Chapter 1: Orientation and Statement of the Problem

1.1 Introduction

The quest for the development of an optimal objective diagnostic procedure to aid in the assessment of persons regarded as *difficult-to-test*, such as neonates and infants, has kept many researchers intensely occupied in the last two decades (Kemp, 1979; Tanaka, O-Uchi, Arai & Suzuki, 1987; Bonfils & Uziel, 1989; Lonsbury-Martin, 1994; Stover, Gorga & Neely & Montoya, 1996a; Koivunen, Uhari, Laitakari, Alho & Luotonen, 2000). Despite phenomenal advances in the ability to record electrical potentials generated at various levels of the nervous system and discoveries of active biological mechanisms in the cochlea, audiologists are still spending large amounts of time (Lee, Kimberley & Brown 1993; Vohr, White, Maxon & Johnson, 1993; Quinonez & Crawford, 1997) and money (Mauk & Behrens 1993; Weber, 1994) to attempt to evaluate difficult-to-test populations with equipment that allows only a limited frequency range of evaluation (Kemp & Ryan, 1993).

The purpose of this chapter is to present a brief overview of the ongoing struggle for the development of an optimal objective diagnostic audiologic procedure to aid in the assessment of difficult-to-test populations. This overview clearly indicates the need for a simple, cost effective, non-invasive yet accurate and objective method and states the reasons for difficulties experienced in this seemingly impossible quest. Furthermore, this chapter will present the purpose of this study, and plot a brief course of how the main objectives would be obtained. Lastly, this chapter will outline the objectives of following chapters to provide a more detailed description of the scope and objectives of the study.

1.2 The Origin of Objective Procedures

For many decades, diagnostic audiology relied on behavioral testing procedures in which hearing thresholds were determined by studying the listener's motor responses (Yantis, 1994). The first behavioral audiology test battery was developed in 1920 when bone conductors and speech channels became a standard feature included in an audiometer's capabilities (Brunt, 1994). For three decades, audiological tests were developed with only these basic features. Tests that were developed included the ABLB test for loudness growth to indicate cochlear pathology in the 1930s, the tone decay test to indicate retrocochlear pathology in the 1940s, and the SISI (Short Increment Sensitivity Index) for cochlear pathology in the 1950s (Brunt, 1994).

Prior to the 1960's, the evaluation of *difficult-to-test* populations, such as neonates, infants and very young children typically consisted of the observation of behavioral responses to an array of noise makers, such as bells, whistles, rattles, rustling paper and a spoon stirring in a cup (Ewing & Ewing, 1944). Hardy (1962) also used phonemes such as "S,S,S" presented behind the child to observe head turning responses but concluded that if the child does not respond, it can be suspected that something is wrong, although not necessarily that a hearing loss existed. Responses observed in neonates usually involved the moro reflex and for older infants localization responses and conditioned orientation reflexes (Suzuki & Ogiba, 1961). Before the development of objective diagnostic procedures in the 1970's, hearing tests to evaluate neonates and infants were not geared to evaluate pure tone thresholds objectively and accurately (Martin, 1984).

The first objective physiological procedure was developed in the 1970s. Progress in technology enabled audiologists to measure minimal changes in air pressure in the external meatus, which resulted in a completely new diagnostic tool, tympanometry. This allowed audiologists to obtain information not only about middle ear pressure and tympanic membrane movement but also about the stapedius reflex. Immittance testing enabled the Audiologist to obtain a variety of objective diagnostic functions, such as an indication of middle ear pathology, cochlear pathology when loudness recruitment is present, and retrocochlear pathology when reflex decay occurs. What is more important is that immittance procedures allowed audiologists to verify results obtained with behavioral audiometry objectively, for the first time. The prediction or evaluation of pure tone thresholds in difficult-to-test populations was still problematic. One application of the acoustic reflex, the SPAR-test (sensitivity prediction with the acoustic reflex), was developed by Jerger in the 1970s to predict hearing ability (Jerger, 1974). SPAR predicts hearing ability as normal, moderately impaired, or severely impaired. However, SPAR was influenced by a number of variables, such as chronological age (children between 0 and 10 are most accurately predicted), minor middle ear abnormalities, and audiometric configuration and still did not predict specific decibel levels for pure tones. Even though prediction of moderate hearing levels was only slightly better than chance, it offered a rapid estimate of hearing sensitivity useful for screening purposes (Northern & Gabbard, 1994).

The second development toward objective audiological measurements also occurred in the 1970s when audiologists began to measure the electric potentials of the nervous system with surface electrodes. Auditory evoked potentials (AEPs) occur in different time intervals after stimulation and provide information about the cochlea (EcoghG), auditory nerve (auditory brainstem response (ABR)), and brainstem (middle latency response (MLR) and late latency response (LLR)). AEPs measure the integrity of the auditory pathway at certain sites and are not a test of hearing such as pure tone measurement, which evaluates the entire auditory system (Cope, 1995). However, AEPs not only enabled audiologists to confirm behavioral test results but also to measure auditory status at certain sites in difficult-to-test populations. (Robinette, 1994). ABR is still currently the preferred objective diagnostic method in the evaluation of neonates and very young infants (Weber, 1994) despite limitations such as a limited frequency area that can be evaluated (Kemp & Ryan, 1993), lengthy test times, expense and expertise required for diagnostic applications and the unfortunate possibility of sedation in the case of very young children (Hall III & Mueller III, 1997). The quest for an optimal procedure to determine pure tone thresholds in difficult-to-test populations rapidly, economically, accurately and across a wide range of frequencies continued.

At the end of the 1970s, another objective way to evaluate hearing ability was discovered by David Kemp (1978), namely otoacoustic emissions—that is, energy generated by a normal cochlea either spontaneously or in the presence of acoustic stimulation. Kemp's (1978) original reports were greeted rather skeptically, and much early research only replicated his study to confirm the presence of otoacoustic emissions. After two decades of intensive research, however, there is currently much excitement among researchers, since certain types of otoacoustic emissions such as transient otoacoustic emission (TEOAE) prove to be highly applicable in the areas of hearing screening and distortion product otoacoustic emissions (DPOAEs) in screening and even diagnostic audiology (Kummer, Janssen, & Arnold, 1998; Martin, Probst, & Lonsbury-Martin, 1990b; Stach, Wolf, & Bland, 1993; Stover, et al. 1996a).

Otoacoustic measurement will certainly never replace pure tone audiometry, immittance, or ABR, but OAEs reveal diagnostic information regarding the auditory system that is not available from any other test and offers the possibility of objective evaluation of pure tone thresholds in special populations. Many researchers hoped that this relatively new field in audiology would prove to be the long-awaited objective, rapid, and accurate test of auditory function (Kemp, 1990; Lee, et al. 1993; Kimberley Hernadi, Lee & Brown 1994b; Danhauer, 1997).

The hope that OAEs are the optimal new objective test of hearing arose despite facts that suggest that this prospect may be impossible. OAEs measure the functioning of the outer hair cells (OHC), which apparently is only involved with the amplification of sounds and fine-tuning of the cochlea to specific frequencies (Kemp, 1978). It is the inner hair cells that receive 95% of the afferent auditory nerve fibers to carry auditory signals to the brain (Dallos, 1997). Furthermore, pure tone threshold estimation involves measurement of the entire auditory system, outer-, middle- and inner ear as well as the auditory nerve, brainstem and cortex. OAEs evaluate OHC functioning only. Despite these fundamental differences in the two procedures, many researchers found a significant correlation between one type of emission, the distortion product otoacoustic emission (DPOAE) and pure tone thresholds (PTTs) (Probst & Hauser, 1990; Lonsbury-Martin, Harris, Stagner, Hawkins & Martin, 1990; Avan, Elbez & Bonfils, 1997; Nieschalk, Hustert & Stoll, 1998). Good correlation between DPOAEs and PTTs was also found for degree and configuration of hearing loss (Martin, Ohlms, Franklin, Harris, Lonsbury-Martin, 1990). These findings fueled expectations that DPOAEs could possibly predict pure tone thresholds objectively (Kemp, 1997).

Many researchers studied the correlation between DPOAEs and PTTs (Martin et al. 1990a; Lonsbury-Martin et al. 1990; Probst & Hausser, 1990; Gorga, Neely, Bergman & Beauchaine, 1993) and some attempted to predict PTTs as normal or hearing-impaired with DPOAEs (Kimberley, Kimberley & Roth 1994a; Kimberey et al 1994b; Moulin et al 1994; De Waal, 1998). Several difficulties were experienced in the development of DPOAEs as a diagnostic procedure: Firstly, the distortion product has numerous stimulus parameters that should be carefully chosen to ensure optimal measurement and many researchers investigated optimal levels and ratios for input stimuli (Gaskill & Brown, 1990; Avan & Bonfils, 1993; Stover et al. 1996a; Mills, 1997). Secondly, the measured responses are often "noisy", incomplete, (Probst & Hauser, 1990; Stover et al. 1996a) idiosyncratic (Lonsbury-Martin, Harris, Stagner, Hawkins, & Martin, 1990) and complex which makes the determination of the non-linear correlation between DPOAEs and PTTs even more difficult (Ruggero, 1993; Kemp, 1997; Nakajima, Mountain & Hubbard, 1998). Thirdly, the non-linear correlation between the two data sets of which one is noisy and incomplete as well as the numerous variables that influence that correlation require a special data processing technique that is capable of predictions of pure tone thresholds based on the determined correlation between the data sets (Kimberley et al. 1994a). Many researchers used conventional statistical methods such as multivariate discriminant analysis (Kimberley et al. 1994b; Vinck, Cauwenberge, Corthals & De Vel, 1998) and struggled with the noisy incomplete data, non-linear correlation and number of variables involved. Fourthly, prediction of normal hearing at frequencies lower than 1000 Hz proved to be problematic for most researchers due to the rising noise floor caused by subject artifacts such as breathing and swallowing (Gorga et al. 1993) and limitations in measuring equipment (Kemp, 1997). Lastly, the research needed to fully understand the fine structure of the distortion product and the significance of other distortions as the cubic distortion tone (2f1-f2) in pure tone prediction is only scraping the surface (Kemp, 1997). The quest to predict pure tone thresholds with DPOAEs objectively, rapidly, economically and accurately is apparently still limited to categorization of hearing ability as normal or impaired at frequencies above 1000 Hz (Gorga et al. 1993; Kimberley et al. 1994a; Kimberley et al. 1994b; Stover et al. 1996a; Kummer et al. 1998a; Zhao & Stephens, 1998).

