ears with cochlear hearing loss, a steep run is found in the whole primary tone level range (Janssen et al., 1998). Thus, the slope differs most in the ranage of high primary tone levels when comparing results from ears with normal hearing and ears with cochlear impaired hearing. For assessing compression loss of OHC amplifiers, the slope of the DPOAE I/O-functions is calculated in an L2 range between 40 and 60 dB. For providing a quick view of place-specific compression loss in the cochlea, slope is calculated for the different f2-frequencies and plotted as slope profile (s(f2)).

2.4. Estimation of hearing threshold by means of extrapolated DPOAE I/O-functions

In the present study estimation of hearing threshold was performed following the method of Boege and Janssen (2002). The method is as follows: DPOAE I/O-functions were recorded in 30 normal hearing ears and in 119 ears with sensorineural hearing loss. The primary tones used to evoke DPOAEs are important in determining the amplitude of the emission recorded in the ear canal. It was found that for yielding maximum DPOAE levels with decreasing primary tone levels, an increasing primary tone level separation L1 – L2 is essential (Janssen et al., 1995; Kummer et al., 2000). The most prominent DPOAE in the human ear is generated at primary tone levels according to the equation L1 = 0.4L2 + 39 dB SPL at f2-frequencies between 1 and 8 kHz and L2 levels between 20 and 65 dB SPL (Fig. 2.2A, B) and at 2f1 – f2.
As already mentioned, the size of the overlapping region changes when either the level or the frequency ratio of the primary tones is altered; see section 1.1 and Fig. 1.5. At L1 = L2 = 40 dB and f2/f1 = 1.2 no emissions can be elicited since there is no overlap; but also at low frequency ratios, like f2/f1 = 1.1, and at low primary tone levels, no emissions can be measured, even though there is a small region of overlap. This fact is a result of the filtering function of the tectorial membrane (Brown et al., 1992). Therefore, a lower L2 level has to be chosen at low stimulus levels, for example, L1 = 55 dB and L2 = 40 dB. It is especially due to the different compressions of the two primaries at f2, that the low frequency primary tone level L1 has to be changed by a smaller step than the high frequency primary tone level L2 (Kummer et al. 2000; Boege and Janssen, 2002).

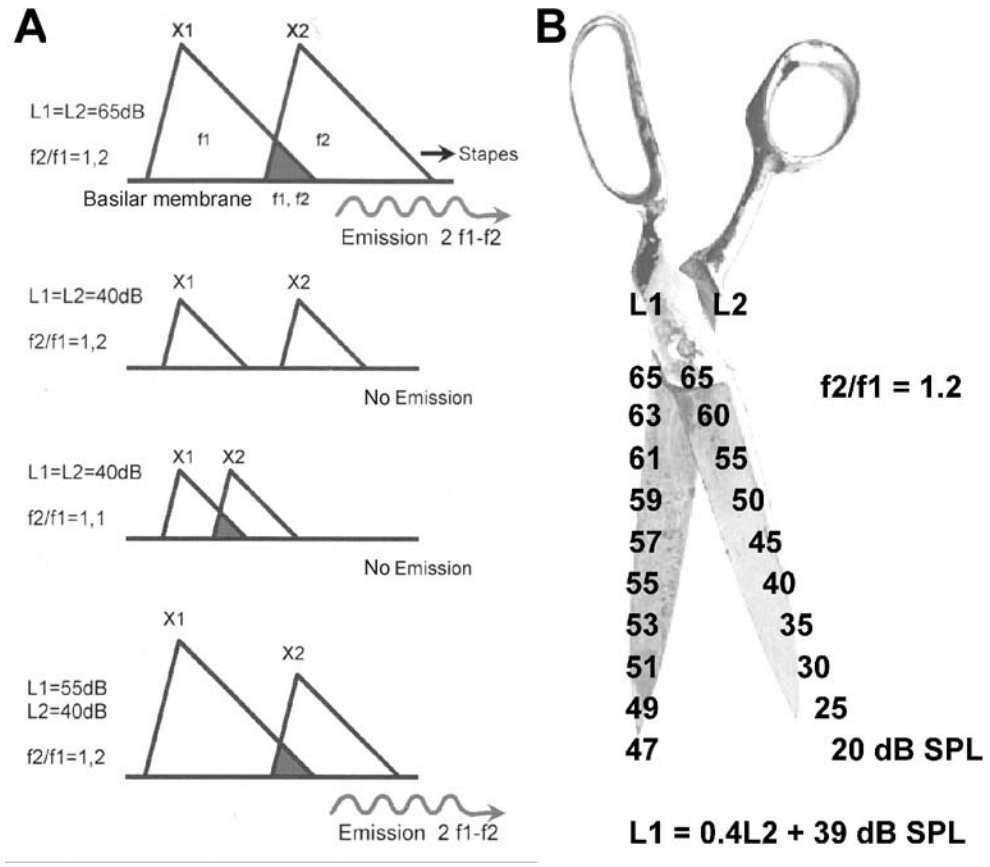

Figure 2.2. *Influence of the frequency ratio f2/f1 and levels L1 and L2 of the primary tones on DPOAE generation.*

(A) The shaded area represents the overlapping region of the traveling waves of the primary tone with maxima at x1 and x2. The size of the overlapping region depends on the level and the frequency ratio of the primary tones. The overlapping region disappears when decreasing the primary tone level under the L1 = L2 condition (for example L1 = L2 = 40 dB, f2/f1 = 1.2; from Janssen, 2000b).

(B) The optimal level ratio is therefore a lower L2 at low primary tone levels (from Janssen et al., 1995; Kummer et al., 2000).

It was shown that the 2f1 – f2 distortion product pressure pdp is a linear function of the primary tone level L2. Therefore, the DPOAE threshold can easily be derived from the semi-log DPOAE I/O-function by extrapolation using linear regression analysis (Fig. 2.3). The linear fit to the data proves the logarithmic dependency of the distortion product sound pressure pdp on the sound pressure of the f2 primary tone (upper panel: semi-logarithmic scale). The correlation coefficient r^2 is a measure for the accuracy of the linear fit. The point of intersection of the regression line with the L2-axes serves as an estimate for the DPOAE threshold level. It is equivalent to the primary tone level L2, which would give a zero DPOAE sound pressure pdp. In the lower panel, the same data is plotted as DPOAE level Ldp as a function of L2 in log-log scale. At low primary tone levels, emissions would disappear in the noise floor (open triangles). Therefore, an extrapolation of the DPOAE I/O-function is made and a point of intersection is obtained for the estimated hearing threshold. Through the

intersection with the abscissa, a value in dB SPL is received. This value is transformed into dB HL using a conversion table (see section 7.1) generated in the laboratory in advance. Only values lying between –10 and 50 dB HL are accepted because reliable DPOAEs at hearing thresholds of more than 50 dB HL are not measurable and a hearing threshold better than –10 dB would seem unrealistic.

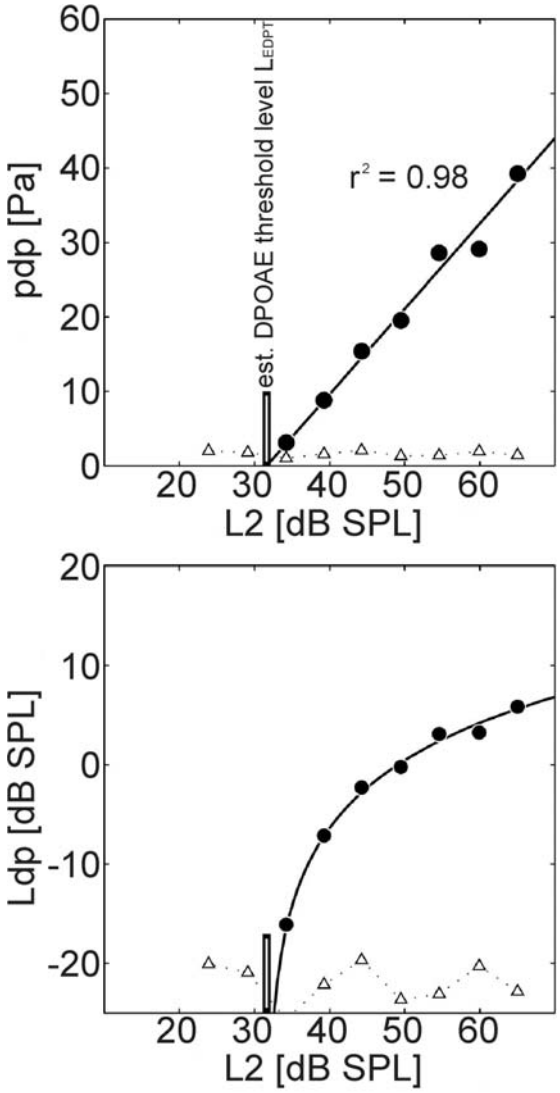

Figure 2.3. *Estimation of DPOAE threshold level.*
In the upper panel the DPOAE sound pressure pdp is plotted as a function of the primary tone level L2 (semi-logarithmic scale).
In the lower panel the same data is plotted as DPOAE level Ldp as a function of L2 but in log-log scale.
Filled circles represent the measured DPOAE level and open triangles the noise floor. The solid line shows the fitted linear function in both scales with a good correlation coefficient (r^2 = 0.98). Through the intersection of the regression line with the L2-axis, an estimated DPOAE threshold level L_{EDPT} is obtained, revealing the logarithmic relationship of the DPOAE pressure to the primary tone level (from Boege and Janssen, 2002).

To compare the agreement between objectively and subjectively assessed thresholds in the group of normal hearing subjects, the psycho-acoustic pure-tone thresholds were recorded immediately after the DPOAE measurement. A computer-controlled method of adjusting the sound pressure level through button press or release was applied at the same frequencies. There was a significant correlation ($p < 0.001$) between objective and subjective measures, especially with regard to hearing-impaired patients. Therefore, DPOAE measurements are likely to provide specific and quantitative information on the dysfunction of cochlear signal

processing. Furthermore, the good frequency correlation underlines the reliability of the new method.

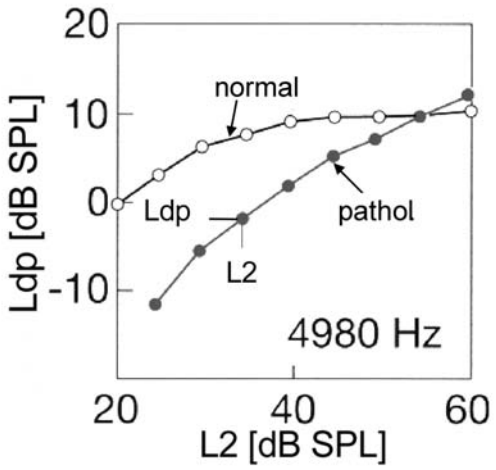

Figure 2.4. *DPOAE I/O-function at f2 = 4980 Hz.*
Open circles represent a normal DPOAE I/O-function. The function is nonlinear showing saturation at high primary tone levels.
Filled circles represent a pathological DPOAE I/O-function resulting from an impaired cochlear amplifier mechanism. The function is steep and linear without showing saturation at high primary tone levels (modified from Janssen, 1996).

In ears with cochlear hearing loss, growth functions are found to be steep, with the DPOAE level being small at low primary tone levels (Fig. 2.4). At high primary tone levels emissions can have normal amplitudes (L2 = 60 and L2 = 55 dB). As already mentioned above, the function is rather linear without showing any saturation. Thus, the cochlear amplifier has lost a part of its nonlinear compression characteristics. Additionally, it shows that the same primary tone setting used for normal hearing subjects can be applied for hearing-impaired patients.

It is important to mention that hearing also includes neural processing and functioning of the IHCs, which cannot be measured with DPOAE testings. Strictly speaking, the estimated threshold and the subjective hearing threshold cannot be identical, but they give information on the nonlinear compression characteristics of the cochlea. Due to the fact that sensitivity and frequency selectivity of hearing are achieved by cochlear signal processing, DPOAE measurements – when measured with the new method – can be used to assess cochlear impairment in detail. There is no other objective method that provides frequency-specific and quantitative information on ears with cochlear hearing loss.