A new form of information processing, called artificial neural networks (ANNs), was applied to this problem (De Waal, 1998; Kimberley et al. 1994a) that excel in dealing with noisy, complex or incomplete data sets (Nelson & Illingworth, 1991), non-linear correlations (Rao & Rao, 1995) and predictions based on learned correlations (Blum, 1992).

Kemp (1994a) found the neural network approach to be more effective in the classification of normal and impaired hearing than multivariate statistical methods. De Waal (1998) predicted normal and impaired hearing at frequencies ranging from 500 Hz to 4000 Hz and predicted normal hearing as low as 500 Hz objectively with 92% accuracy for the first time. The fore mentioned study also indicated that it is probable that pure tone thresholds could be predicted for impaired hearing within 10dB for hearing loss up to 65dB HL if the neural network has enough data to train on. The application of the neural network approach to this field of diagnostic audiology revealed that distortion product otoacoustic emissions are suitable as a diagnostic test of hearing to evaluate pure tone thresholds in normal and hearing-impaired ears objectively, accurately, rapidly, economically across a wide range of frequencies.

However, certain difficulties were encountered in the De Waal (1998) study that could have influenced prediction accuracy negatively. These included:

- The search for optimal neural network topology such as desired number of middle level neurons, input data manipulation and error tolerance levels.
- Variables included in neural network training such as DPOAE amplitude that made the neural network so complex that no convergence was possible and the question of specificity of which the age variable can be presented to the neural network.
- Optimal definition of DPOAE threshold, to ensure that all present responses are valid yet no valid responses are discarded.
- Which aspect of the distortion product to best correlate to pure tone thresholds- the f1 frequency, f2 frequency, 2f1-f2 frequency or a combination of frequencies.

1.3 Purpose of This Study

Against this background it seems possible to develop DPOAEs as an objective pure tone predictor with the use of artificial neural networks to aid in the assessment of difficult-to-test populations.

The purpose of this study is therefore to further develop DPOAEs as an objective diagnostic test of hearing by addressing the problems experienced in the De Waal (1998) study to improve prediction accuracy of pure tone thresholds from 500 Hz to 4000 Hz with DPOAEs and artificial neural networks. Optimal parameters for DPOAE measurement will be identified with an in-depth literature study and applied to measure DPOAE responses in subjects with normal hearing, various degrees of sensorineural hearing loss and of various ages. The correlation between DPOAEs and pure tone thresholds (PTTs) will be studied with the use of artificial neural networks. There will be extensively experimented with optimal neural network topologies, error tolerance levels, manipulation of input data and the inclusion of DPOAE amplitude for neural network training. The effect of DPOAE threshold defined as 1, 2 or 3dB above the noise floor, the effect of the inclusion or omission of noisy low frequency data on prediction accuracy and specificity of which the age variable should be presented to the neural network will be investigated. The main purpose of this study is to improve prediction accuracy of PTTs at 500, 1000, 2000 and 4000 Hz with DPOAEs and ANNs

1.4 Outline of the Thesis

Chapter One: Orientation and Statement of the problem

This chapter provides a brief overview of the development of objective tests in audiology, formulate the need for an accurate, cost effective procedure and delineate the purpose of this study, which is to further investigate DPOAEs as a diagnostic test of hearing by improving prediction accuracy of PTTs with DPOAEs and artificial neural networks (ANNs).

Chapter Two: The Quest for Optimal Pure Tone Threshold Prediction

The second chapter will focus on current objective diagnostic procedures for pure tone evaluation purposes, motivate their need and discuss their limitations in the evaluation of certain populations. This chapter will also concentrate on specific prerequisites that objective tests should have as well as the data processing techniques used to develop these tests, to be considered effective and efficient. Special attention will be given to the history of the use of distortion product otoacoustic emissions (DPOAEs) to predict pure tone thresholds (PTTs), the limitations of previous studies and reasons for their struggle.

Chapter Three: Parameters that Influence Pure Tone Threshold Prediction Accuracy with Distortion Product Otoacoustic Emissions and Artificial Neural Networks

The third chapter will be a discussion of all the parameters that influence prediction accuracy of PTTs with DPOAEs and ANNs. The discussion will be divided into two segments, first, parameters that influence the distortion product in the recording, analysis and interpretation of measurements and second, parameters that influence the neural network in the designing-, training-, prediction- and analysis phase of operation.

Chapter Four: Research Methodology

Chapter four will be a discussion of the methodology for data collection, preparation and analysis, apparatus, subjects, the research design and the procedures chosen for optimal neural network functioning.

Chapter Five: Results

Chapter five will present results of all experiments: Pure tone threshold prediction accuracy at 500, 1000, 2000 and 4000 Hz, and the effect of subject-, DPOAE-, and ANN variables experimented with to determine effects on prediction accuracy.

Chapter Six: Discussion and Interpretation of Results

Chapter six will discuss and interpret all findings in terms of significance as well as readiness for broad clinical use. A few interesting case studies will also be discussed.

Chapter Seven: Summary, Evaluation of the Study and Conclusion

The last chapter will evaluate this study in terms of validity, reliability and limitations and make recommendations for future research.

References

Only references mentioned in this thesis appear alphabetically in the reference list.

1.5 Conclusion

> "It should be clear that in spite of the technical advancements made in detecting [DPOAEs], the relation between DPOAEs and sensorineural hearing loss is not fully understood. There is no physiological basis for assuming that DPOAE measures ought to perfectly correlate with pure-tone threshold, even in the case of a purely cochlear hearing loss. Currently available empirical evidence, however, suggests that the general relationships between pure-tone threshold and DPOAE will serve as an important tool for the audiologist" (Kimberley, Brown & Allen, 1997:201).

Chapter 2: The Quest for Optimal Objective Pure Tone Threshold Prediction

2.1 Introduction

David Kemp (1978) first described otoacoustic emissions (OAE) from the human ear and ignited a tremendous interest in these measurements to develop another objective diagnostic test of hearing. These relatively easy measurable active responses from the cochlea to sound stimulation, due to the basilar membrane's natural ability to amplify sound and tune in to specific frequencies, have kept many researchers occupied in the last two decades (Elberling, Parbo, Johnsen & Bagi, 1985; Bonfils, Avan, Francois, Marie, Trotoux & Narcy, 1990; Brass & Kemp, 1994; Kossl & Boyan, 1998). The main interests of most studies were to attempt to categorize pure tone sensitivity with these measurements as normal or impaired (Kimberley, et al. 1994b; Hurley & Musiek, 1994; Kimberley, et al. 1994a) or to gain more information regarding the site-of-lesion in diagnostic audiology (Tanaka, et al. 1987; Ohlms, Lonsbury-Martin & Martin, 1990; Robinette, 1992; Moulin, Bera & Collet, 1994). Most researchers, however, found it extremely difficult or even impossible to predict impaired pure tone thresholds (PTTs) or to categorize hearing ability at low frequencies as normal or impaired with distortion product otoacoustic emissions (DPOAEs)(Gorga, et al. 1993; Kimberley et al. 1994b; Stover, et al. 1996a; Zhao & Stephens, 1998). This unsatisfactory prediction of PTTs with DPOAEs is probably due to the large number of DPOAE stimulus parameters that influence optimal measurement (Bonfils, Avan, Londero, Trotoux & Narcy, 1991; Gorga, et al. 1993), the complex nonlinear nature of the measured responses (Nakajima, et al. 1998; Kummer, et al. 1998) and the inability of conventional statistics to address this problem sufficiently (Kimberley et al. 1994a).

This seemingly impossible quest to predict pure tone thresholds (PTTs) accurately with DPOAEs arises not from the need to replace existing conventional behavioral evaluation procedures, but to aid in the assessment of pure tone sensitivity in difficult-to-test populations such as neonates, infants, malingerers and the crucially ill (Balfour, Pillion, & Gaskin, 1998).

The purpose of this chapter is to evaluate current objective diagnostic procedures available in the assessment of pure tone thresholds in difficult-to-test populations, to identify their need and limitations and formulate the requirements for an optimal objective diagnostic procedure. The history of the development of DPOAEs as a pure tone predictor will be reviewed extensively, and evaluated to identify limitations and postulate reasons for their struggle. Prerequisites for optimal data processing techniques in the development of an objective diagnostic procedure will also be formulated.

The following section will discuss objective procedures in audiology to better understand the need for an optimal non-invasive, rapid, accurate, simple and cost-effective test to aid in the assessment of difficult-to-test populations.

2.2 Objective Diagnostic Procedures

What is meant with an *objective* test, why does audiologists have to rely heavily on these measures when assessing *difficult-to-test populations* and who is regarded as difficult-to-test?

2.2.1 Overview and Definition of Terms

An *objective test* according to Cope (1995) requires no voluntary response from the patient that an auditory stimulus was perceived. Even though the patient may still influence the results by interfering with the procedure, the subjectivity is transferred to the clinician who interprets the results. Objective tests are not a measurement of hearing as such, but evaluate the integrity of the auditory pathway at various levels, never in its entirety. The value of objective tests becomes apparent in the evaluation of subjects who cannot participate in conventional behavioral audiometry to respond to auditory stimuli voluntarily. Subjects who are too young, critically ill, subconscious, mentally incapable of providing cooperation or subjects who refuse to cooperate for whatever reasons, are all considered to be *difficult-to-test* and it is in the evaluation of these populations that audiologists have to rely heavily on objective evaluation procedures (Balfour, et al. 1998).

2.2.2 Current Objective Procedures Available to Predict Pure Tone Thresholds

As was stated in the definition of an objective test in the previous paragraph, objective tests measure the integrity of the auditory pathway at various levels and is not a measurement of hearing such as pure tone audiometry. Objective tests such as acoustic immittance measurements evaluate the mobility of the middle ear when air pressure is varied with tympanometry, or the ease of flow of energy through the middle ear in static acoustic immittance, or the lowest intensity needed to elicit a muscle contraction in the middle ear with acoustic reflex measurements (Block & Wiley, 1994). These measurements are valuable in site of lesion testing in diagnostic audiology and provide useful information regarding certain components of the auditory system but do not provide information about hearing sensitivity as such (Cope, 1995). Certain objective measurements however, have been adapted in an attempt to predict pure tone thresholds, such as the SPAR, ABR and some types of OAE measurements. Since the scope of this chapter is to discuss the quest for optimal objective pure tone threshold prediction, only those objective procedures that attempt to predict pure tone thresholds will be discussed in more detail.

2.2.2.1 Sensitivity Prediction with the Acoustic Reflex (SPAR)

SPAR was developed by Jerger in 1974 (Jerger, Burney, Mauldin & Crump, 1974) to predict hearing ability into categories as normal, moderately impaired, or severely impaired. This technique uses the difference between the thresholds of pure tone acoustic reflexes at 500, 1000 and 2000 Hz and broadband noise reflexes to predict hearing sensitivity. Normal hearing ability was accurately predicted 100% of the time when the 1000 Hz acoustic reflex threshold (ART) is 95 dB SPL or less and the noise-tone reflex difference is more than 20 dB. Severe hearing loss was accurately predicted 85% of the time when the broadband noise (BBN) threshold is more than 95 dB SPL. Moderate hearing losses were predicted accurately 54% of the time when the noise-tone ART difference is less than 20 and the BBN reflex threshold is 95 dB SPL or less. However, SPAR is influenced by a number of variables, such as chronological age (children between 0 and 10 are most accurately predicted), minor middle ear abnormalities, and audiometric configuration. Even though prediction of moderate hearing levels is only slightly better than chance, in difficult-to-test populations SPAR can often offer a rapid, economical, and objective estimate of hearing sensitivity and is also useful in screening (Northern & Gabbard, 1994).

2.2.2.2 Sensitivity Prediction with Auditory Evoked Potentials

The measurement of auditory evoked potentials (AEPs) involve the extraction of tiny electrical amplitudes of the auditory system from larger signals such as electroencephalographic (EEG) activity and other general muscular activity by using surface electrodes and signal averaging techniques.

Auditory evoked potentials (AEPs) occur in different time intervals after stimulation and provide information about the cochlea, auditory nerve, and brainstem. AEPs are usually classified by their "latency epoch," the time domain within which the response occurs after stimulus onset (Ferraro & Durrant, 1994). AEPs occurring in the first 10–15 milliseconds are known as short latency responses (SLRs). SLRs include the auditory brainstem response (ABR) as well as components preceding the ABR that are recorded via cochleography (ECoghG). ECoghG can be used in pure tone sensitivity prediction to enhance wave I in ABR testing, when test conditions are less than optimal or when a hearing loss is present. SLRs arise from the periphery and brainstem (Ruth, 1994).

Middle latency responses (MLRs), which refer to components in the latency epoch of 10–50 milliseconds, are generated in structures beyond the inferior colliculus (Kraus, Kileny, & McGee, 1994). MLRs are clinically used to objectively determine hearing ability in the lower frequencies. They are also used to assess the cochlear implant function and to localize auditory pathway lesions (Kraus et al. 1994). However, MLRs are affected by sleep and cannot be detected in certain phases of sleep. It is possible to monitor sleep phases with EEG measurements and to conduct MLR testing only in favorable sleep periods, but this requires much more expertise and expensive equipment. The fact that MLRs are affected by the subject's level of consciousness has limited their popularity as an objective diagnostic procedure (Ferraro & Durrant, 1994).

Components generated beyond 50–80 milliseconds post-stimulus onset are long latency responses (LLRs) and are cortically generated (Kraus et al. 1994). An example of an LLR measurement is the N_1-P_2 Complex, which was successfully used as an indicator of hearing sensitivity in difficult-to-test populations and also to detect lesions in the central auditory pathway (Ferraro & Durrant, 1994). Just like the MLR, the N_1-P_2 Complex is sensitive to the subject's state of consciousness. Another example of LLR is the $P_{300,}$ whose most common uses include studies of aging, dementia, and attention disorders (Ferraro & Durrant, 1994).

The ABR dominated clinical attention to AEPs for about a decade and is still a very popular test of auditory function for difficult-to-test populations (Ferraro & Durrant, 1994). Behavioral evaluation of very young infants relies on spontaneous responses such as eye and head movements. Even with some kind of reinforcement, these responses cannot be elicited near the threshold value. Presentation of stimuli is via loudspeakers, which does not provide information about hearing ability in separate ears. All these limitations of behavioral hearing testing made ABR the preferred objective audiologic technique for infants younger than 6 months (Weber, 1994). With ABR, stimuli are presented via earphones, making it possible to test the hearing status of the individual ears. ABR enables the audiologist to obtain responses to low stimulus intensity levels from sleeping infants. As Robinette (1994) stated, the ABR is popular in the evaluation of hearing when traditional behavioral tests are precluded or their results are equivocal.

The ABR is, however, not without its own shortcomings. First, the frequency range in which hearing ability can be determined with ABR is limited. ABR testing with click stimuli provides only a one-point audiogram in the 2000–4000 Hz region. This is due to the type of stimuli needed to elicit an ABR—namely, abrupt onset acoustic clicks. The more abrupt the stimulus onset, the more neural fibers will respond in synchrony and the more clearly defined the ABR (Weber, 1994). The acoustic click has its greatest energy around 3000 Hz, therefore creating the stimulus range from 2000 to 4000 Hz.

This aspect implicates another limitation: If hearing in the 2000 to 4000 Hz region is normal, a hearing loss in lower frequencies can be overlooked. According to Kemp and Ryan (1993), a passable ABR response can be obtained during screening from a limited region of normal high frequency hearing although medium and low frequency hearing may be seriously impaired.

Attempts to gain information about the low frequencies created a new set of problems. The use of low frequency tone bursts with abrupt stimulus onset resulted in high frequency contamination. (An abrupt stimulus onset might stimulate broad areas of the basilar membrane.) Investigators have used several alternative techniques in an attempt to gain reliable and frequency-specific low frequency information such as masking techniques and filtering. A study by Balfour et al. (1998) conducted in clinical settings in the United States, indicated that the availability of filters and attenuators in ABR equipment in most clinical settings is very limited and that if tone burst stimuli are utilized, that they are unmasked for most facilities. Therefore, the quest continues for a sensitive electrophysiologic measure of low frequency hearing status that can be used with difficult-to-test populations (Weber, 1994).

The second shortcoming of ABR testing is the amount of time the test requires. It can take more than 30 minutes to obtain a single ABR threshold for each ear (Weber, 1994).

The third weakness is the possibility of sedation. When testing hearing ability close to the threshold, it can be affected by movement artifacts. The child should therefore be as still as possible, preferably asleep. When infants younger than 6 months are tested, it can be assumed that there will be periods of sleep long enough for ABR testing. For older infants, it is unfortunately often necessary to ensure adequate test conditions by giving the child some form of sedative, usually administered orally (Weber, 1994).

Lastly, ABR performed for diagnostic purposes requires highly trained personnel and is a relatively expensive procedure (Musiek, Berenstein, Hall III, & Schwaber, 1994).

At the end of the 1970s, David Kemp discovered a feature of normal cochleae that led to another objective way to evaluate hearing ability. He discovered otoacoustic emissions, which is tiny amounts of energy released by the outer hair cells. The energy is generated from a normal cochlea either spontaneously or in the presence of acoustic stimulation. It appeared that normal cochleae emitted these responses, whereas ears with a hearing loss >35 dB HL did not.

Kemp's (1978) original reports were greeted rather skeptically, and much early research only replicated his study to confirm the presence of otoacoustic emissions. After two decades of intensive research, this method is now generating much excitement among researchers, since certain types of otoacoustic emissions are proving to be highly applicable in the areas of hearing screening and even diagnostic audiology (Kummer et al. 1998; Martin, et al. 1990b; Stach, et al. 1993; Stover, et al. 1996a). Many researchers hope that this relatively new field in audiology will prove to be the long-awaited objective, rapid, and accurate test of auditory function to aid in the assessment of difficult-to-test populations.

Otoacoustic measurement will certainly never replace pure tone audiometry, immittance, or ABR, but OAEs offer diagnostic information regarding the auditory system that is not available from any other test. This new objective procedure deserves to be evaluated.

2.2.2.3 Otoacoustic Emissions

Otoacoustic emissions are low intensity acoustic signals generated by the outer hair cells (OHC) in the organ of Corti on the basilar membrane either spontaneously or in the presence of acoustic stimulation. Brownell (1990) describes the outer hair cell motility as a lengthening or shortening of the outer hair cells in response to acoustic stimulation. This active biological mechanism in the outer hair cells causes a vibration of the basilar membrane in an attempt to enhance the ear's sharpness and sensitivity (Attias, Furst, Furman, Haran, Horowitz, & Breslof, 1995) by providing the appropriate stimulus to the inner hair cell receptors (Kummer et al. 1998). This vibration, called an otoacoustic emission, can be recorded using a very sensitive microphone placed in the ear canal. Otoacoustic emissions are therefore not, themselves necessary for hearing but reflect processes in the cochlea necessary for hearing (Norton, 1993).

The primary value of otoacoustic emissions is that their presence indicates that the preneural cochlear mechanism (and middle ear as well) can respond to sound in a normal manner. A large area of the basilar membrane is stimulated, and the measured emissions are frequency specific and frequency selective, so it is possible to gain information about different areas of the cochlea simultaneously. "No other clinical test," wrote Kemp, Ryan, and Bray (1990), "specifically tests cochlear biomechanisms or combines the operational speed, non-invasivity, objectivity, sensitivity, frequency selectivity, and noise immunity of otoacoustic emission testing" (p. 94).

Kemp (1978) described two main classes of otoacoustic emissions: spontaneous otoacoustic emissions (SOAEs) and evoked otoacoustic emissions (EOAEs), which will be described below.