2.5. Conduction of measurement and processing of data

Three to four newborns were seen every day at the neonatal care unit of the gynecological hospital. Each newborn undergoes TEOAE screening performed by an audiological assistant on the second or third day after birth. Since the DPOAE measurement was mostly performed after that screening, canal debris was already removed. The most readily accessible ear was

tested first. The still-sleeping child was then turned on its other side, and the second ear was measured. Time of measurement was preferably after feeding and during spontaneous sleep in the cradle. The room was not as quiet as an insulation cabin, but the noise level was sufficiently low for testing (acceptable SNR).

A probe tip of suitable size was inserted into the baby's ear canal and was tested to see if a perfect seal was achieved by sound pressure calibration. If the calibration with a chirp signal was all right, the measurement was started. Measurement was stopped only if the newborn was too restless or started crying.

The data were processed using Matlab software (Mathworks). Statistics were calculated using SPSS 10.1 (SPSS Inc.). Figures were made using Excel (Microsoft).

3. Results

3.1. Example of a measurement report

After a measurement has been finished, several kinds of information about the hearing capability of the patient can be derived (Fig. 3.1).

Figures 3.1A and B plot DPOAE I/O-functions in parts at f2 = 2 and 4 kHz. Figure 3.1C shows the DPOAE-grams, which are constructed from the DPOAE I/O-functions at the f2-frequencies. The slope of the DPOAE I/O-functions calculated between L2 = 40 and L2 = 60 dB is plotted over f2 in Fig. 3.1D. Figure 3.1E plots the estimated DPOAE threshold at the 12 frequencies after converting dB SPL into dB HL in the form of a clinical audiogram.

The gray areas indicate normative data for the different measures evaluated on the basis of 30 adults with normal hearing (mean ± standard deviation). In Fig. 3.1A and B filled circles represent the DPOAE level elicited at the ten different primary tone levels of the scissor paradigm; open circles represent the noise floor. The standard deviation at the DPOAE level is a measure of accuracy for the DPOAE test. It marks the variability of the DPOAE level depending on the SNR that is known from normative data (Janssen, 2000b). The gray area below the noise floor is the expected level of noise under optimal conditions in a sound booth (Fig. 3.1A, B, C). Open circles represent conditions in which the SNR is smaller than 6 dB, for example with L2 = 20 dB at 4 kHz where there is a high standard deviation for the DPOAE level. The SNR is essential for the stability of the DPOAE level. If the SNR is high, the variability of the DPOAE level is small, allowing reliable results to be assumed and vice versa.

Whith decreasing primary tone level, the DPOAE level also decreases (Fig. 3.1A, B). Due to physiological noise, measurement of DPOAEs below L2 = 20 dB SPL is restricted. Therefore, an intersection with the abscissa is made by extrapolation (see section 2.3) in order to receive a value in dB SPL that would elicit DPOAEs at threshold. This value is transformed into dB HL using the conversion table (see section 7.1), then plotted in the audiogram (Fig. 3.1E).

At f2 = 2 kHz, the DPOAE level (Ldp) of the newborn was much higher than that of the normative adult group, and it was higher than the Ldp at the high frequency (4 kHz) as well; the function in the 4 kHz panel complied with the growth function at 2 kHz. At f2 = 2 kHz, high emissions for all primary tone levels could be measured. Even for L2 = 20 dB SPL the SNR was sufficient. At f2 = 4 kHz, emissions were obviously lower. For L2 = 25 and 20 dB SPL, emissions disappeared in the noise floor.

The difference between high- and low frequency DPOAEs can be seen in the reconstructed audiogram (Fig. 3.1E). At 4 kHz, the DPOAE I/O-function decreased more rapidly in comparison with the one at 2 kHz, resulting in an estimated hearing loss of 20 dB. The measurement revealed an apparent loss of high frequency hearing, whereas the results at lower frequencies coincided well with the normative data or even exceeded these values, for example at f2 = 1 or 1.5 kHz. This was confirmed by the DPOAE-gram, which showed single curves for each primary tone pair related to the frequency (Fig. 3.1C).

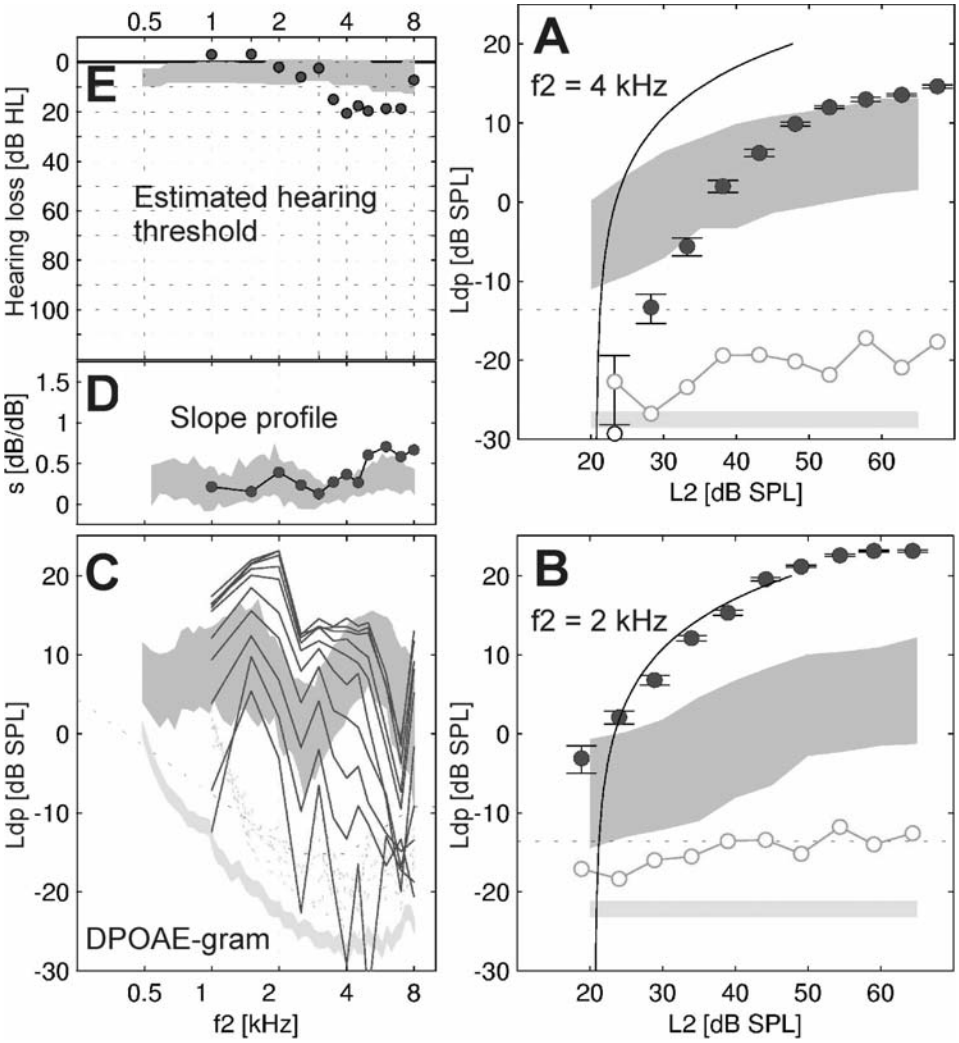

Figure 3.1. *Example of a measurement report.*
(A) , (B) DPOAE I/O-functions at f2 = 2 and 4 kHz. (C) DPOAE-gram.
(D) Slope of the DPOAE I/O-function calculated between L2 = 40 and 60 dB.
(E) Estimated hearing threshold (audiogram form).
Through extrapolation of the DPOAE I/O-function an intersection point with the abscissa and consequently a value in dB SPL is obtained. This value is converted into dB HL and plotted in the audiogram. The gray areas indicate normative data evaluated on the basis of 30 adults with normal hearing.

In the example, the data from the newborn matched the slope of the normative subjects well, except for high frequencies (Fig. 3.1D). Values lay between 0.2 and 0.7 dB/dB. For ears with normal hearing, the mean average of the slope was 0.2 dB/dB. Steep DPOAE I/O-functions and, as a consequence, high slope profiles would account for OHC impairment (Janssen et al., 1998). The unchanged slope in the example thus indicates that the inner ear was not affected.

3.2. Early postnatal period and normative data

3.2.1. DPOAE-grams

The DPOAE-grams were reconstructed from originally recorded data of the DPOAE I/O-functions. They plot the emission amplitude across twelve f2-frequencies at a distinct primary tone level.

The averaged DPOAE-grams of all neonates were M-shaped in form with maxima at 2000 and 5000 Hz and a minimum at 3500 Hz (Fig. 3.2A). At high primary tone levels the DPOAE-grams lay close together, indicating saturation, whereas at low primary tone levels they were more separated, reflecting compressive growth. Changes in the DPOAE levels increased along with decreasing primary tone level in the range around 4500 Hz, with a difference of about 17 dB noted between L2 = 20 dB and L2 = 65 dB. At other frequencies the values lay close together, and the growth functions had therefore more compressive shapes.

In general, the lower the primary tone level the lower the DPOAE level. However, an exception was found at 1000 Hz, where DPOAEs for L2 = 30 dB SPL were higher than those for 65 dB SPL, for example. Since the DPOAE levels for all primary tone levels were nearly the same, the DPOAE I/O- function was flat (Fig. 3.3A). The reliability of results at 1000 Hz was critical and is described in detail in the discussion.

The DPOAE-grams of the adult subject sample were M-shaped, too (Fig. 3.2B). Maxima lay at 1500 and 5000 Hz and a minimum at 2000 Hz. As already described for the neonates, the DPOAE-grams of the adults at high primary tone levels lay closer together than at low primary tone levels, indicating saturation and compressive growth, respectively.

Consideration of single frequencies revealed that the DPOAE-grams lay close together in the low frequency range, indicating saturation (see section 3.2.2.). In contrast, the DPOAE-grams in the 4.5 – 6 kHz region were widely spaced. The greatest difference between the highest and lowest DPOAE levels was circa 20 dB at 6 kHz.

The rule that the lower the primary tone level the lower the DPOAEs was valid for nearly all frequencies and sound pressures. Less than five values existed for 20, 25 and 30 dB SPL at 8000 Hz, so these DPOAE-grams stopped at 7000 Hz.

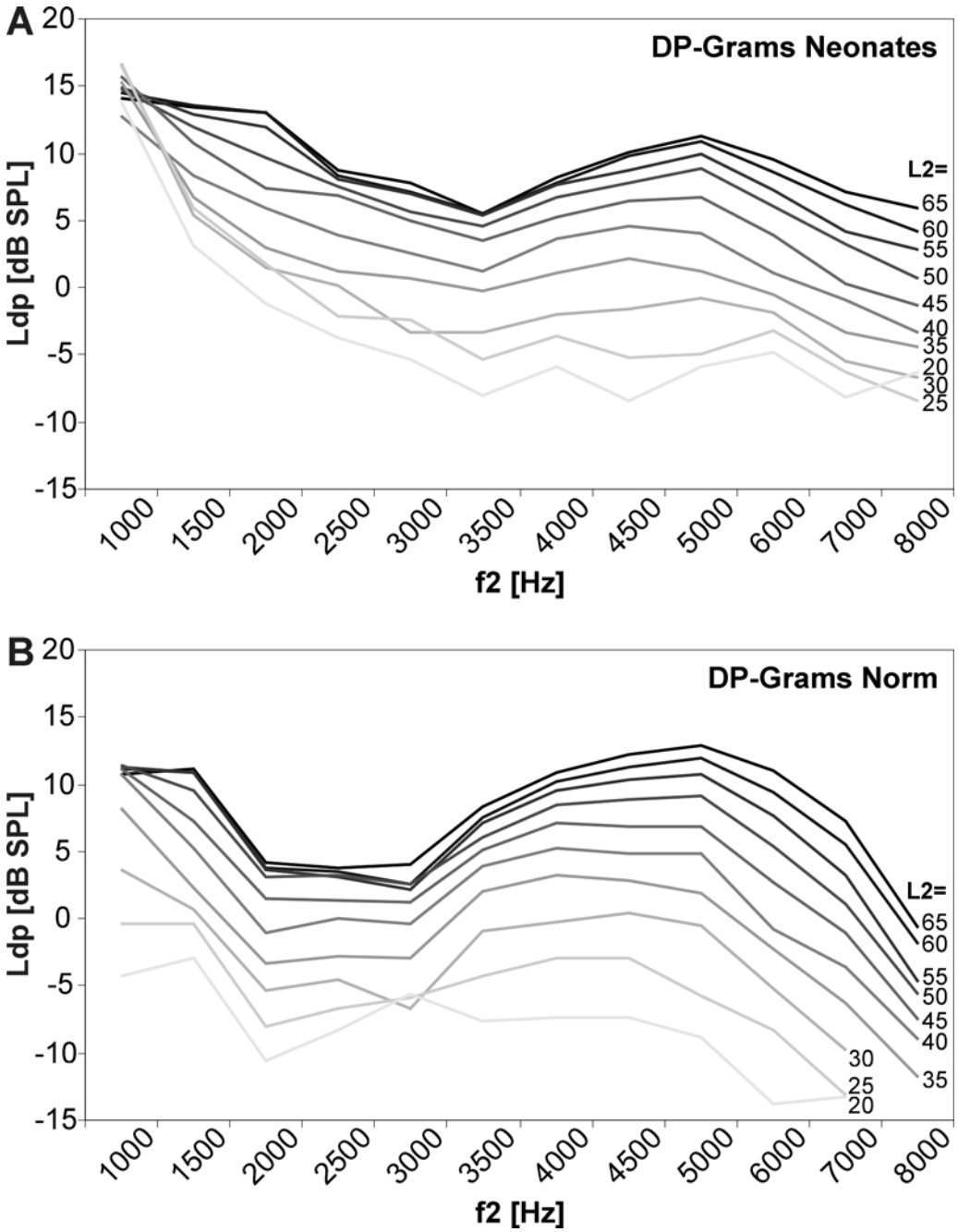

Figure 3.2. *DPOAE-grams of the neonatal (A) and adult (B) subject samples.*
The DPOAE-grams were reconstructed from the DPOAE I/O-functions and plot the emission amplitude across f2-frequencies at a distinct primary tone level.

3.2.2. DPOAE I/O-function

The DPOAE I/O-functions represent the level of distortion product as a function of the level of L2 stimulus. Shown are the mean values and standard deviations of the DPOAE levels of

the pediatric and adult populations at ten different primary tone levels for each of the twelve f2-frequencies (Fig 3.3A-L).

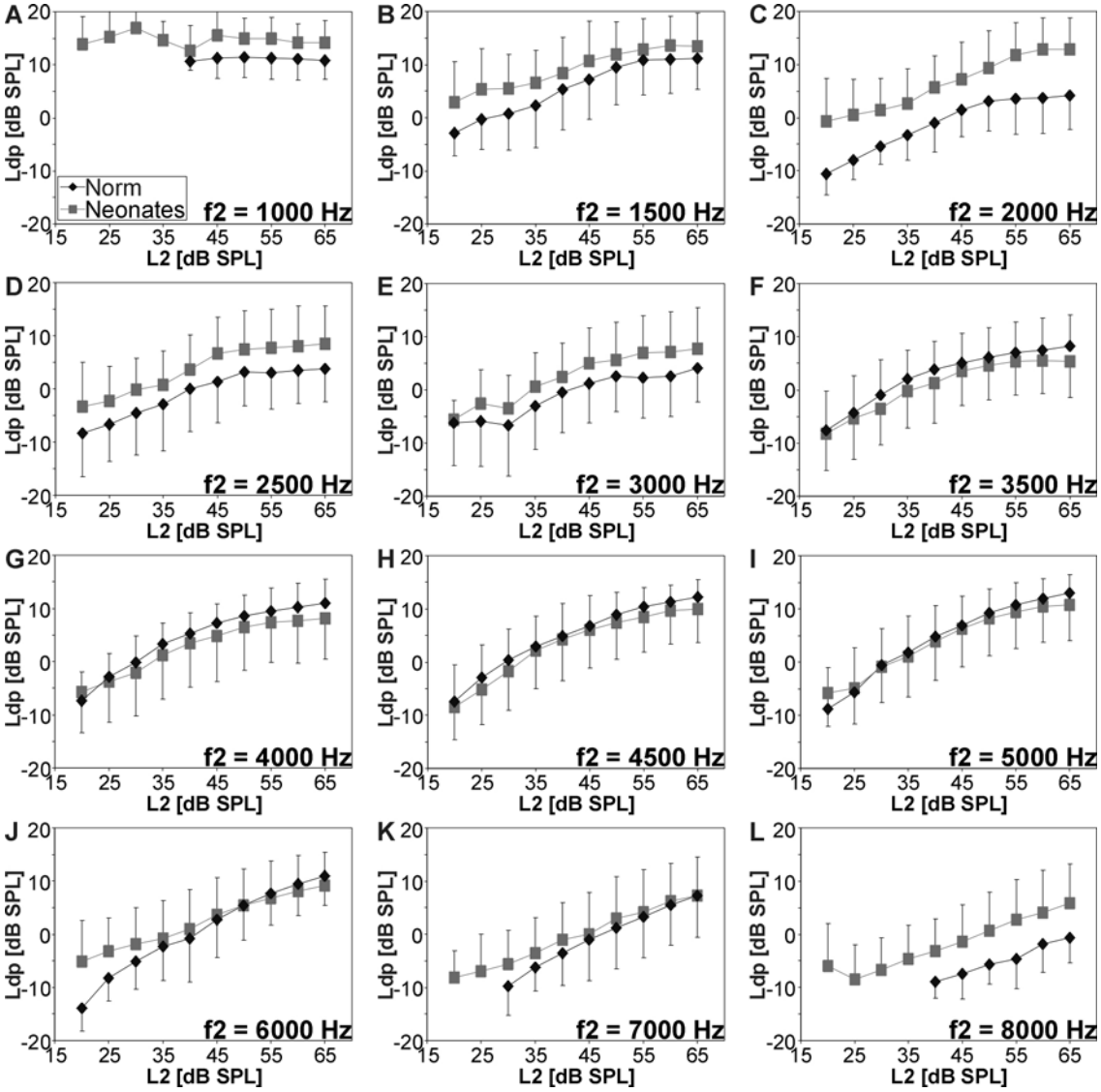

Figure 3.3. *DPOAE I/O-functions of the neonatal (square) and adult (diamond) subject samples. DPOAE I/O-functions for both groups are shown at twelve different frequencies between 1000 and 8000 Hz. The DPOAE I/O-functions of the newborns and adults were averaged using data of 127 ears and 26 ears, respectively (mean value and standard deviation).*

In the 3500 to 5000 Hz range the DPOAE I/O-functions of the neonatal and adult subject samples were nearly congruent (Fig. 3.3F-I). At 6000 and 7000 Hz the curves of both groups lay close together (Fig. 3.3J, K) and between 1500 and 3000 Hz the DPOAE I/O-functions ran relatively parallel (Fig. 3.3B-E). The greatest averaged distance, with approximately 8 dB, was measured at 2000 Hz, while circa 5 dB was found at 2500 Hz and about 4 dB at 1500 and 3000 Hz.

With some exceptions (for example at 1000 Hz) as L2 increased, the DPOAE level also increased. The highest DPOAE level related to frequency in the neonatal group was measured at 1000 - 2000 Hz (Fig. 3.3A, B, C). It should be noted that data of only 41 ears entered the statistical evaluation at 1000 Hz. Mostly due to the SNR criterion, no DPOAEs could be obtained for the missing ears. Except for the 1500 Hz function (86 ears), all functions were averaged from data of more than 100 ears. In the adult population, an average value was only calculated if more than five data points for the corresponding L2 existed. This explains why less than ten values appear at some frequencies. Here, the highest amplitudes occurred at 4000 - 5000 Hz (Fig. 3.3G, H, I).

The shape of the mean newborn and adult DPOAE I/O-functions were similar and can be described as straight (Fig. 3.3J-L), saturated (Fig. 3.3F-I), with a plateau (Fig. 3.3A-D) and notched (Fig. 3.3E), although a clear classification was sometimes difficult. This kind of characterisation of DPOAE I/O-functions was proposed by Popelka et al. (1995). The degree of saturation increased along with increasing f2 frequency in the range between 3500 and 5000 Hz. From 6000 Hz onwards there was no clear saturation level since the growth functions were growing rather monotonically. Growth functions of the adults were steeper than those of the newborns.

In the range from 1000 to 3000 Hz the DPOAE I/O-functions of the neonates were above those of the adults (Fig. 3.3A-E). These positions inverted at 3500 to 4500 Hz and partly at 5000 Hz but were restored at frequencies from 6000 to 8000 Hz.

3.2.3. Estimated hearing threshold

The DPOAE threshold is estimated by fitting the extrapolated DPOAE I/O-functions and determining the point of intersection between the regression line and the L2-axis. The estimated hearing loss and standard deviation averaged using data obtained from 127 ears (of 134) of 98 neonates (of 103) at eleven frequencies is shown in Fig. 3.4A.

Five newborns had no DPOAEs or were too restless for the hearing threshold to be measured. Since there were only two data points (two of 127) at 1000 Hz, this frequency was not taken into account. The reconstructed values for the hearing threshold were only accepted if they lay between -10 and 50 dB HL (see section 2.3).

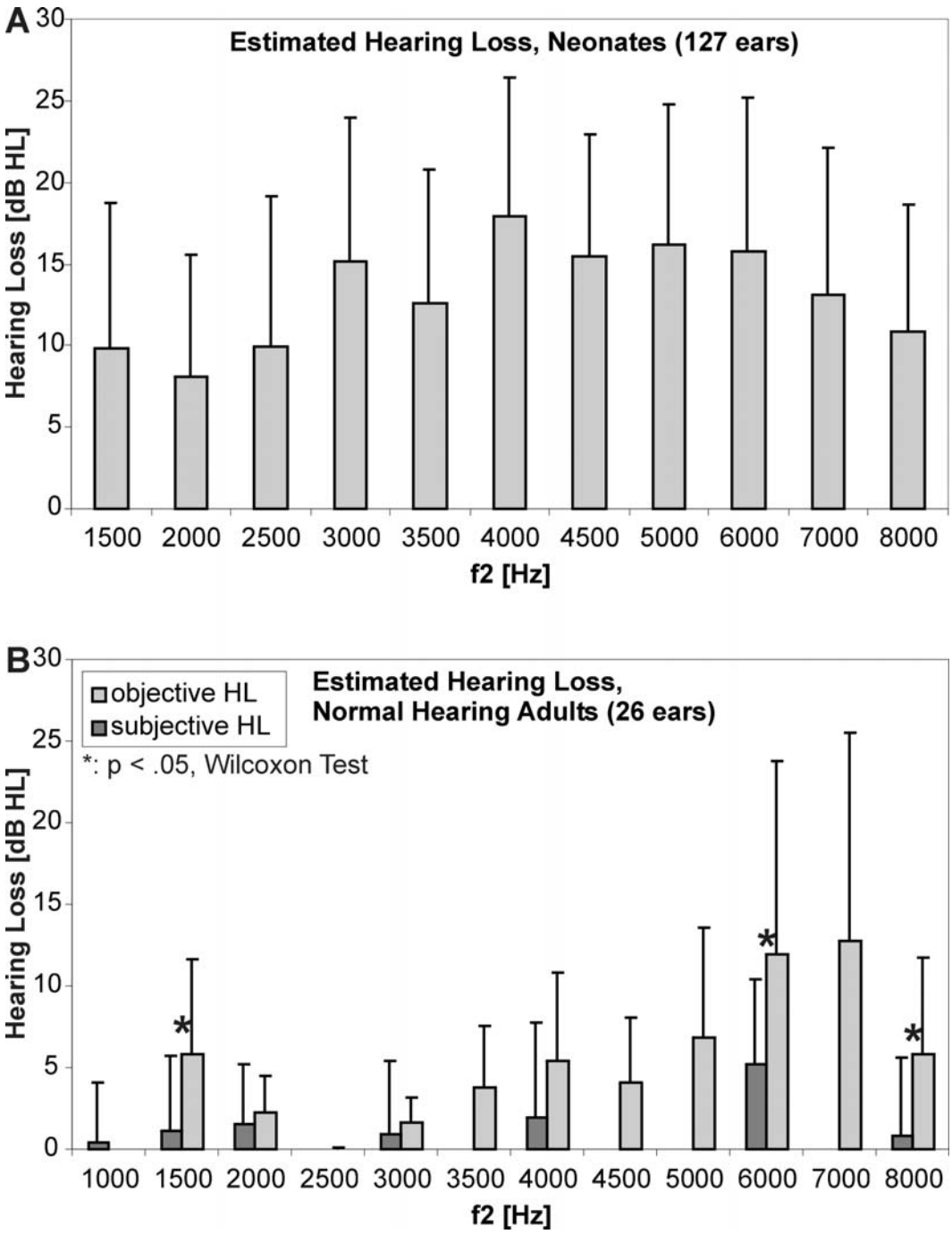

Figure 3.4. *Estimation of hearing loss by means of extrapolated DPOAE I/O-functions (mean value and standard deviation).*

(A) For the neonates only two data points could be obtained at 1000 Hz so this frequency was disregarded.