2.2.2.3.1 Spontaneous Otoacoustic Emissions (SOAEs)

SOAEs are tonal or narrowband low level signals that can be recorded in the absence of any auditory stimulation in only 50% of all persons with hearing levels <20 dB HL and in 60% of persons with hearing levels <30 dB HL (Lonsbury-Martin, 1994). Because of this low incidence of SOAEs, they are not viewed as a suitable clinical indicator of the mechanical activity of the cochlea (Lonsbury-Martin, 1994; Norton & Stover, 1994). After Kemp (1978) reported the existence of SOAEs, many clinicians hoped that they would be the objective basis for tinnitus. It has been proved, however, that most people are unaware of their spontaneous otoacoustic emissions, and only a very small percentage of people with tinnitus have recordable SOAEs that can be linked to their tinnitus (Norton, Schmidt, & Stover, 1990).

An interesting study by Kulawiec and Orlando (1995) investigated the effect of SOAEs on evoked OAEs and found that SOAEs contribute greatly to the level and shape of the frequency spectrum of TEOAEs. Present SOAEs increased the levels of the peak amplitudes at corresponding frequencies and as the number of SOAEs increased, the TEOAE levels increased. This phenomenon causes a large range of different levels found in TEOAE testing, which in turn is according to these authors, the primary reason why TEOAEs fail to predict actual hearing thresholds.

SOAEs can be used as a complementary technique for evoked otoacoustic emissions (Bonfils, et al. 1990) but due to the low incidence cannot be used as a screening or diagnostic procedure.

Several types of evoked OAEs exist, depending on the type of stimulus used during the measurement. Evoked emission types include stimulus frequency emissions, transient evoked otoacoustic emissions, and distortion product otoacoustic emissions.

2.2.2.3.2 Stimulus Frequency Otoacoustic Emissions (SFOAEs)

A stimulus frequency otoacoustic emission (SFOAE) is the most stimulus frequency specific of all emission types, but it is also probably the least clinically applicable (Norton & Stover, 1994). SFOAEs reflect the response of the cochlea at a certain pure tone, occurring simultaneously with and at the same frequency as the stimulus presented. When a tone is presented to the ear, the sound pressure measured in the ear canal is the sum of the sound pressure of the stimulus and the response. In the case of other evoked emission types, the stimulus sound pressure level is separated from the response either spectrally (as in the case of distortion product otoacoustic emissions) or temporally (as in the case of transient evoked otoacoustic emissions). Due to the lack of temporal or spectral separation techniques in measuring SFOAEs, more sophisticated equipment and processing of data are required, and therefore SFOAEs are not currently practical for clinical use (Lonsbury-Martin & Martin, 1990; Norton & Stover, 1994). Lonsbury-Martin, (1994) described this phenomenon quite effectively: "SFOAEs are technically difficult to measure, due to the complexities of separating the in-going acoustic stimulus from the out-going emitted response. Thus, to date, little information has accumulated concerning either their basic nature or their clinical utility" (p. 2). One possible way to overcome this problem is to use the nonlinearity of the cochlea by performing multilevel tests and with subtractions determine which part is due to the cochlea's nonlinear response (Kemp & Ryan, 1993). This can be time consuming and not a practical resolution for a screening test.

Another type of evoked otoacoustic emissions is transient otoacoustic emissions.

2.2.2.3.3 Transient Evoked Otoacoustic Emissions (TEOAEs)

TEOAEs are responses that follow a brief acoustic stimulus such as a click. TEOAEs can be recorded in nearly all persons with normal hearing (hearing levels < 20 dB from 500 Hz to 4000 Hz) and are absent in all ears with a hearing loss 30–40 dB HL. (Hearing loss > 40 dB HL according to Glattke, Pafitis, Cummiskey, & Herer, 1995; hearing loss > 35dB according to Robinette, 1992; or hearing loss > 30 dB according to Kemp et al. 1990.) The latest research indicated that when tone bursts are used to elicit TEOAEs instead of clicks, emissions can be evoked in ears with hearing losses at least up to 60 dB HL (Vinck, et al. 1998).

In measuring a TEOAE, a probe is inserted into the ear canal, containing a miniature sound source for delivering the stimulus and a very sensitive microphone for detecting the response. TEOAEs are obtained by using synchronous time-domain averaging techniques. Responses to several stimuli (e.g., 500–2000 clicks) are averaged to improve the signal-to-noise ratio and make the response distinguishable from the noise floor (Glattke et al. 1995). The ear canal sound pressure is amplified, filtered, and then digitized, and the first 2.5 seconds of the response are eliminated to remove the stimulus (Norton & Stover, 1994).

TEOAEs are frequency dispersive: high frequencies coded basally on the basilar membrane have a shorter latency (4 ms for 5000 Hz) than low frequencies, coded apically on the basilar membrane (20 ms for 500 Hz). According to Kemp et al.

(1990), this provides for temporal separation of the stimulus's and response's sound pressure level, both measured in the ear canal.

When it comes to the discussion of the frequency specificity of TEOAEs, the issue is often misunderstood because there are different areas of AOE measurement and analysis that involve frequency specificity. Kemp and Ryan (1993) distinguish between the three kinds:

- First, ***stimulus frequency specificity*** refers to the similarity of the stimulus to a pure tone. TEOAEs use broad band clicks and stimulate broad areas on the basilar membrane. However, when a pure tone is used for stimulation, it does not mean that only one point on the basilar membrane is stimulated as is often supposed. The traveling wave resulting from pure tone stimulation vibrates all the basilar membrane up to the place representing that frequency. Furthermore, excitation of the basilar membrane by a completely pure tone can involve up to a third octave range.
- Second, ***cochlear frequency specificity*** is the cochlea's ability to respond to the frequency of a stimulus in a certain place representing that frequency, and to generate responses for every frequency being stimulated independently. This is still not very specific: in the human cochlea only within a third octave specific.
- Third, ***response frequency specificity*** refers to the relationship between the response and the frequency area of the basilar membrane tested. In other words, can the frequency area on the basilar membrane being tested be determined by looking at the response?

It is evident that the use of frequency specific stimuli does not guarantee or create a frequency specific response.

The stimulus frequency specificity of TEOAEs is determined by the bandwidth of the stimuli being used to elicit a response. Emissions can be evoked at most frequencies in the normal cochlea. The broader the stimulus spectrum, the broader the emission spectrum (Norton & Stover, 1994). Broadband clicks are usually used for measuring TEOAEs, which allows for simultaneous multifrequency testing (Kemp & Ryan, 1993). TEOAEs provide simultaneous information regarding the functioning of the outer hair cells on the basilar membrane for a very broad region of frequencies (Kemp et al. 1990; Norton & Stover, 1994). Some cochlear frequency-specific information can be gained by analyzing the spectral distribution. Ueda, (1998) found that if certain frequencies are over stimulated in guinea pigs, the temporal shifts could be measured in the TEOAE spectrum and therefore proved that TEOAEs are frequency specific. Kemp et al. (1990) successfully used TEOAEs to identify frequency ranges of normal hearing in pathological ears. In a case with a high frequency hearing loss, they obtained emissions up to the frequency of the hearing loss and no emissions for the pathological frequencies. It should be noted, however, that no information regarding the thresholds of the pathological frequencies could be obtained. Many other researchers have also had difficulty in making comparisons between frequency-specific audiometric thresholds and frequency information provided by TEOAEs (Bonfils et al. 1990; Lee, et al. 1993; Lonsbury-Martin & Martin, 1990). The fact that no click emissions can be obtained when the hearing loss exceeds 30–40 dB HL has proven TEOAEs to be more applicable in the area of hearing screening than diagnostic audiology (Harris & Probst, 1991; Lee et al. 1993).

TEOAEs were the first method to be tried and recommended for neonatal hearing screening and are currently the most widely used OAE method for screening (Kemp & Ryan, 1993). TEOAEs can be measured very effectively in newborns. Both ears can be screened in a sleeping infant in about 10 minutes, compared to about 20 minutes with screening ABR (Norton & Stover, 1994). Another advantage of TEOAEs is that a broader frequency spectrum is being evaluated than with ABR, they do not require highly trained personnel, and they are objective and non-invasive (Lonsbury-Martin, McCoy, Whitehead & Martin, 1992; Stevens Webb, Hutschinson, Smith & Buffin, 1990).

TEOAEs do, however, have limitations. The first is that they are only recordable in normal and near-normal ears (30–35 dB HL) when clicks are used as stimuli. This implies that TEOAE data cannot be translated into "threshold data." An ear with a hearing loss of 65 dB will have the same absent response as an ear with a hearing threshold of 40 dB (Kemp et al. 1990). Although TEOAEs function as a wonderful screening procedure (Stevens et al. 1990), no information regarding hearing status can be obtained once the emission is absent, as in the case of mild and moderate hearing losses. A recent study by Harrison and Norton (1999) however, found that a broadband tone burst, which has all of its energy concentrated in a narrow bandwidth, could sometimes evoke and emission where a click could not. In a few isolated cases, they could elicit emissions with broadband tone bursts in ears with mild and moderate hearing losses. It is thus probable that with more research, it may be possible to distinguish between mild and moderate losses using broadband bursts. Vinck et al. (1998) also made a remarkable breakthrough in pure tone threshold prediction with tone burst otoacoustic emissions (TBOAE) and proved that TBOAEs could predict hearing sensitivity within 10dB for hearing losses up to 60 dB HL for all frequencies, 250 Hz to 8000 Hz. The authors considered a statistical artifact for these astounding findings but eventually attributed the results to several other explanations including the new use of TBOAEs, the use of multivariate statistical techniques, and the fact that pure tone thresholds are highly inter-related. Normal hearing at any given frequency might influence prediction accuracy of frequencies with absent emissions. In other words, prediction of PTTs at frequencies where there is a 60dB HL hearing impairment could have been influenced by inter-related frequencies where the hearing loss was less than 45 dB HL. The only limitation that they identified was that this process of emission measurement is still very time consuming and questionable for the use of small children. Advances in OAE software will hopefully enable audiologists to use tone bursts to predict PTTs more rapidly and easily in the future.

The fact that a more frequency specific stimulus has all of its energy concentrated in one area, instead of spreading it out over the basilar membrane, provides for more efficient basilar membrane stimulation and enables researchers to measure emissions in populations with hearing loss. This is the primary reason why TBOAEs and DPOAEs can be recorded in ears with a hearing loss and TEOAEs cannot.