(B) For the adults an additional subjective hearing test was performed (dark bar). Asterisks mark frequencies with significant differences between subjective and objective hearing loss. In the objective hearing test less than five values could be obtained at 1000 Hz.

The estimated hearing loss revealed a slight hearing loss (> 15 dB HL) within the high frequency region (17.92 dB HL ± 8.51 at 4000 Hz). The lowest hearing loss was observed at 2000 Hz (8.13 ± 7.45 dB HL). Ninety-two data points could be obtained at 5000 Hz, which

was the highest number. In contrast, a minimum of 44 values were obtained at 1500 Hz. Data points were recorded at 7000 and 8000Hz for one half of the neonates.

In comparison, the adult sample of normal hearing subjects had the greatest hearing loss in the objective test at 6000 (11.9 ± 9.12 dB HL) and 7000 Hz (12.8 ± 8.64 dB HL, Fig. 3.4B), while the lowest figures were found at 2500 Hz (0.05 ± 7.49 dB HL).

A comparison between objective and subjective hearing loss was made at six frequencies since test frequencies differed in the two test methods. Significant differences ($p < 0.05$, Wilcoxon test) in hearing loss existed at 1500, 6000 and 8000 Hz. At those frequencies, hearing loss in the objective test was between 5 and 10 dB HL greater than that denoted in the subjective test. At 2000, 3000 and 4000 Hz the results were closely related. For the objective measurement there were less than five values existing at 1000 Hz. At 5000 Hz data points were found for all subjects, while at 8000 Hz data points were found for only 15. In the subjective test, values were available for all subjects and all audiometric frequencies. However, in both test groups the majority of the data points were measured at 5000 Hz.

3.2.4. Slope of DPOAE I/O-functions

Mean and standard deviation of the slope of the DPOAE I/O-functions are shown in Fig. 3.5.

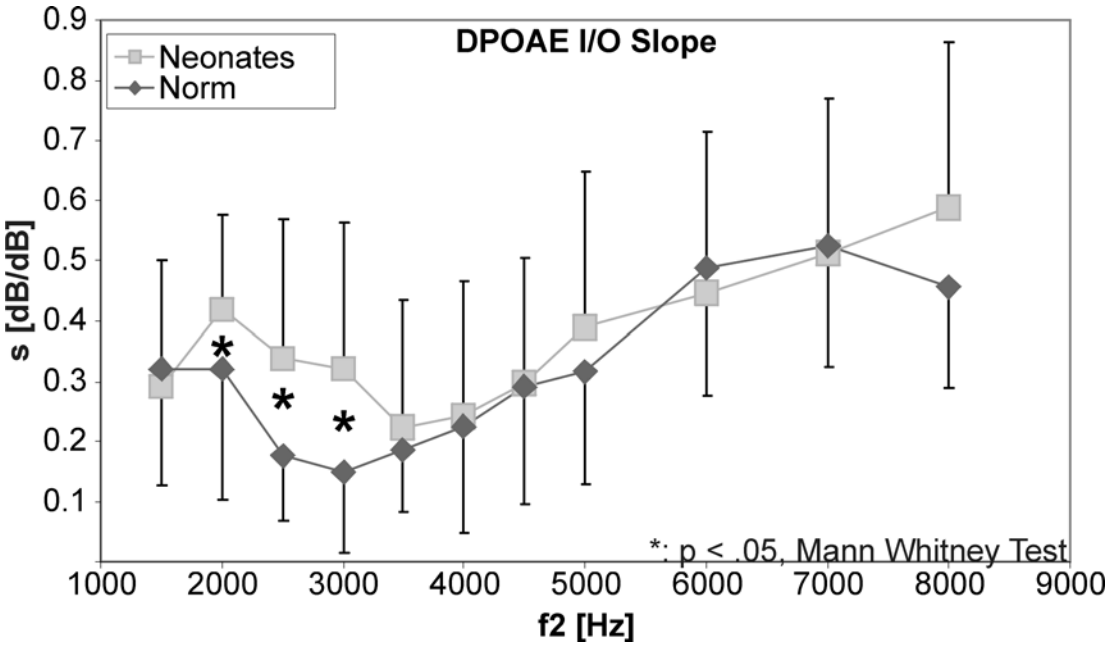

Figure 3.5. *DPOAE slope profile of the neonatal (squares) and adult (diamonds) subject sample (mean value and standard deviation).*
Asterisks mark frequencies with significant differences between the values of both groups.

The adult subject sample exhibited a slope with values varying from 0.15 to 0.53 dB/dB. In the newborn sample the slope varied from 0.22 to 0.59 dB/dB. The slope for the mean overall growth function of adults was 0.3 ± 0.13 dB/dB and for neonates 0.34 ± 0.14 dB/dB.

Since only a few data points were recorded in both test groups at 1000 Hz, this frequency was not taken into consideration. For all other frequencies in the norm group, except 8000 Hz which had 14 values, at least 20 data points were entered for averaging. In the neonatal group the lowest number of data points (51) was also obtained at 8000 Hz, but more than 80 data points were obtained for all frequencies between 3500 and 6000 Hz.

For the norm group, the slope in the low frequency region decreased to 3000 Hz then increased continuously to 7000 Hz before decreasing again.

For the neonates the slope increased between 1500 and 2000 Hz then decreased to 3500 Hz; a continual increase followed. In the region of 3500 - 7000 Hz the averaged growth rates were similar. Except for values at 1500, 6000 and 7000 Hz, all values of the neonates were above those of the norm group.

Significant differences between the postnatal and adult data existed at 2000 - 3000 Hz ($p < 0.05$, Mann-Whitney-test).

As mentioned above, high values or steep functions indicate pathology in the inner ear.

3.3. Follow-up study data

3.3.1. Change of DPOAE I/O-function

Sixteen ears of 13 children underwent a second measurement at their home. Comparison of the DPOAE I/O-functions at first measurement (mean age of 3 days) and some weeks (> 4) later revealed noticeable differences (Fig. 3.6A-K, fig. 3.7). Again, the 1000 Hz measurement was missing due to lack of data.

Whereas the two measurements of DPOAE I/O-functions showed little difference at 1500 Hz, the DPOAE I/O-functions were considerably different at all other frequencies, with the DPOAE level most often being higher in the second measurement. Higher emissions at first measurement were measured at only a few primary tone levels (1500 and 2500 Hz). The greatest difference in the DPOAE level was seen at 3500 Hz with about 9 dB at L2 = 65 dB (Fig. 3.6E). The difference at L2 = 65 dB amounted to around 4 dB on average. At 2000, 3000, 3500, 6000, 7000 and 8000 Hz more data points were obtained in the follow-up examination, especially for the low primary tone levels.

The predominant shape of growth functions in the follow-up sample was the saturated one. Nevertheless, making a clear classification remained difficult in many cases. At 2000 Hz the initially saturated shape of growth function transformed into a shape with a plateau (Fig. 3.6B). At 2500 Hz growth functions at both test periods showed a plateau (Fig. 3.6C), and at 3500 Hz a saturated shape followed a formerly notched one (Fig. 3.6E). The initially straight function at 8000 Hz became a saturated one with a notch at L2 = 45 dB (Fig. 3.6K). The two curves were clearly parallel at 4500, and at 2500, 4000 and 5000 Hz.

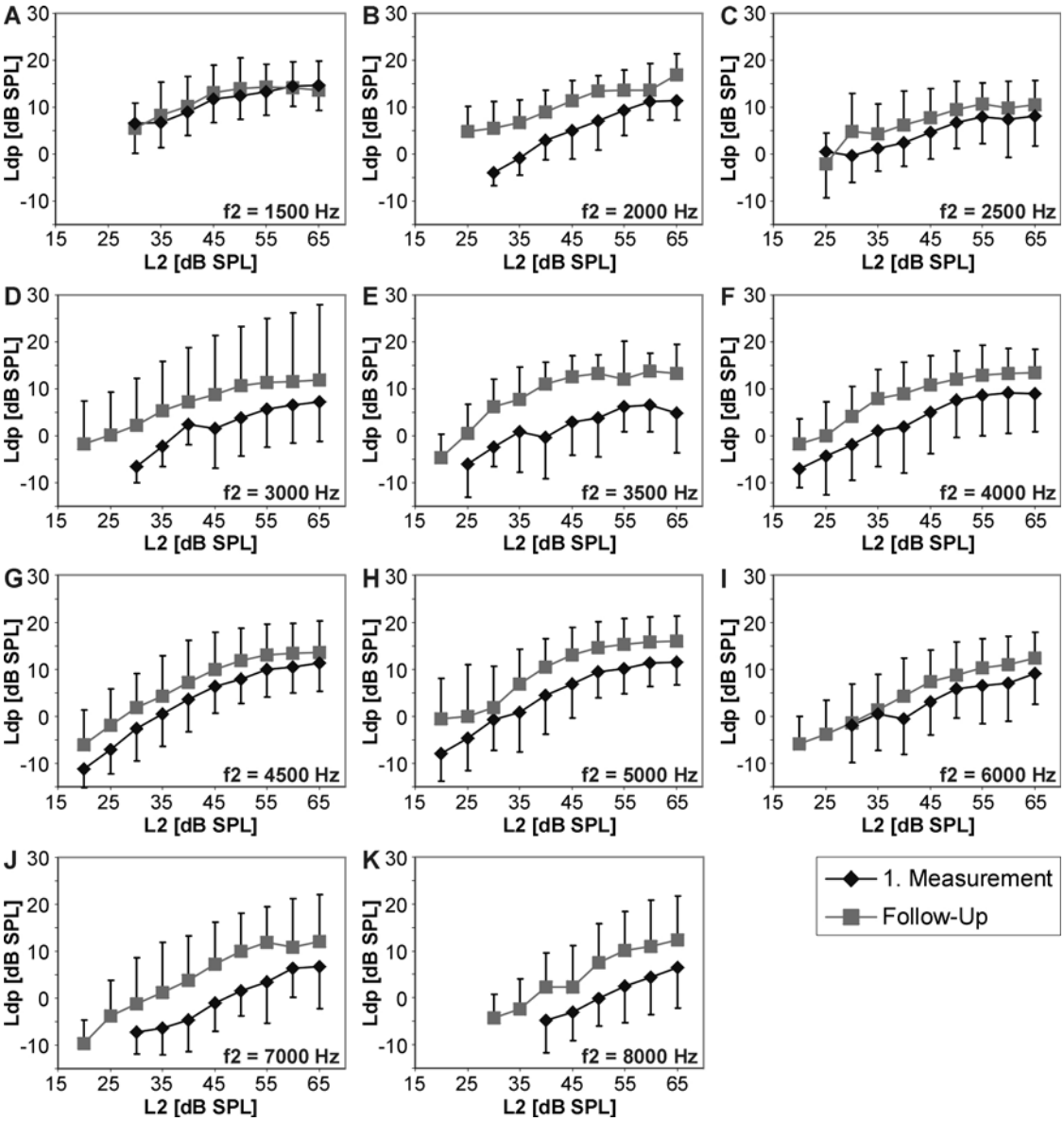

Figure 3.6. *DPOAE I/O-functions of first measurement (diamonds) and follow-up (squares), n = 16 ears of 13 neonates (mean value and standard deviation).*
Since only few data points were recorded at 1000 Hz, this frequency was disregarded The same explanation accounts for missing data points for low primary tone levels at several frequencies.

Consideration of the estimated hearing loss confirmed the assumption that hearing ability improves over time (Fig. 3.7). Significant differences ($p < 0.05$, Wilcoxon-test) existed at all frequencies except 1500, 2000 and 8000 Hz. The greatest difference could be seen at 3000 Hz, with an improvement of 11.26 dB HL, in contrast to only a 2.84 dB HL improvement at 4500 Hz. Aside from the value at 4500 Hz, all averaged values of estimated hearing loss lay below 9 dB HL. In comparison with the adult group (Fig. 3.4B), the values, especially at high frequencies, were better; for example, the values at 6000 / 7000 Hz were 8 dB versus 12 / 13 dB HL. Concerning the maximum values of the individual data (Fig. 3.7), the curve of the second measurement lay below that of the first measurement, except for the 4500 Hz value.

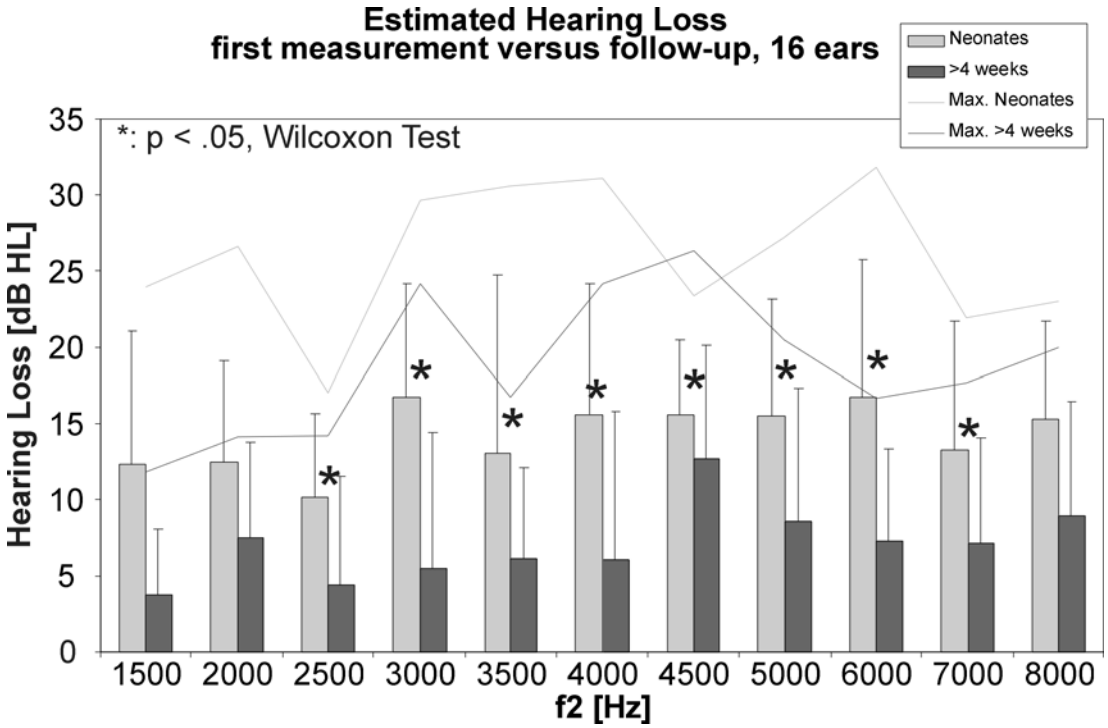

Figure 3.7. *Estimated hearing loss of first (bright bar) and second (dark bar) measurement of 16 ears (mean value and standard deviation).*
The solid lines represent the corresponding maximum values of the individual data. Asterisks mark frequencies with significant differences between the first measurement and follow-up.

3.3.2. DPOAE slope profile

Compared to the DPOAE level the slope of the I/O-function showed significant differences ($p < 0.05$, Wilcoxon test) at just a few frequencies (2500, 3000 and 3500 Hz; Fig. 3.8). The slope of the DPOAE I/O-function obtained during the first measurement started as an M-shape (with maxima at 2000 and 3000 Hz) and increased steadily from 3500 Hz onwards, with a slight decrease found between 7000 and 8000 Hz.

The slope of the DPOAE I/O-function obtained during the follow-up measurement, however, also started as an M-shape (maxima at 2000 and 4500 Hz) at high frequencies then increased steadily above 5 kHZ. All values lay below those of the first measurement.

The mean overall slope at first measurement was 0.39 ± 0.11 dB/dB with a maximum at 0.59 dB/dB and a minimum at 0.26 dB/dB. At follow-up measurement the average slope amounted to 0.28 ± 0.13 dB/dB with a maximum at 0.54 dB/dB and a minimum at 0.13 dB/dB. At 8000 Hz there were only five values in the data analysis, whereas ten or more data points existed for each of the frequencies between 3500 and 7000 Hz. Again, the number of data points collected at 1000 Hz was insufficient and therefore not included.

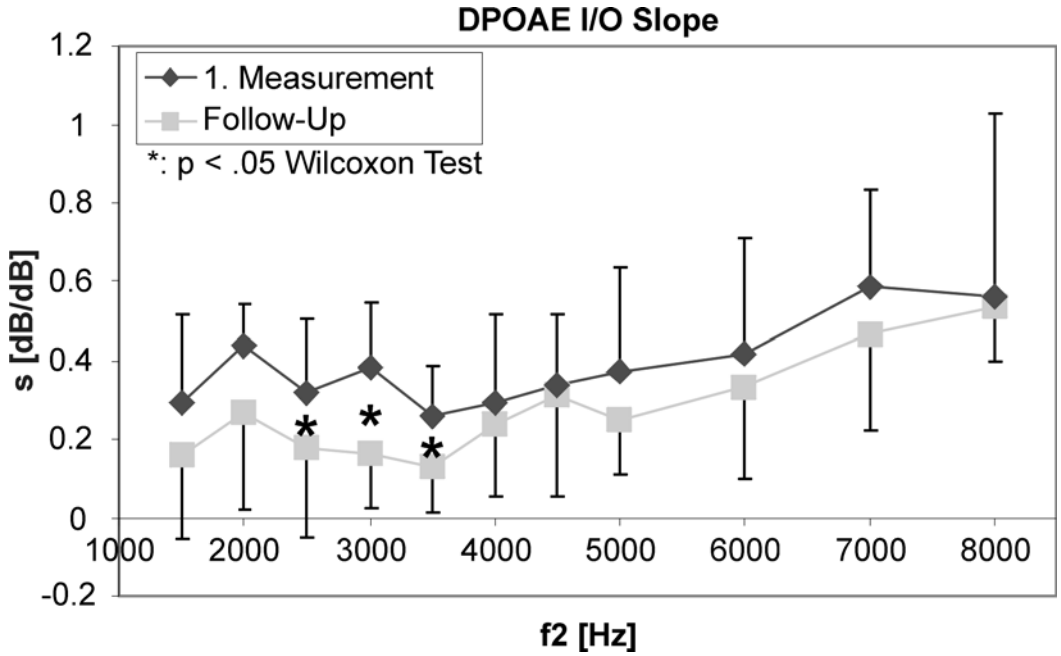

Figure 3.8. *DPOAE slope profile of first measurement (diamonds) and follow-up (squares) of 16 ears (mean value and standard deviation).*
Significant differences between first and second measurement existed at three frequencies (asterisks).

3.3.3. Slope profile of follow-up versus norm group

When comparing the slope of the normal hearing adults (Fig. 3.9) with the follow-up slope of the newborns only a slight difference could be seen. This was in contrast with the large difference found between both data sets for the DPOAE level of the I/O-functions (normative data from Fig. 3.3 and follow-up data from Fig. 3.6).

Significant differences existed at 6000 Hz only ($p < 0.05$, Mann-Whitney-Test). At 7000 and 8000 Hz values were close. Only at the 1000 and 5000 – 7000 Hz levels did the data points of the norm group clearly exceed those of the follow-up group, while the reverse was true at 8000 Hz.

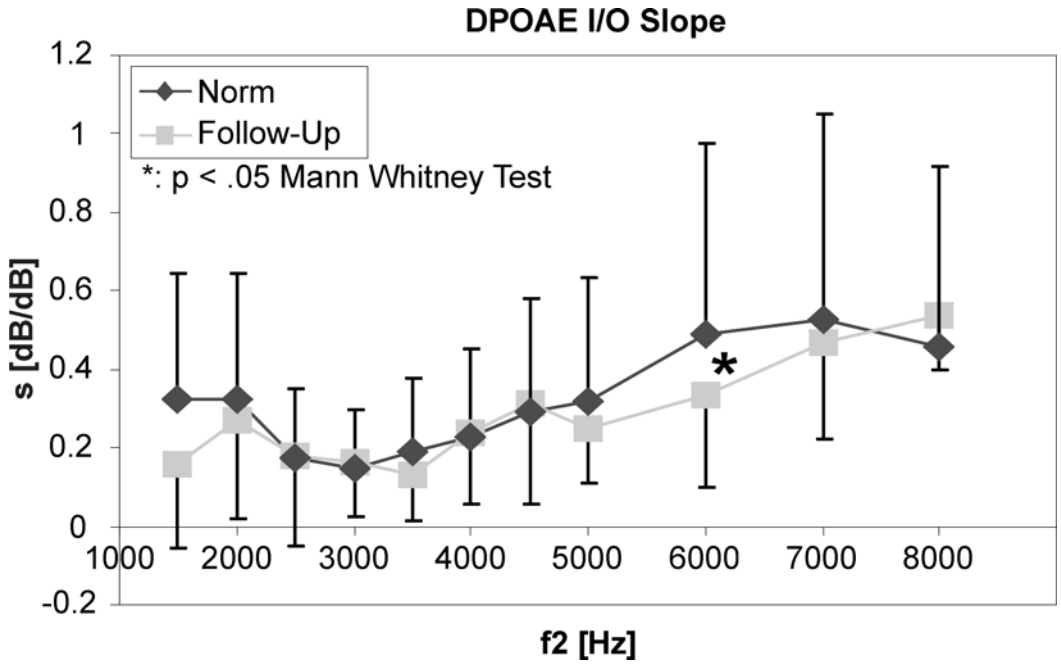

Figure 3.9. *DPOAE slope profile of the norm group (diamonds) and the follow-up (squares). Significant differences (asterisks) between the two subject samples were found at 6000 Hz (mean value and standard deviation).*

3.4. Examples of noticeable screening results

Among the 134 ears tested only six ears of five neonates demonstrated no DPOAEs during the first measurement. Five ears of those newborns (CH, NB, MV, NC) turned out to have normal hearing after further examination by TEOAE screening, ABR and tympanometry. Only in one subject (MP) did a final diagnosis remain unclear.

Two days after birth neither TEOAEs nor DPOAEs were measured in both ears of subject NC (positive screening). However, five weeks later both tests were negative. Similar results were obtained for subject MV, but in this case TEOAE screening with its negative result was already repeated the next day while the DPOAEs were measured again six weeks later.

For subject CH both tests provided a positive screening result for the left ear whereas the right ear was normal. Repeating the TEOAE screening the next day and seven weeks later did not change the result. Ten weeks after birth DPOAEs were measured at home. The reconstructed audiogram showed normal hearing at frequencies between 2500 and 4000 Hz and a slight hearing loss at higher frequencies. When perfomed nearly four months after birth, the TEOAE screening was still positive, so an ABR was done at the age of five and a half months. This last examination confirmed normal hearing.

The four-day-old subject NB had positive TEOAE and DPOAE screening results for both ears. Follow-up measurements scheduled seven and twelve weeks later were difficult to perform since the infant had repetitive colds. DPOAEs in the 3000 – 5000 Hz region were

measurable, but they were of low amplitude. Additionally, the child was very restless, so the noise floor in the low frequency region was elevated. It took four months to diagnose normal hearing through TEOAEs and tympanometry.