Another weakness of TEOAEs is the variability in TEOAE spectrums for normal populations. Hurley and Musiek (1994) indicated that TEOAEs are affected by small changes in cochlear physiology that do not result in comparable changes in auditory threshold. In other words, they found considerable TEOAE variability among ears with similar hearing sensitivity. This aspect makes it almost impossible to predict hearing thresholds with TEOAEs. According to Kulawiec and Orlando (1995), the TEAOE variability is greatly influenced by the presence of SOAEs. A study by Avan, et al. (1997) indicated that ultra high frequency hearing status (8 to 16 kHz) also influences the TEOAE spectrum even though hearing in the normal frequency range (0.5 to 8 kHz) might be normal. This factor, together with age and probe tip placement is the reason why there is so much variability in TEOAE spectrums of normal hearing people. TEOAEs can therefore only classify hearing levels as normal (<20 dB HL) or abnormal (>20 dB HL) but fail to predict hearing sensitivity of specific frequencies.

Another aspect that should be kept in mind is the difference in the application of stimulus level in TEOAE recordings compared with its use in ABR recordings. According to Kemp and Ryan (1993) ABR measures a physiological threshold dependant on synaptic events and the ABR threshold is the dividing line between stimulus levels where one results in a response and the other doesn't. OAEs do not have such a threshold because they are presynaptic and for OAEs a detection threshold has to be determined which is the lowest point where a response can be distinguished from he noise floor. With TEOAE detection threshold determination, the exact threshold level can be a function of the equipment, background noise and subject cooperation and therefore TEOAE screening usually uses suprathreshold stimuli. It can be argued that the use of suprathreshold stimuli limits the sensitivity of a screening test for minor hearing impairments might be overlooked with high-level stimuli.

Finally, it seems that TEOAE amplitude and occurrence are negatively affected by increasing age. Norton and Widen (1990) reported a statistically significant decrease in TEOAE amplitude with increasing age even in a carefully screened sample. Kemp et al. (1990) also indicated stronger responses as well as responses at more frequencies for neonates than adults. It is still unclear whether the age-associated changes are due to normal developmental changes in the middle ear or to progressively impaired cochlear function.

All the emission types previously discussed—namely, SOAEs, SFOAEs, and TEOAEs—have one limitation in common. **None of these emission types can function as an objective test of hearing where pure tones can be predicted given only the otoacoustic emissions** (Bonfils et al. 1990; Hurley & Musiek, 1994; Lee et al. 1993; Lonsbury-Martin, 1994). The requirement for an emission type to be able to potentially predict pure tone thresholds given only the otoacoustic emissions is that the emission type should be present in normal and hearing-impaired ears (Kimberley, et al. 1994b). It should also be frequency-specific and easily compared to the frequencies of the behavioral thresholds (Lee et al. 1993). There is one emission type that might prove to be clinically applicable in the prediction of behavioral pure tone thresholds—namely, distortion product otoacoustic emissions (Lee et al. 1993; Lonsbury-Martin & Martin, 1990).

2.2.2.3.4 Distortion Product Otoacoustic Emissions (DPOAEs)

Distortion Product Otoacoustic emissions (DPOAEs) were identified by Kemp (1979), only one year after the initial identification of transient evoked otoacoustic emissions (TEOAEs) and spontaneous otoacoustic emissions (SOAEs). Distortion product otoacoustic emissions are different from the other emission types in a number of ways. Firstly, DPOAEs are elicited by the simultaneous presentation of two pure tones and the emission is an internal produced frequency different from the two stimuli, in frequency and amplitude. Secondly, in contrast to other emission types such as TEOAEs, SOAEs and SFOAEs, the distortion product can very easily be measured in many common vertebrae laboratory animals (Mills, 1997). Research on laboratory animals allows experimental control of certain factors that contribute to a better understanding of the characteristics of distortion product emissions and OAEs in general (Zhang & Abbas, 1997). DPOAEs have even been measured in the ear of a grasshopper with a complete different morphology. The hearing organ of a grasshopper does not have any sensory hair cells, but the dendrites of the ciliated receptor cells are responsible for generation of distortion (Kossl & Boyan, 1998). Distortion product otoacoustic emissions have therefore been proven useful in both clinical and research settings. Thirdly, DPOAEs can be measured in hearing impaired ears with elevated threshold levels of up to 65dBHL (Moulin, et al. 1994). This feature enables DPOAEs to provide more than just hearing screening information.

These interesting differences between DPOAEs and other emission types led to an extensive investigation of DPOAEs to determine the clinical applicability of DPOAEs (Bonfils & Uziel, 1989). This clinical interest in DPOAEs is twofold. The first interest lies in the development of an objective test of auditory function. The second as a basis of a test uniquely sensitive to the functioning of the outer hair cells, and therefore a useful tool in differential diagnosis testing (Durrant, 1992). This research project focuses on the first interest: **To develop an objective, noninvasive test of auditory function with distortion product otoacoustic emissions.**

2.3 DPOAEs as an Objective, Non-invasive Technique

2.3.1 Definition

Distortion product otoacoustic emissions (DPOAEs) are elicited by the simultaneous presentation of two different pure tones, f1 and f2, where f1<f2. The distortion product response is a third tone of frequency, produced internally and in a frequency region different from the two primary frequencies. Responses can be expected at several different distortion product frequencies such as 2f1-f2, 3f1-2f2, 4f1-3f2, etcetera. Of all the distortion products, the cubic distortion product is the most prominent in humans and occurs at 2f1-f2 (Nielsen, Popelka, Rasmussen & Osterhammel, 1993).

The normal cubic distortion product is typically 60dB lower than the overall level of the primaries (Nielsen, et al. 1993). The relationship of the distortion product (2f1-f2) and the two primary frequencies (f1 and f2) can very clearly be seen in the spectrum of the ear canal sound pressure of normal hearing subjects undergoing DPOAE testing. This relationship is illustrated in Figure 2.1.

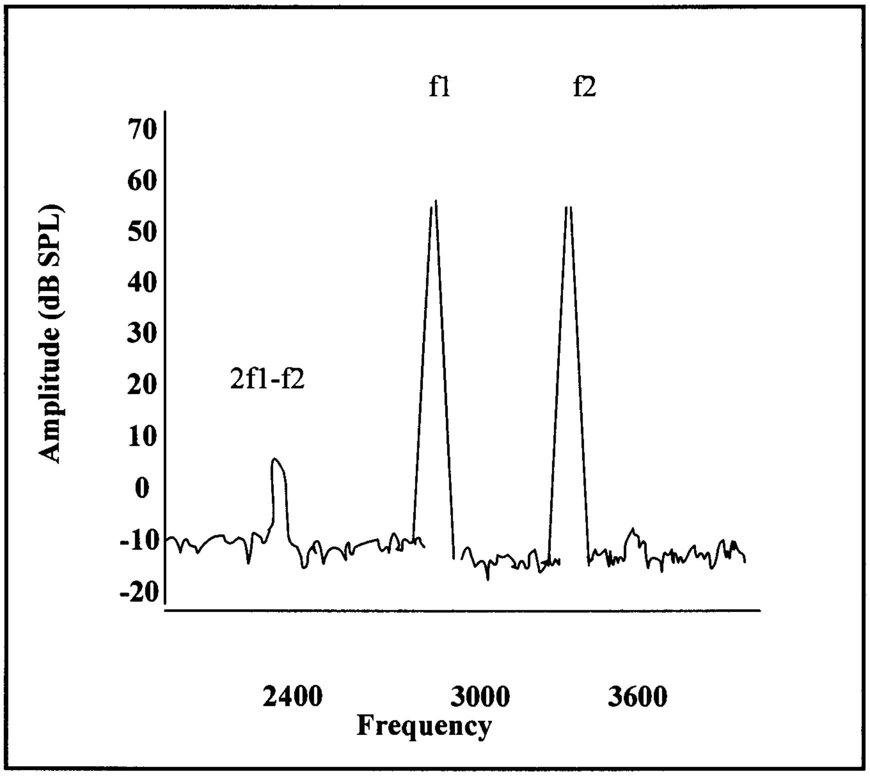


Figure 2.1: The spectrum of the ear canal sound pressure of a normal hearing adult undergoing DPOAE testing. f1 and f2 are the stimuli and 2f1-f2 is the response (from Norton & Stover, 1994:457).

The next section will discuss the measurement procedures and instrumentation necessary to elicit a distortion product otoacoustic emission.

2.3.2 Measurement Procedures and Instrumentation for DPOAEs.

For the measurement of a distortion product otoacoustic emission, two separate channels for stimulus generation and attenuation are necessary. These two channels should be electrically isolated to prevent distortion. The signals are presented to the ear canal via a probe microphone assembly with two delivery ports. Probe microphone systems for DPOAEs consist of a miniature sound source and a very sensitive microphone built into a unit small enough to fit snugly into a human ear canal (Siegel, 1995).

After the two signals are presented to the ear canal, the ear canal sound pressure is averaged to reduce the noise floor and spectrally analyzed for the levels of the primaries (fl and f2) and the response (2fl-f2). Figure 2.1 shows the spectrum of the sound pressure measured in the ear canal, depicting the two primary stimuli fl and f2, as well as the response, 2fl-f2.

A complete DPOAE system is presented schematically in Figure 2.2.

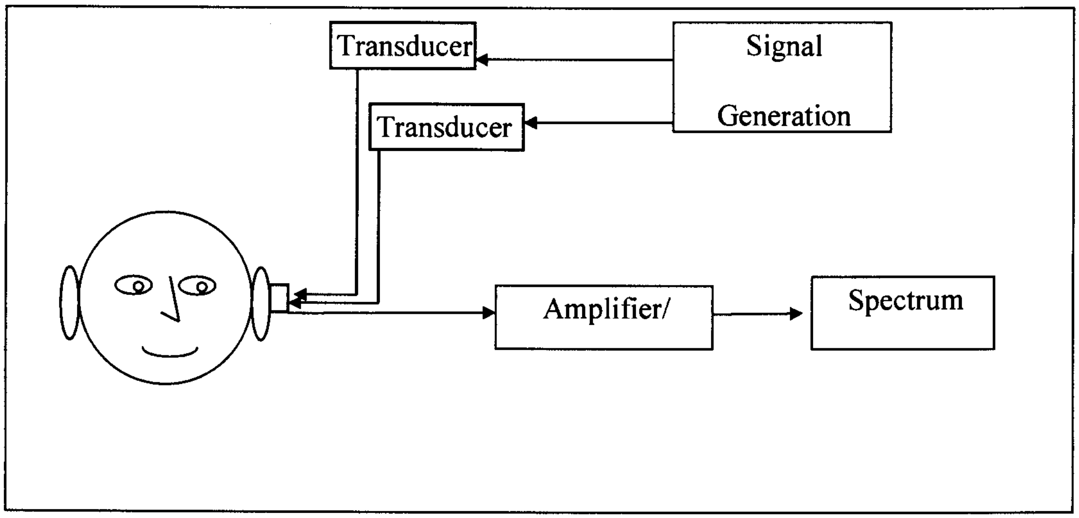


Figure 2.2: Schematic representation of a system used to measure distortion product otoacoustic emissions (Norton & Stover, 1994:456).