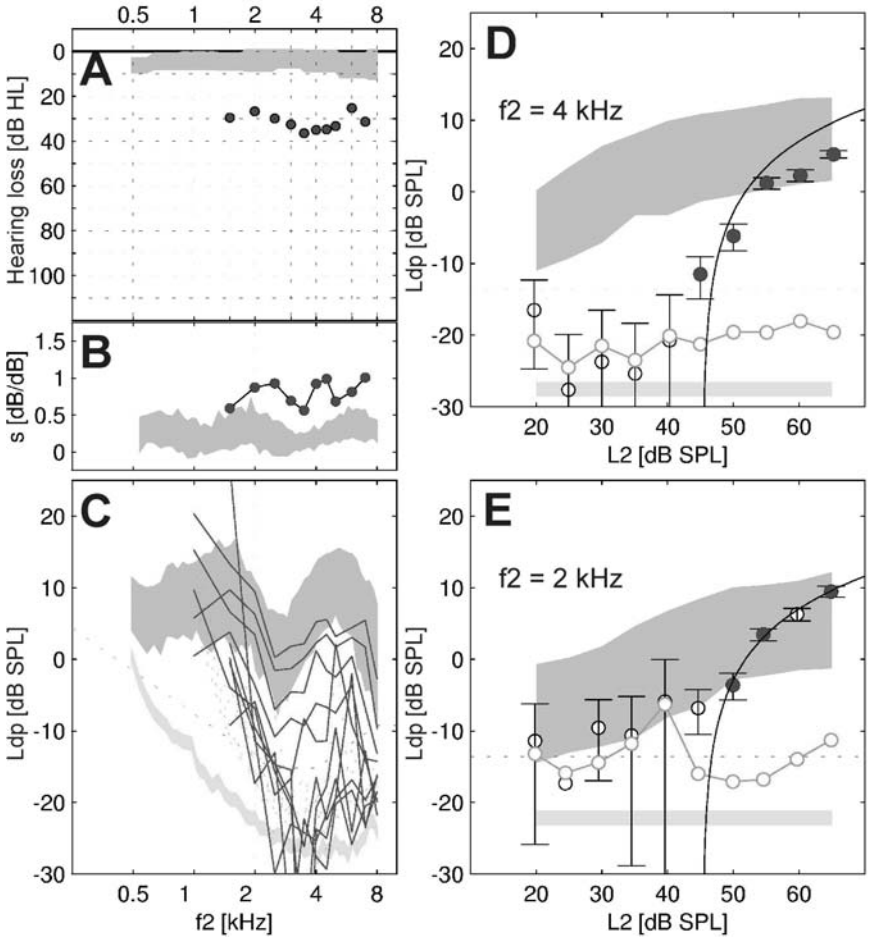

Figure 3.10. *Measurement report of subject MP.*
For detailed information see Fig. 3.1.

The special case (MP) in which the final diagnosis remains unclear is illustrated in Fig. 3.10. Three days after birth TEOAE screening of both ears was without pathological findings but DPOAEs were not measurable on the left side (no DPOAE measurement was performed on the right side). Four weeks later the measurement was repeated at home (Fig. 3.10). The slope profile showed values above the normative data for all frequencies tested (Fig. 3.10B). Examples of DPOAE I/O-functions showed this at 2000 (Fig. 3.10B) and 4000 Hz (Fig. 3.10E). Emissions were only measurable at high primary tone levels and resulted in steep DPOAE I/O-functions. The objective audiogram showed a mean average hearing loss of 30 – 40 dB HL (Fig. 3.10A). To confirm the hearing loss an ABR was planned but, unfortunately, the mother did not keep the appointment. Therefore a final diagnosis could not be made.

4. Discussion

4.1. Comparison of newborn and adult outcomes

4.1.1. DPOAE I/O-functions and DPOAE-grams

DPOAE I/O-functions mirror sensitivity and compression of OHC amplifiers at a distinct location on the cochlea. When measured at different f2-frequencies DPOAE I/O-functions provide a specific test reflecting the proper functioning of the cochlea. The question is whether DPOAE I/O-functions differ in neonates in the early postnatal period and in adult subjects. Three main factors may cause potential differences: (i) acoustic properties due to different ear canal length, (ii) middle ear transduction properties due to different mass, (iii) cochlear sound processing depending on cochlear maturity.

The DPOAE I/O-functions of the neonate and adult subjects were nearly congruent in the 3500 to 5000 Hz range (Fig. 3.3F-I) and very similar at 6000 and 7000 Hz (Fig. 3.3J, K) with respect to emission amplitude and slope of the I/O-functions. At the remaining frequencies the DPOAE I/O-functions of the neonates surmounted those of the adults, mostly by some decibels.

DPOAE-grams plot the emission amplitude across f2-frequencies at a distinct primary tone level. DPOAE-grams are constructed using the measurements of the DPOAE I/O-functions and serve for a better comparison of DPOAE level in subject samples.

In the DPOAE-grams of the neonate and adult subject samples maxima appeared in the 1500/2000 Hz and the 5000 Hz region for both groups (Fig. 3.2A, B). In neonates the minimum DPOAE level was found at 3500 Hz, and in adults it was around 2000 Hz. At high primary tone levels the DPOAE-grams of both subject samples were close together indicating saturation, whereas at lower primary tone levels they were more separated reflecting compressive growth.

The observation that DPOAEs of both groups behaved similarly was surprising since one would expect higher emission amplitudes in neonates due to their shorter ear canals and corresponding higher sound pressure. In the present study, the calibration of sound pressure in the individual ear canals was performed by applying a broadband chirp signal via the loudspeakers. The smaller volume between the probe and the eardrum was measured as a higher sound pressure level. Thus, stimulus parameters were adapted so that the actual primary tone level at the ear drum was nearly the same in both test groups. However, while

measuring DPOAEs, the smaller volume was no longer irrelevant and resulted in higher DPOAE amplitudes.

Our results obtained at low f2-frequencies, between 1000 and 3000 Hz, confirmed these observations (Fig. 3.3A-E). The shapes generated for the two subject samples were very similar, sometimes nearly parallel, but the emissions of the neonates surmounted those of the adults mostly by some decibels. At levels between 3500 and 7000 Hz, however, the DPOAE I/O-functions coincided well.

Residual amniotic fluid in the middle ear of neonates (Ochi et al., 1998) or fluids in general damper sound and work as sound filters, respectively. The fluid enhances the mass of the middle ear and reduces mechanical motion of the ossicular chain. This effect concerns especially high frequencies. The consequences for DPOAE measurement are reduced amplitudes for all primary tone levels in the high frequency range. This could explain the observation in the present study that, in comparison with the adults, the neonates did not exhibit higher emission amplitudes in the high frequency region (Fig. 3.3F-K). In contrast, DPOAE I/O-functions of the newborns had higher amplitudes than the adults in the low frequency region (Fig. 3.3A-E). For further details see section 4.2.1.

Similar results for DPOAEs in neonates and adults can be expected because the cochlea is functionally mature by 35 weeks of conceptional age (Pujol and Uziel, 1988). Only one of the newborns tested in the present study was younger than 36 weeks, by a slight margin. Therefore, cochlear maturity for the entire group of neonates was assumed. Nevertheless, other authors have suggested that minor developmental changes in the human cochlea occur in the postnatal period (Smurzynski, 1994), especially in preterm to term neonates (Quinonez and Crawford, 1997). Smurzynski saw this as an explanation for the variation of DPOAE amplitudes at different postconceptional ages.

Several researchers came to the conclusion that cochlear function is relatively mature in term neonates (Abdala et al., 1996; Lasky, 1998a; Brown, 2000), but proposed that further changes take place in the outer and middle ear. Keefe et al. (1993) reported that neonates have very compliant canal walls that absorb more sound in the ear canal. The walls of the ear canal thicken in the postnatal period, and the authors saw this as an important factor for longitudinal changes, for example, growth of DPOAE amplitudes with increasing postconceptional age. A second factor contributing to these changes was the observation that resistance in the middle ear was higher in neonates than in adults. Therefore, the power transfer into the middle ear could be lower for neonates.

Finally, it remains difficult to compare newborn and adult DPOAE I/O-functions because of age-related differences in the outer and middle ear. Therefore, some of the disagreements found may be explained by developmental differences in noncochlear structures.

Several authors have reported either similar or greater DPOAE amplitudes in term neonates compared with adults (Abdala, 1996; Bonfils et al., 1992). Lasky (1998a) noticed higher DPOAE amplitudes in the low frequency region and similar amplitudes at high frequencies in neonates compared with adults.

In the present study, the shapes of the DPOAE I/O-functions (i.e., straight, notched, saturated, plateau) were very similar in newborns and adults. Dallos (1992) explained those nonlinearities with active cochlear processes and Popelka et al. (1995) concluded that the same procedure occurs in the neonatal ear. In addition, it is a sign of the integrity of the OHC system. Other authors (Stover et al., 1996) considered it difficult to interpret the different shapes of I/O-functions.

The DPOAE growth functions in the present study often showed amplitude saturation and nonmonotonic growth for both age groups, thus confirming the results of Abdala (2000). Other authors have reported that saturation and nonlinearity of growth functions were more apparent in neonates than in adults (Lasky, 1998b). These authors attributed this to the fact that higher primary tone levels could be presented to newborns without producing acoustic problems in the ear canal.

In the present study, it was difficult to speak of saturation for the norm group beginning at 5000 Hz (Fig. 3.3I). The growth functions at the following three frequencies were rather straight, whereas those of the neonates were shallower and showed a slight hint of saturation. Either higher primary tone levels should have been applied or a compression deficit was already present in the cochlear amplifier of the adults. This would be consistent with the high frequency hearing loss in adults described in section 4.1.2.

The DPOAE-grams revealed that while the neonates had increasing Ldps for decreasing frequency after a minimum at 3000 Hz and high Ldps at 8000 Hz, the norm group had minima at 2000 and 8000 Hz. Oswald et al. (2002) explained these minima at 2 and 8 kHz as calibration errors caused by standing waves in the ear canal.

The DPOAE-grams in a study of Stover et al. (1996) were M-shaped and also showed a minimum at 2000 Hz. Unfortunately, though, they represented only one subject and were not averaged for all normal hearing adults. As the ear canal in neonates is much smaller, standing waves might have played an inferior role in this population (Abdala, 1996).

In the present study, data of only 41 of the 127 total neonates entered the evaluation at 1000 Hz due to an elevated noise floor. At low frequencies and at all primary tone levels the DPOAE level scattered around 15 dB so the DPOAE I/O-function was shallow without showing non-monotonic growth (Fig.3.2A). Apparently, there was a calibration problem for low frequencies and small ear canal volumes. However, in the norm group only 12 of 27 ears had measurable DPOAEs at 1000 Hz. Less than five values were obtained for primary tone levels lower than L2 = 40 dB. The reason for this was also an elevated noise floor, even though the measurement was performed in an insulation cabin.

Due to movement and a higher breathing rate, the noise floor in measurements of neonates is higher than that in adults. Especially at low frequencies, like 1000 Hz, where noise contains greater energy (Gorga et al., 2000), DPOAEs are often not measurable due to an insufficient SNR (Gorga et al., 2000; Marco et al., 1995). In the present study, those observations were confirmed for the 1000 Hz values and resulted in a very shallow DPOAE I/O-function (Fig. 3.3A). Prieve et al. (1997) also reported that flat I/O-functions occurred most often at 1000 and 1500 Hz, although this pattern accounted for only 3 % of shapes. As only half of the adults in the present study had measurable DPOAEs at 1000 Hz, the criteria for accepting DPOAE measurements was possibly too strict in this frequency range considering the inevitable physiological noise.

Results at 8000 Hz should also not be overestimated for lack of data and the assumption of a calibration mistake (see section 4.4.3). It was striking that on the one hand the mean average DPOAEs at 8 kHz were significantly higher in the neonates than in the adults (Fig. 3.2), while on the other hand it was a minimum region. At primary tone levels < 35 dB less than five of the adults had DPOAEs and those that were measurable were of very low amplitude.

Brown et al. (2000) tried to determine the optimum f2/f1 ratio of the primary tones to evoke the highest DPOAE amplitudes. They found that no significant differences exist for the optimum frequency ratio between neonates and adults. Therefore, the frequency ratio of the primary tones was suggested to be the same for both groups.

4.1.2. Estimated hearing loss

The intersection point of the DPOAE I/O-function with the L2-axis delivers an estimated hearing threshold. An overview of the hearing threshold at 12 different frequencies obtained during clinical testing can be seen in the reconstructed audiogram (Fig. 3.1).

In our data, the estimated hearing threshold for neonates within the early postnatal period exhibited a slight hearing loss at high frequencies (Fig. 3.4). The adults had a slight hearing

loss at 6000 and 7000 Hz in the objective hearing test, whereas the subjective test was without pathological findings.

In the neonates the results could be attributed to the fact that residual amniotic fluid after birth might enhance the mass of the middle ear and reduce mechanical motion of the ossicular chain at high sound frequencies. This finding corresponds with the findings of Ochi et al. (1998) and Kok et al. (1993) who found reduced DPOAE and reduced TEOAE amplitude, respectively, in newborns tested immediately after birth.

The highest estimated hearing loss, 17.92 dB, occurred at 4000 Hz, corroborating the former hypothesis that fluids in the middle ear particularly affect the high frequency range.

For the adults in our study significant differences between subjective and objective hearing loss did not exist at 2000 Hz but were found at 1500 and 8000 Hz (Fig. 3.4B; Oswald et al., 2002), which led again to the conclusion that the problems were caused by standing waves.

Striking were the elevated values for the objective hearing loss of the adults at 6000 and 7000 Hz. A closer look at the I/O-functions at these two frequencies (Fig. 3.3J, K) might help explain the cause for this hearing loss. At 7000 Hz no emissions were obtained for L2 < 30 dB SPL. At 6000 Hz emissions at low primary tone levels were of very small amplitude, whereas results at high primary tone levels were very similar in both test groups and at both frequencies. Since subjects included in the norm group were rather young (mean age = 24.7 years), it can be assumed that they were exposed to noise regularly. This includes the high noise floor in discotheques, at concerts and produced by headphones. Damage in the cochlea caused by an elevated noise floor initially affects high frequencies. The OHCs responsible for the high frequency region lie next to the oval window, thus at the beginning of the basilar membrane and are affected first. In case of damage, hearing problems occur especially at low primary tone levels.

A second explanation could be found in the shape of the growth function, which was more linear than compressive in both groups. Either the neonatal cochlea was not yet mature at birth or the cochlea of the adults had already forfeited a part of its nonlinear compression characteristics.

Most data points were collected at 5000 Hz which led to the conclusion that minor problems with calibration and standing waves were present at that frequency.

It is difficult to compare these results with other studies since the estimation of hearing threshold by extrapolated DPOAE I/O-functions is a new method that is not yet widespread (Boege and Janssen, 2002). Nonetheless, Gorga et al. (2003) recently applied the same method and extended it by applying primary tone levels higher than 65 db SPL.

4.1.3. Slope profiles

The slope s serves to quantify the DP growth and to measure compression of the OHC amplifiers. It is calculated between L2 = 40 and L2 = 60 dB SPL because that is the range in which normal and pathological DP growth differ most. Pathological findings result in steep functions and high values in the slope profile s(f2). It should be emphasized that this is only true in ears with OHC impairment (Janssen et al., 1998).

The DPOAE slope profiles of the neonates and the adult subjects were very similar (Fig. 3.5). Significant differences between the two groups existed in the low frequency range only. Although differences were noted for values between 2000 and 3000 Hz, these data points lay within the normal range (Fig. 3.1D). Therefore, pathological processes in the inner ear could be excluded. The slope profile revealed outstanding values at 2000 Hz and at high frequencies for both subject groups. This was possibly a result of problems caused by standing waves in that frequency range. On the other hand, standing waves should play an inferior role in the small ear canal of newborns.

Abdala (2000) reported the slope of the DPOAE I/O-function to be between 0.8 and 1 dB/dB in neonates as well as in adults, with the difference not being significant. However, DPOAE I/O-functions were fit with a regression equation in that study, not linearly between 40 and 60 dB SPL as in the present study. Furthermore, the whole monotonically growing portion was taken into consideration while applying primary tones ranging from 30 to 80 dB SPL at 1500, 3000 and 6000 Hz. Therefore, it is not possible to make a direct comparison between the data of Abdala and that of the present study.

4.2. Follow-up study

4.2.1. Amplitudes of DPOAEs

To examine changes in the auditory function of neonates, 13 of the children underwent the same measurement again some weeks later at home. Thus, differences in DPOAE amplitudes obtained at two time-points could be seen easily. The data for the DPOAE I/O-functions obtained in the follow-up study surmounted those of the first measurement at nearly all frequencies and for most of the primary tone levels.

The greatest difference in DPOAE amplitude between the first and second measurements existed at 3500 Hz (Fig. 3.6E), i.e., in the high frequency region. Here, the mean average difference between measurements was 7.88 dB, with values ranging from 5.12 to 11.3 dB. At

3000 Hz the mean average difference was 6.2 dB, while the smallest difference (1.18 dB) existed at 1500 Hz.

An important finding in this study was that the DPOAE amplitude reduction was independent of primary tone stimulus. As already mentioned, the DPOAE amplitude was higher for nearly all frequencies and primary tone levels in the second measurement. At some frequencies the DPOAE I/O-functions of the second measurement reflected a simple parallel shift by some decibels of those obtained in the first measurement. This means there was no change in the course of growth function and thus provided evidence for middle ear sound conduction disturbances. Cochlear dysfunction would result in a stimulus-dependent change in the DPOAE level and a consequent steep DPOAE I/O-function (Janssen et al., 1998).

A comparison of the DPOAE I/O-functions of the norm group (Fig. 3.3) with those obtained in the follow-up study of the newborns revealed higher emission levels for the latter at all frequencies. Looking at the results obtained at the 4000 Hz frequency showed a saturation threshold of about 10 dB SPL for the adults and 12 dB SPL for the neonates at follow-up. Evident differences existed at low frequencies; for example, at 2500 Hz the saturation threshold for adults was 3 versus 10 dB SPL for the newborns. At all frequencies except 8000 Hz, all growth functions were non-monotonic and showed a saturation level. This would support the hypothesis that linear functions and slight hearing loss at high frequencies in adults result from cochlear damage.

It is known that DPOAE amplitudes increase with increasing postconceptional age (Smurzynski, 1994; Quinonez and Crawford, 1997). In longitudinal studies Smurzynski tested 13 ears of seven preterm newborns from week 33 through week 41. He defined a significant increase in DPOAE amplitude with increasing PCA as a > 3 dB difference between the initial and the final test sessions. Using this definition, significant increases were found at 2.8 and 4 kHz, which is similar to the findings in our study. Similar results were also observed in the study of Quinonez and Crawford. One explanation was seen in the fact that minor developmental changes in the cochlea and changes in the middle-external ear transfer function do occur postnatally.

As already mentioned in 4.1.1, Keefe et al. (1993) identified postnatal changes occurring in the outer ear or the walls of the ear canal as additional factors contributing to longitudinal variation of otoacoustic emissions. They revealed the most significant increase in power absorbed in the ear with increasing age occurs in the 2 – 4 kHz region, which is also in agreement with the results of the present study. Finally, the question of how important each

factor is remains open, not forgetting the assumption of residual amniotic fluid in the middle ear.

In contrast, other authors have reported finding no differences in amplitude between 34 and 42 weeks conceptional age, but they only conducted tests at 2 and 4 kHz (Popelka et al., 1995).

As mentioned before (4.1.1), amniotic fluid in the middle ear during the first days of life seems to play an important role. Kok et al. (1993) made the same suggestion. In their study the prevalence of TEOAEs rose from 78% in newborns younger than 36 h to 99% in neonates older than 108 h. Apparently, this fluid is reabsorbed after several weeks, so neonatal DPOAE amplitudes obtained later surmounted those of the adults in the high frequency region as well.

Priner et al. (2003) studied postnatal changes of auditory function in guinea pigs; an animal model with a lot of similarities to the human acoustic organ. Their results confirmed the suggestion of amniotic fluid-induced temporary hearing loss, with low amplitude otoacoustic emissions being found shortly after birth and adult values found on postnatal day 2. They even drained the middle ear cavity of neonate guinea pigs with different amounts of fluid on the day of birth, and nearly no residual fluid was present three days after birth.

4.2.2. Shift of hearing level and changes of slope profiles

The hearing loss identified in the follow-up study compared to that of the first measurement was lower at all frequencies. The slope of the DPOAE I/O-function determined in the first and follow-up measurements were very similar, with slightly higher values in the second measurement. The slope profiles of the norm and neonatal subject groups were very similar, except for a few high frequency values and the 1500 Hz value.

A significant difference in hearing loss could be seen at all frequencies except 1500, 2000 and 8000 Hz. The greatest difference existed at 3000 Hz. Since values varied considerably, it was not possible to assign the greatest differences of hearing level to a certain frequency range. Results of the estimated hearing level for infants were much better than those for adults, especially at 6000 and 7000 Hz, so it was assumed again that problems with standing waves in the former group play an inferior role.

Looking at the slope profiles from the first and second measurements revealed significant differences at only three frequencies. It was interesting to see that significant differences existed between the slope of the infants and that of the norm group (Fig. 3.5) in the same frequency range. However, values obtained at follow-up were lower, thus arguing for slightly shallower growth functions.

Comparing the slope of the norm group to that of the neonates at follow-up led to the interesting observation that values in the 2000 – 5000 Hz region were very similar and significant differences remained only at 6000 Hz. This led to the conclusion that the DPOAE I/O slope of neonates was already adult-like at a few weeks following birth.

4.3. Discussion of neonates with positive screening results

Positive screening results can have different causes such as residual earwax or an inadequately fitting ear probe. In the present study, six ears of five neonates had no demonstrable DPOAEs during the first measurement and five of them had previously had a positive TEOAE screening result. One subject had a negative TEOAE screening result but no measurable DPOAEs.

The cause of the initially positive screening results for subjects NC and MV remained uncertain. However, in these two cases DPOAE screening provided no advantage over TEOAE screening because both methods had a positive result at first measurement. In contrast, the diagnosis of normal hearing through DPOAE screening in subject CH was made 6 weeks before the final diagnosis was made through ABR testing. TEOAEs were also not measurable at the second screening, but our method was not officially accepted as a screening device. Thus, the parents had an extended period of uncertainty and the child was subjected to the additional stress associated with elaborate examinations.

In the case of subject NB, repetitive colds possibly caused middle ear problems. Nevertheless, DPOAEs were detected since they are measurable at hearing loss levels up to 50 dB HL in ears with cochlear hearing loss (Boege and Janssen, 2002). Whereas the measurement after seven weeks revealed an estimated hearing loss of 30 – 40 dB HL at frequencies between 3500 and 4500 Hz, the values improved up to 20 – 30 dB HL after twelve weeks in the same frequency region. Due to the subject's blocked nose, breathing sounds resulted in an elevated noise floor. Since at least some otoacoustic emissions were measurable and a slight improvement was detected despite ongoing colds, the parents could be somewhat reassured.

Subject MP was the only infant with a negative TEOAE screening but no measurable DPOAEs. The results indicated a hearing loss of 30 dB HL at. Since TEOAEs disappear at even a slight hearing loss of 20 – 30 dB HL, the two results were not congruent. No further examinations could be done, however, so it remained unclear whether the TEOAE screening was false negative or the DPOAE measurement was false positive.

UNHS generally achieves a sensitivity of about 90% (Welzl-Müller, 1998). For DPOAEs, however, no values are available since the method is not standardized and pass criteria do not exist for this kind of hearing screening measurement in newborns (Barker et al., 2000).

4.4. Requirements for a screening

4.4.1. Criteria of normal DPOAEs

DPOAEs are often defined as normal through the SNR, which was 6 dB in the present study. Sufficient SNRs in neonates have been reported by Gorga et al. (2000) at 2, 3 and 4 kHz. Thus, these authors came to the conclusion that screening programs using DPOAEs should require reliable results at the mentioned frequencies.

Barker et al. (2000) also chose a SNR of 6 dB, and they required a DPOAE level exceeding –5dB. Other authors considered a SNR of 3 dB (Smurzynski, 1994) or 4 dB to be sufficient (Ochi et al., 1998), but they required a certain number of frequencies at which DPOAEs were measurable.

In the present study, DPOAEs were tested at 12 different frequencies and 10 pairs of primary tone levels so up to 120 data points could be obtained. Therefore, the criteria mentioned before were not taken into consideration in this study. Even if the subject woke up after one or two minutes, when only one or two frequencies for all of the ten different primary tone pairs had been tested, this was not seen as a reason for excluding the data from the analysis. Barker et al. tested only three frequencies for one pair of primary tone levels. Therefore, it was rather difficult to compare measurement criteria. The advantage of obtaining a large quantity of information had the disadvantage of an increased duration of measurement time. In our study 8 – 10 minutes were required per ear, but the number of frequencies and primary tone levels tested could easily be reduced in a future study.