DPOAEs can be recorded in virtually all normal hearing ears (100% according to Lee et al. 1993; and 95% according to Kimberley et al. 1994b). DPOAE measurement uses frequency specific pure tone stimuli. The facts that specific input frequencies can be selected and that responses are measured at certain frequencies make it easier to make comparisons between DPOAE results and conventional pure tone thresholds. This feature of DPOAE measurement makes it the best-suited emission type to relate to behavioral thresholds (Lee et al. 1993). Although one should be careful to state that DPOAE is a more frequency specific type of emission due to its stimulus frequency specificity, there are studies to support the notion that DPOAEs are frequency specific in the sense that there are good correlations between shapes of audiograms and DPOAE emission spectrums (Gaskill & Brown, 1990; Gorga et al. 1993).

Furthermore, DPOAEs are the only otoacoustic emission type that can be recorded in the presence of a mild to moderate hearing loss. TEOAEs can only classify a person's hearing as normal or impaired (Bonfils, Piron, Uziel & Pujol, 1988). DPOAEs can classify hearing ability as normal, slightly impaired, mildly impaired, moderately impaired, or severely impaired (in cases where no emissions can be measured) (Durrant, 1992; Gaskill & Brown, 1990; Lee et al. 1993). This advantage of DPOAEs allows emission testing of a much larger population with varying hearing sensitivity, making this one of the best reasons to investigate DPOAEs as an additional objective test of hearing.

The use of DPOAEs to predict hearing sensitivity will be reviewed in the next section to better understand the struggle of previous researchers and to set the goals for what such a project might hope to accomplish. It is however a challenging task to compare one study with another because of the numerous DPOAE and demographic features that influence predictive accuracy of hearing sensitivity and that differ greatly in the various studies. Some studies use DPOAE amplitude as predictors (Stover et al. 1996a; Kimberley et al. 1994b), others use DPOAE threshold (Moulin, et al. 1994).

Some use DP Grams (Lonsbury-Martin, 1994), others I/O functions (Lonsbury-Martin & Martin, 1990). Furthermore, the DPOAE frequencies chosen in DPOAE measurement seldom overlap and include different frequency ratios. In the analysis of data some studies correlate PTT frequency to the frequency of f1 (Gaskill & Brown, 1990), f2 (Harris, Lonsbury-Martin, Stagner, Coats & Martin, 1989; Kimberley et al. 1994a; Kimberley et al. 1994b; Kummer et al. 1998), 2f1-f2 or the geometric mean (GM) (Lonsbury-Martin and Martin, 1990; Martin et al. 1990b; Bonfils et al. 1991; Zhao & Stephens, 1998) of the primaries. Most studies use only one frequency in correlation determination but some included adjacent frequencies (Kimberley, et al. 1994a).

It might seem logical to attempt to concentrate the findings of previous researchers into a table to summarize achievements. After several attempts it became clear that the format of such a table would be too complex due to the hundreds of different measurement and analysis techniques and styles of reporting findings. Very few researchers expressed their findings in percentage correct prediction values and percentage false positives and false negatives. Furthermore, researchers used different statistical techniques that add to the rich terminology not expressible in table format. The following discussion will attempt a succinct yet informative overview.

2.3.3 Literature Overview of Studies Attempting to Predict Hearing Sensitivity with DPOAEs.

An early study by Kimberley and Nelson (1989) investigated the correlation between distortion product otoacoustic emissions and hearing threshold. Subjects were selected without regard to age, sex, etiology of hearing loss or pattern of hearing loss. The frequency ratio of the primaries (f2/f1) was 1.2. Distortion product otoacoustic emissions were measured over a stimulus range from 30 dB SPL to 80 dB SPL in 6 dB steps. DPOAE I/O functions were measured covering the frequency range from 700 Hz to 6000 Hz. Kimberley and Nelson (1989) then plotted emission thresholds and auditory thresholds of 21 ears on a scattergram. (Emission thresholds represent the stimulus level required to just raise the emission above the noise floor.) Kimberley and Nelson's (1989) scattergram can be viewed in Figure 2.3. The linear fit shown with the data points has a slope of 1.0 and a correlation coefficient of .86.

The results displayed in this scattergram in Figure 2.3 suggest that DPOAE measurements can predict auditory thresholds within 10 dB over a range from 0 dB SPL to 60 dB SPL. The authors claim that this was the first report of such a precise correlation.

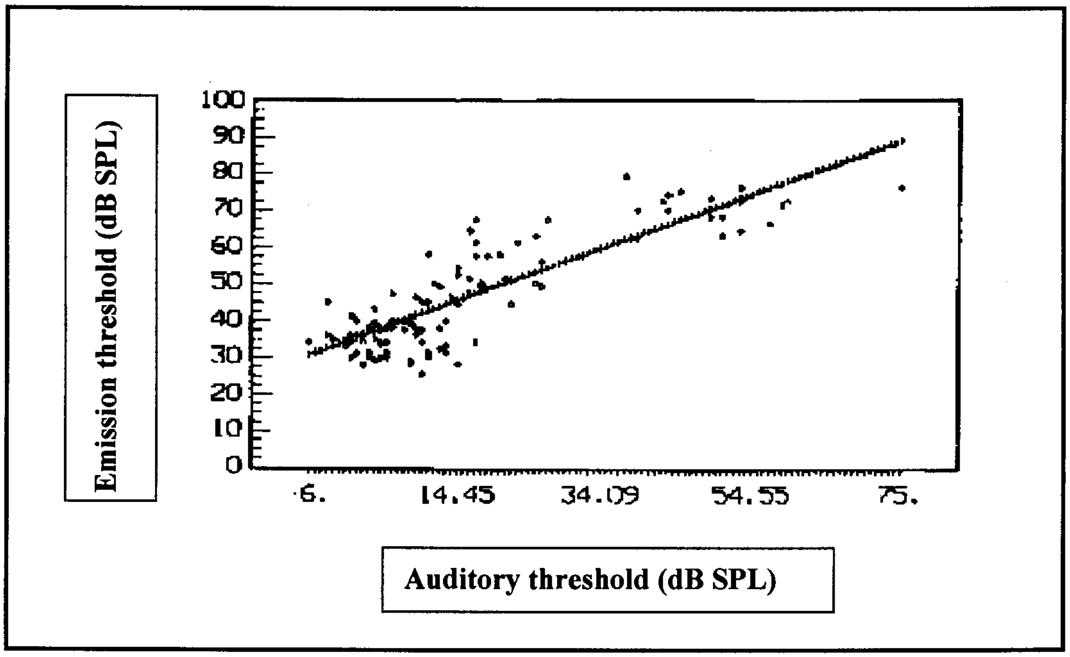


Figure 2.3: Scattergram of emission threshold versus auditory threshold as measured by Kimberley and Nelson, (1989: 368)

Gaskill and Brown (1990) investigated the behavior of the acoustic product in humans and it's relation to auditory sensitivity. They concluded that with certain optimal stimulus parameters (stimulus levels below 60 dB SPL; L1>L2 by 15 dB; f1/f2 = 1.225), half of the subjects showed a statistically significant correlation between DPOAE results and auditory sensitivity at the corresponding f1 stimulus.

Avan and Bonfils (1993) confirmed these findings. The authors conducted a study on DPOAEs in 25 normal hearing and 50 hearing impaired ears. Their results indicated that the DPOAEs evoked by low intensity primary tones (below 62 dB SPL) were strongly correlated with the auditory threshold at the mean frequency of f1 and f2 and that DPOAEs disappear for hearing losses larger than about 30dB. This research also suggests that when low intensity primaries are used, DPOAEs provide frequency specific information on the local cochlear state of the primaries.

A few other studies indicated positive relationships between DPOAEs and pure tone thresholds. Spektor, Leonard, Kim, Jung and Smurzynski (1991) reported a positive qualitative relationship between pure tone thresholds and DPOAE thresholds in 19 children (although these authors did not quantitatively correlate DPOAE thresholds with pure tone thresholds). It seemed that the configuration of the hearing loss correlated well with the frequency pattern of the DPOAEs. Lonsbury-Martin and Martin (1990) assessed DPOAEs in subjects with noise induced hearing loss. They found that DPOAE thresholds provide reasonable good estimates of hearing loss in cases where primary damage to the outer hair cells can be assumed (such as noise induced hearing losses). The authors found a relatively strong correlation between DPOAE thresholds and magnitude of hearing loss. In the subjects they examined, for every 1dB increase in DPOAE threshold, hearing level increased by 1dB. When DPOAE threshold was > 63 dB SPL, the accompanying hearing level was > 20 dB HL. Such a strong correlation between DPOAEs and pure tones in subjects with OHC pathology proves it as an efficient measurement of cochlear functioning. DPOAEs could potentially be successfully applied to other cochlear pathologies such as Meniere's disease and ototoxity.

Gorga, et al. (1993) measured DPOAEs in normal hearing and hearing-impaired human subjects. They investigated the extent to which DPOAEs can be used to correctly distinguish between normal and impaired hearing. DPOAE amplitude was able to distinguish between normal and impaired subjects at 4000 Hz, 8000 Hz and to a lesser extent at 2000 Hz. At 500 Hz, performance was no better than chance, due to high biological noise levels such as breathing and swallowing. They concluded that DPOAE measurement could successfully be implemented to identify high frequency hearing loss, but that it was not an accurate predictor of hearing loss in the lower frequencies.