To minimize the measuring time, stopping criteria could be defined, like fewer sweeps for the averaging procedure if the SNR is sufficiently high. On the other hand, the duration of measurement is acceptable when DPOAEs are seen as a second step in the diagnostic sequence.

Nevertheless, it was remarkable that only 6 of 134 ears had no demonstrable DPOAEs and for five of them the result was compliant with the TEOAE screening. Reproducibility was not tested since too much time would have been required; however, from the literature it is known that DPOAEs in neonates are less reproducible than those of adults because of higher noise floors.

One further aspect making it difficult to define normal criteria is the fact that all researchers have used different stimulus parameters in various subject populations. It was therefore difficult to compare the results.

Mean DPOAE levels in neonates and adults varied in certain frequency ranges depending on postconceptional age. Therefore, it might be necessary to use separate norms for newborns

tested some days after birth, for infants who are a few weeks old and for adults. In comparison to the adults, normative data for neonates might be the same for frequencies beyond 3000 Hz. In the lower frequency region, higher amplitudes of DPOAEs might be expected. For infants, higher DPOAEs might be expected at all frequencies, with mean average differences between 2 and 8 dB SPL.

4.4.2. Follow-up study and its consequences for hearing screening

The results obtained through the follow-up study showed that in the weeks following birth different processes take place in the neonatal ear. As already mentioned, it was assumed that residual amniotic fluid, maturational processes in the cochlea and ear canal impedance each seem to play an important role. Therefore, a slight hearing loss detected during the first days following birth does not have to have a pathological background. Results should be checked critically. As long as DPOAE amplitude is reduced for all primary tone levels at a specific frequency, i.e., slope of the DPOAE I/O-function is nearly unaffected, middle ear processes can be assumed. Additionally, a slight hearing loss detected solely in the high frequency region is a further criterion for detecting transitory sound conduction disturbances. Further diagnostic steps should not be considered until unusual slope profiles and steep growth functions are seen.

Besides the amplitudes of the DPOAE I/O-functions, the results of the follow-up study in neonates were quite similar to the results obtained for the norm group, i.e., similar slope profiles and shape of growth functions. Since the higher amplitudes in neonates were mainly a result of a smaller ear canal volume, it can be concluded that after a few weeks residual amniotic fluid, in particular, plays an inferior role. In case of a positive screening result shortly after birth, these possible causes should be explained to the infant's parents.

DPOAE testing demonstrates superior frequency specificity compared to TEOAEs and ABR, making it a desirable complement to further diagnostic evaluations. A reliable and easy test is especially important for children who are at risk for hearing impairment and for whom regular hearing evaluation is necessary.

4.4.3. Possible source of error during measurement

An important aim of screening methods is to avoid false positive results. For obtaining a reliable DPOAE measurement in subjects with normal hearing, several aspects play an important role, especially for neonates.

A good probe fit is one important factor for obtaining reliable results. Since neonates often move their head during measurement, it is very difficult to assure proper placement of the

probe. In general, it is more complicated to test newborns than cooperative adults, except while sleeping. Restlessness results in longer test time, elevated noise floor, reduced reproducibility, and, in the worst case in false screening results.

Neonates are more likely to have obstructed ear canals, but earwax, for example, should have been removed prior to testing since TEOAE screening shoul have already been performed. Otoacoustic emissions are very sensitive for middle ear problems. Maxon et al. (1993) assumed the presence of more birth-related debris in the ear canal of younger children and thus proposed a cleaning procedure. Additionally, they suggested testing more than 24 h after birth would decrease the false positive rate.

Neonates have a shorter ear canal and thus a much smaller volume than adults. Through calibration, the smaller volume was measured and the stimulus parameters were adapted in our study. Nonetheless, a calibration mistake in the high frequency region was assumed since the correlation between the subjective and objective hearing tests of the adults was not very satisfying (Fig. 3.4.B). Data at 1000 Hz should also be treated critically when looking at the growth functions of the neonate and norm groups (Fig. 3.3). In contrast to all other DPOAE I/O-functions this one was shallow without showing any saturation. As already mentioned, physiological noise plays an important role especially at low frequencies like 1000 Hz.

Standing waves were a problem for calibration, but in the shorter ear canal of the newborns they played an inferior role. They had to be taken into account primarily for the norm group.

Furthermore, the room in which the measurement was performed was not as quiet as an insulation cabin. From time to time, nurses or other clinical staff had to enter. This contributed to a elevated background noise or caused the neonate to wince, possibly changing the probe fit. However, when leafing through the measurement reports, improvements were noted, especially concerning the noise level. These were considered to result from increased experience in performing the test. Finally, there were a lot of factors that were difficult to control and these certainly contributed to the false positive rate of screening results.

4.5. Comparison of TEOAE-screening and DPOAEs

4.5.1. Clinical application of DPOAEs and TEOAEs

Otoacoustic emissions have potential as a screening tool for auditory dysfunction in neonates. Kok et al. (1993) recommended not screening neonates before the fourth day of life, while Ochi et al. (1998) favored the third day. However, there is one important factor in favor of screening children during the first days of life: they sleep during most of the day. The older they become, the less they sleep and the test conditions become increasingly difficult. This

was confirmed in the present follow-up study in which waiting periods of 1 – 2 hours were sometimes necessary before the newborns fell asleep, thus allowing the measurement to be performed. The best results were obtained shortly after feeding. Even though appointments for testing were made with the parents, waiting periods occurred. One reason is that neonates have no fixed circadian rhythm, so exact feeding times cannot be predicted.

For UNHS it is important to test babies at a time when they are readily available; thus, the period just before hospital discharge is ideal. Afterwards, children are regularly seen in the practice of their pediatrician but only for a short period of time. If the child is too restless or is crying, a repetition of measurement is difficult to perform. This problem is much easier to manage in the hospital, where a second attempt can be made some hours later, perhaps soon after feeding. In the neonatal care unit of the gynecological hospital of the Technical University Munich, UNHS is not performed before 48 hours after birth. In case of a "fail" result, babies are retested one day later. After hospital discharge the compliance of parents is not very good. Therefore, the new method used in this study could become an important step in optimizing hearing screening, since it can detect transitory sound conduction disturbances that are possibly responsible for a false positive screening result.

The applicability of an examination in children is greatly influenced by the duration of the test. Heinemann and Bohnert (2000) tested a TEOAE-screening-device and measured each ear for 1.2 minutes with an additional minute for preparation. Even in restless babies the measurement could be performed. As already mentioned in 4.4.1, further stopping criteria can reduce the measuring time of DPOAE testing. Especially when considering DPOAE testing as a second measurement in a two-step screening process, the tests have significant advantages in comparison to ABR. Heinemann and Bohnert also tested two new ABR-screening-devices. The measuring time for both was around 5 minutes per ear, with 5-10 minutes required for preparation because electrodes had to be fixed to the head. Thus, the testing time was comparable to our method, but information received in comparison was neither frequency-specific nor quantitative concerning hearing capability. No other testing method was able to present such detailed information on the functioning of the cochlea as measurement of DPOAEs.

4.5.2. Agreement between TEOAE and DPOAE outcomes

Since DPOAE screening has not been standardized and no universally accepted pass criteria has been devised, it is difficult to compare the method with TEOAE screening. Shi et al. (2000) tried to compare the two methods and came to the conclusion that agreement between the test outcomes was very poor. In their study, two groups with mean ages of 2.7 and 37.5

months were tested. Especially for the younger age group, agreement of screening outcomes for various pass/fail criteria were low; this was attributed to higher physiological noise in that group and the greater probe tip instability in younger infants due to uncontrollable behavior. Furthermore, the cochlear responses were evoked through different kinds of stimulation (transient stimulus versus two pure tones) and different stimulus levels. Thus, different portions of the cochlea were concerned.

Test results depend on the alertness of the child. In general, the reason for few data points in the subjects of this study was an elevated noise floor. TEOAE screening has a much shorter test time in comparison to DPOAE measurement. This explains the normal outcomes obtained at some frequencies and the lack of emissions at others during a single test procedure.

Among the neonates with positive screening results, there was only one case (subject MP) in which the test results differed. For the applied method, a good correlation between DPOAE and TEOAE screening results was assumed. Smurzynski (1994) also reported good correlation between the two types of OAEs. He even observed increasing amplitudes with increasing PCA for both types of OAEs.

4.5.3. Advantages of the new method and future application

The method of DPOAE measurement described in the present study has the advantage of providing frequency-specific and quantitative information on hearing capability. There is currently no other objective testing method that provides such detailed information on the functioning of the cochlea. The method was previously applied successfully in adults (Boege and Janssen, 2002).

In the early postnatal period the neonates tested had a slight hearing loss in the high frequency range. Nevertheless, the DPOAE I/O-functions did not show a steep run or high values in the slope profile. Steep DPOAE I/O-functions would speak for pathological processes in the inner ear. Therefore, transitory sound conduction disturbances can be assumed. This means it is possible that the new method could additionally distinguish between pathological and non-pathological processes in case of a positive TEOAE screening result.

In the present study, four of 103 neonates had a positive TEOAE screening result shortly after birth, but DPOAEs were not measurable. Nevertheless, in two of those four newborns (CH and NB) normal hearing status could have been diagnosed much earlier by testing DPOAEs rather than TEOAEs or ABR. As the subject sample was small, these results are preliminary and further examinations are necessary.

A possible next step is the development of a hand-held system that can measure TEOAEs as well as DPOAEs. In case of a positive TEOAE screening result DPOAEs could be measured afterwards. Since parental compliance is best during hospitalization, it is important to detect hearing impairment as early as possible following birth. Both test methods should be performed automatically so that they can be implemented by a nurse or an audiological assistant.

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5. Summary

A lot has been done recently to examine the applicability of DPOAE measurement in neonates and to evaluate UNHS, since the method provides frequency-specific information on cochlear function. The aim of this study was to examine the applicability of estimating hearing thresholds in neonates by means of extrapolated DPOAE I/O-functions. A further question was whether the method can detect transitory sound conduction disturbances caused by residual amniotic fluid in the early postnatal period.

In the study, DPOAEs were recorded in 134 ears of 103 neonates shortly after birth. DPOAE I/O-functions were measured at 12 frequencies between 1000 and 8000 Hz, and an auditory threshold was reconstructed using the estimated DPOAE threshold level from extrapolation. Sixteen ears of 13 neonates underwent a follow-up measurement at least four weeks later to examine changes in the transitory sound conduction disturbances.

The results of the first measurement were similar to those in adults, except in the high frequency region, where a slight hearing loss was estimated. The DPOAE I/O-functions showed a decreased DPOAE level in the high frequency range, while the compressive shape of the growth functions, indicating transitory middle ear disturbances, remained the same. In the follow-up study, the DPOAE level was higher at nearly all frequencies in comparison to the first measurement. The estimated hearing loss between the first and second measurement was significantly lower for nearly all frequencies.

The temporary reduction in DPOAE amplitude seen during the first days after birth was primarily due to residual amniotic fluid in the middle ear and thus constituted a temporary hearing loss related to sound conduction. This view was supported by the fact that the DPOAE I/O-functions at the first measurement demonstrated no steep run or high values in the DPOAE slope profile. Residual amniotic fluid offers a further explanation for false positive screening results obtained shortly after birth.

The results of this study support the view that measurement of DPOAEs is a useful method for obtaining more detailed information on the hearing status of infants. It is more frequency-specific than both TEOAE and ABR screening. Furthermore, the testing time is shorter than that of ABR, and the method is easier to handle. Measurement and data analysis are performed automatically. Therefore, the method fulfills essential criteria for UNHS.

Using the new method of extrapolating DPOAE I/O-functions for estimating the hearing threshold, DPOAE screening is able to quantify hearing loss at selected frequencies. The

presented method could thus play an important role in audiologic hearing screening, perhaps as a second step following a positive TEOAE screening result.

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7. Appendix

7.1. Table I

SPL > HL

f [kHz]	dL [dB]
1	-11
1.5	-14
2	-19
2.5	-14
3	-11
3.5	-9
4	-7
4.5	-9
5	-12
6	-15
7	-22
8	-26

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