A study conducted by Stover et al. (1996a) examined the effect of the primary stimulus levels on the ability of DPOAE measurements to separate normal hearing from hearing impaired ears. Clinical decision theory was used to assess both DPOAE threshold and DPOAE amplitude as diagnostic indicators of hearing status. This research suggests that DPOAE threshold and DPOAE amplitude perform equally well in distinguishing normal from impaired hearing but DPOAE amplitude is more suited as a screening method due to shorter testing times. Probst and Hauser (1990) performed similar research in 1990 and concluded that the measurement of DPOAE amplitude alone might fail to detect a mild hearing loss. To determine hearing ability more accurately, more detailed measurements such as I/O functions with DPOAE thresholds should be performed.

Kummer et al. (1998) investigated the growth behavior of DPOAEs and its relationship to auditory sensitivity in 20 normal ears and 15 ears with cochlear hearing loss at the f2 frequency with probe tone levels varying from L2 = 20 - 60 dB SPL. They concluded that this relationship is strongly dependant on stimulus levels. For normal ears, statistically significant correlations could be determined for 14/15 ears when lower stimulus levels were used (L2 = 25 dB SPL) and for 17/20 hearing impaired ears when moderate primary tone levels were used (L2 = 45 dB SPL).

Kimberley et al. (1994b) predicted hearing status in normal and hearing-impaired ears with DPOAEs at six frequencies ranging from 1025 - 5712 Hz. The significance of variables such as DPOAE levels, age and gender were determined in the definition of normal versus abnormal PTTs and then applied to a new set of unfamiliar data to determine their predictive accuracy at each frequency. Classification accuracy of normal hearing varied from 71% at 1025 to 92% at 2050 Hz. Kimberley et al. (1994b) concluded that DPOAE measures can reliably categorize pure tone thresholds as being normal or impaired in a population with varied cochlear hearing status.

Kimberley et al. (1994a) compared an artificial neural network (ANN) approach to multivariate discriminant analysis to classify PTTs with DPOAEs in 229 normal and hearing-impaired ears as normal or impaired. Prediction accuracy varied from 57% correct classification of hearing impairment at 1025Hz to 100% at 2050Hz when normal hearing was defined as PTTs < 20dB HL. Overall classification accuracy was 80% for normal PTTs and 90% for impaired PTTs. They concluded that the neural network approach was more successful in classifying hearing sensitivity due to this technique's ability to model complex relationships or more specifically, the nonlinear relationship between DPOAEs and PTTs. The discriminant analysis technique is restricted to modeling purely linear relationships.

Many previous studies attempted to develop DPOAEs as a possible new objective method of hearing sensitivity prediction. Most researchers attempted to classify hearing status as normal or impaired and did not attempt to predict specific pure tone thresholds for impaired ears. Still, most researchers found it extremely difficult or even impossible to classify impaired PTTs at low frequencies as normal or impaired with DPOAEs (Gorga et al. 1993; Kimberley et al. 1994b; Stover et al. 1996a; Zhao & Stephens, 1998). This unsatisfactory prediction or classification of PTTs with DPOAEs is due to many factors influencing the measurement of DPOAEs (Gorga, et al. 1993; Nieschalk, et al. 1998), the complex nonlinear nature of the measured responses (Lonsbury-Martin, Martin & Whitehead, 1997; Nakajima et al. 1998; Kummer et al. 1998) and shortcomings in data analysis techniques used to date (Kimberley et al. 1994a).

There are also more general issues that influence prediction of PTTs with DPOAEs that should be overviewed to put PTT prediction with DPOAEs in perspective. Chapter three will discuss the issues relating to DPOAE measurement, the complex DPOAE response and analysis of DPOAEs in detail. More general issues contributing to the unsatisfactory prediction of PTTs with DPOAEs will be discussed in the following section.

2.3.4 PTT Prediction with DPOAEs in Perspective.

2.3.4.1 Audiometric Threshold is Determined by Factors Not Included in OAE Generation.

According to David Kemp (1997) the following factors assist in the sensitivity of hearing threshold:

1. An open external auditory meatus.
2. A mobile light and stiff tympanum.
3. A light and well articulated ossicular chain.
4. A mobile and low-loss attachment of the stapes to the oval window.
5. A well formed mobile and low-loss basilar membrane supporting a normal traveling wave.
6. Optimum electrochemical environment of the scala media.
7. Optimum condition of the outer hair cells.
8. Optimum configuration of the outer hair cells (including the medial efferent systems)
9. Optimal coupling of motion within the organ of Corti, especially from basilar membrane to outer hair cell to inner hair cells.
10. Optimum condition and functioning of the inner hair cells.
11. Optimum synaptic function at the inner hair cell- including efferent interaction.
12. Optimal neural transmission out of the inner ear.

13. Optimal mapping and processing of the neural signals reaching the cochlear nucleus.
14. Optimum function of the entire auditory pathway.

Auditory threshold depends on the sum of all 14 factors above. OAE generation depends on only the first eight factors. There is an additional factor in OAE generation that is not present in the hearing threshold factor list. The cochlea delivers a vibratory force to the eardrum and this sound pressure depends on the acoustics of the enclosed ear canal in which the probe microphone is situated and that is different from the open ear canal in PTT testing. Furthermore, in OAE generation the energy travels backwards through the system and such a reverse process might have different acoustic parameters.

At first early studies made no claims that OAEs could predict hearing sensitivity but only that it could distinguish between normal and impaired hearing (Probst, Lonsbury-Martin, Martin & Coats, 1987; Bonfils et al.1990; Collet, Gartner, Moulin, Kauffmann, Disant & Morgon, 1989; Kemp et al. 1990). However, the need for an objective test to aid in the assessment of difficult-to-test populations and the superficial similarity between the audiogram and DPOAE intensity-frequency displays fueled expectations that DPOAEs predicts PTTs spontaneously. OAEs are a sensitive indicator of cochlear dysfunction and are partially correlated with threshold but there are numerous factors influencing PTTs that cannot be measured by OAEs. David Kemp (1997) very effectively summarizes the fact that there is such a seemingly strong correlation between the two measures: "It is an accident of biology that the most common auditory disorders affect this region. Even some retrocochlear disorders exert a negative impact on the cochlea. It is an accident of biophysics that a correlate of sound vibration in the cochlea prior to its arrival at the sensory cells can be so easily recorded." (Kemp, 1997: p19).

The fact that there are so many factors contributing to PTTs that are not measured with OAEs is one of the reasons why researchers struggle to develop OAEs as a diagnostic test of hearing.

2.3.4.2 Nonlinearity is at the Heart of OAE Generation.

When the living human cochlea is stimulated with two pure tones simultaneously, it perceives a combination of tones that can be measured even though these tones are not present in the stimuli. According to Ruggero (1993) only an active process requiring energy can explain the perception of these tones that suggests the presence of significant nonlinearities. In 2f1-f2 DPOAE measurement, there is energy measured at f1, f2, 3f1-f2, 2f1-f2 and sometimes even more. It is tempting to believe that the 2f1-f2 component is sufficient, but it is not (Kemp, 1997). About 80% of all the information in discarded and with the instrumentation up to date, it would be very time consuming to measure all the energy tones. In order to form a model of cochlear nonlinearities to fully understand the dynamics of DPOAEs, enough data will have to be assimilated. Current TEOAE and DPOAE measures only scratch the surface.

2.3.4.3 The Sound Calibration Issue.

Most DPOAE measurement devices on the market today calibrate the DPOAE stimuli by adjusting the speaker voltage levels as a function of frequency to produce a constant SPL as measured by the probe microphone. This in-the-ear calibration method poses a potential problem because of the presence of standing waves in the ear canal that cause variations of stimulus levels at the eardrum as a function of frequency (Lonsbury-Martin et al. 1997). This sound calibration issue causes problems when impaired ears have to be compared to a group of normal ears, or for the prediction of PTTs with DPOAEs. Some agreement has to be reached by investigators, clinicians and DPOAE-testing equipment manufacturers regarding the best method to calibrate stimuli in order to make comparisons between studies and to set a norm for normal DPOAE occurrence in large populations.

Despite these problems, many researchers still hope to develop DPOAEs as an objective PTT prediction procedure. The requirements for such a procedure will be reviewed in the following section.

2.4 Requirements for an Optimal Objective Pure Tone Threshold Prediction Procedure

An extensive literature overview indicated that the "wish list" for an optimal objective procedure includes the following attributes:

2.4.1 Frequency Specificity

A frequency specific test of hearing is needed to predict hearing ability at specific pure tones. The procedure's measurements have to correlate well with conventional pure tone threshold measurements (Harris et al. 1989; Durrant, 1992; Lonsbury-Martin et al. 1992; Lee et al. 1993).

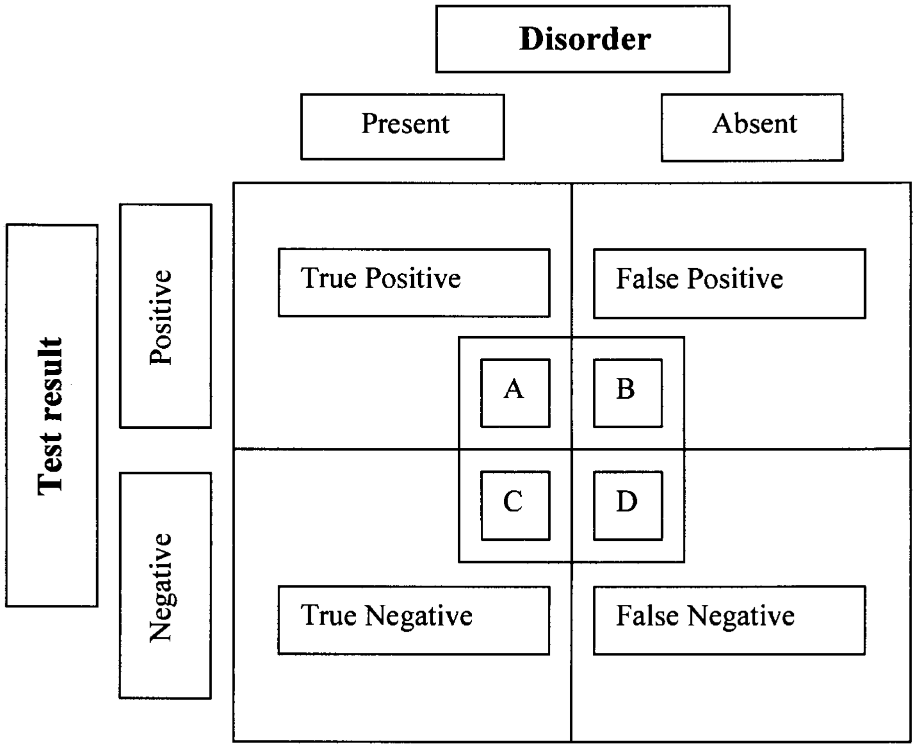
2.4.2 Evaluation of Broad Frequency Span

The measurement procedure must be able to evaluate as many frequencies as possible, (Vinck, Vel, Xu & Cauwenberge, 1995; Whitehead, Lonsbury-Martin, Martin & McCoy, 1996) and not just a one point audiogram as in the case of ABR (Weber, 1994).

2.4.3 Efficiency of the Procedure

The efficiency of a test is an expression of the percentage of individuals who are accurately identified as either normal or abnormal (Glattke et al. 1995). Efficiency can be divided into ***sensitivity*** which is the percentage of impaired ears correctly labeled as hearing impaired (Hussain, Gorga, Neely, Keefe & Peters, 1998) and ***specificity*** which is the number of normal hearing ears correctly labeled as normal (Stevens et al. 1990). Sensitivity is also known as ***the true positive rate*** and specificity as ***the true negative rate***. The ***predictive value*** of a test therefore indicates how many hearing impaired ears tested positive and how many normal ears tested negative.

For practical purposes, these characteristics move in opposite directions as the definition of a positive outcome changes: If sensitivity is raised, specificity is lowered and vice versa. The sensitivity and specificity of a test must be chosen in such a way that most ears with hearing loss is correctly identified without having too many false positive responses. The summary of calculations for test characteristics by Fechtner (1992: p9) can be seen in Figure 2.4.



$$\text{Sensitivity} = \frac{\text{True Positive}}{\text{True Positive} + \text{False Negative}}$$

$$\text{Specificity} = \frac{\text{True Negative}}{\text{True Negative} + \text{False Positive}}$$

$$\text{Positive Predictive Value} = \frac{\text{True Positive}}{\text{True Positive} + \text{False Positive}}$$

$$\text{Prevalence} = \frac{A+C}{A+B+C+D}$$

Figure 2.4: Calculation of test characteristics such as sensitivity, specificity, positive predictive value and prevalence (Fechtner 1992:9).

2.4.4 Good Test-Retest Repeatability

If a person's hearing sensitivity stayed exactly the same from one day to the next, so should the DPOAE responses measured in that ear (Lonsbury-Martin et al. 1992). Another aspect that can be mentioned here is the interaural difference between the two ears of a subject that should be small if the two ears have similar PTTs. According to Tanaka et al. (1987) this aspect is very useful in the identification of unilateral hearing losses and functional unilateral hearing losses.

2.4.5 Differential Diagnosis between Sensory and Neural Hearing Impairment

A test that can accurately discriminate between cochlear and retrocochlear hearing losses would be welcomed (Durrant, 1992; Robinette, 1992; Norton, 1993; Whitehead et al. 1996).

2.4.6 Fast Test Performance

In the assessment of difficult-to-test populations, time is of the essence. DPOAEs have to be measured in a relatively quiet stage, where the subject is still and calm and most difficult-to-test subjects cannot be instructed to cooperate. The test therefore has to be quick to perform (Stevens, et al. 1990; Cane, O'Donoghue & Lutman, 1992; Lonsbury-Martin et al. 1992; Lee et al. 1993; Mauk & Behrens, 1993; Vohr, et al. 1993).

2.4.7 Economic Test Performance

If such a test is extremely expensive to perform, many people for lower socioeconomic groups will refuse the test and turn to less effective but more economic tests. The cost of a test is partly influenced by the ease in which the test can be performed and interpreted. If highly trained and specialized personnel are necessary, the cost will be considerably more (Bonfils et al. 1990; Mauk & Behrens, 1993; Vohr et al. 1993; Whitehead et al. 1996; Kim et al. 1997).

2.4.8 Non-invasive, Comfortable for the Patient

The test is usually performed when the subject is awake and in the case of neonates and children a painless and comfortable method of measurement is needed to ensure a calm and still posture (Bonfils et al. 1990; Lonsbury-Martin et al. 1992; Lee et al. 1993; Mauk & Behrens, 1993; Kim et al. 1997).

2.4.9 Age Differences

A test is required where the responses are not diminished by an increase in age. In other words, an infant should have similar measurable responses as an adult (Quinonez & Crawford, 1997; Abdala, 1998; Lasky, 1998a; Lasky, 1998b; Popelka, Karzon & Clary, 1998).

2.5 DPOAEs as an Optimal Objective Pure Tone Threshold Prediction Procedure

The feasibility of DPOAEs as an optimal objective procedure will be discussed according to the requirements set in the previous section.

2.5.1 Frequency Specificity

Many studies found positive correlations between certain frequencies concerning the measurement of DPOAEs and the frequencies of the PTTs and found DPOAEs to be highly frequency specific in the prediction of PTTs (Kemp et al. 1990; Lee et al. 1993; Nielsen, et al. 1993; Rasmussen, Popelka, Osterhammel & Nielsen, 1993; Kimberley et al. 1994a; Kimberley et al. 1994b; He & Schmiedt, 1997; Kummer et al. 1998; Zhao & Stephens, 1998). Recent research indicated that although the generation of the distortion product due to the interaction of the two primaries is in principle spread out over the whole basilar membrane, it is only the about 1mm around the f2 place that gives maximum contribution to the DPOAE measurement (Mauermann, Uppenkamp, Hengel & Kollmeier, 1999a+b).

2.5.2 Evaluation of Broad Frequency Span

Compared to TEOAEs evoked with click stimuli and ABR, DPOAEs are currently the objective test that evaluates the broadest frequency range: ABR currently evaluates a single area on the basilar membrane in the region of 2000 – 4000 Hz and provides a one point audiogram (Weber, 1994) and this aspect limits this procedure because a passable response can be obtained from normal hearing in these frequencies even if other frequencies are abnormal (Kemp & Ryan, 1993). Balfour et al. (1998) indicated that the attempt to measure a broader frequency range with ABR is limited due to the limited availability of filters and attenuators in ABR equipment in most clinical settings.

The measurement of TEOAS with clicks is currently the most widely used procedure (Harris & Probst, 1991; Prieve, Gorga & Neely, 1996; Avan, et al. 1997) and is limited to frequencies above 1000Hz and below 4000 Hz with most of the energy concentrated in the 2000 – 4000 Hz region (Probst & Harris, 1993). Researchers are investigating the measurement of TEOAEs with tone bursts and find it to be more accurate in the classification of normal and impaired hearing in frequencies higher than 1000 Hz (Vinck et al. 1998). Even though DPOAEs are also limited in the measurement of frequencies lower than 1000 Hz due to the rising noise floor (Durrant, 1992), it can measure frequencies much higher than 8000 Hz and that makes it the emission type that evaluates the broadest frequency range (Whitehead et al. 1996).

2.5.3 Efficiency of the Procedure

The efficiency of DPOAEs as a screening procedure was evaluated by Bonfils, Avan, Landias, Erminy and Biacabe (1997) and although this discussion is about DPOAE as an objective PTT prediction procedure which is more diagnostic, many applicable aspects can be extracted from their study. They investigated what the presentation level of the stimuli should be to have an ideal sensitivity, specificity, positive predictive value (PPV) and negative predictive value (NPV). The ideal discrimination level would allow the separation of all subjects without false negative or false positive responses. Bonfils et al. (1997) identified two test conditions according to what he primary goal of the test is: If the goal is to identify normal hearing (<30dB HL), then DPOAE primary stimulus levels of ≤50 dB SPL will discriminate between subjects with PTTs better or worse than 25-30 dB HL with great sensitivity and specificity. If the objective is to discriminate between profound and severe hearing losses, then primary stimulus levels of ≥ 60 dB SPL will discriminate between subjects with a hearing loss greater or lower than 55-60dB HL with great sensitivity and specificity. The main argument in the measurement of DPOAEs at high intensity levels (such as ≥ 60 dB SPL) is that only passive properties of the cochlea is measured and that it is not a true measurement of OHC functioning and therefore not a true measurement of hearing. Bonfils et al. (1997) argues that these passive emissions are only present in persons with a hearing loss greater than 60dB HL and that there is still an active component measurable in hearing losses <60 dB HL even if high intensity stimuli are used. This aspect makes DPOAEs even more applicable in PTT prediction of hearing impairment over a large decibel range.

2.5.4 Differential Diagnosis Between Sensory and Neural Hearing Impairment

Cane et al. (1992) found that OAEs alone are not sufficient enough to discriminate between cochlear and retrocochlear hearing losses, it should be used in conjunction with other tests such as ABR to determine etiology of sensory-neural hearing loss. Lonsbury-Martin and Martin (1990) discussed two cases where OAEs could discriminate between sensory and neural hearing losses but Robinette (1992) warned that many people have a cochlear condition in conjunction with the retrocochlear hearing loss and that only 18% of retrocochlear losses could be accurately identified with OAEs alone. Telischi, Roth, Stagner, Lonsbury-Martin and Balkany, (1995a) confirmed these findings by reporting that many tumors on the eight nerve causes pressure on the organ of Corti influencing its blood supply. It seems therefore, that DPOAEs can only be useful in differential diagnosis when used in conjunction with acoustic reflex measurements and ABR.

2.5.5 Good Test-Retest Repeatability

Lonsbury-Martin and Martin, (1990) measured high test-retest repeatability with DPOAEs for every ear they tested that demonstrated the same PTTs over a period of time and found it useful to monitor dynamic changes in outer hair cells. Kim, Sun, Jung and Leonard (1997) confirmed these findings. It seems that DPOAEs have excellent repeatability over a long period of time as long as the PTTs stays the same.

2.5.6 Fast Test Performance

The measurement of DPOAEs have been proven to be one of the fastest test available (Bonfils, et al. 1990; Cane, et al. 1992; Lonsbury-Martin, et al. 1992; Mauk & Behrens, 1993; Vohr, et al. 1993; Kim, et al. 1997).

2.5.7 Economic Test Performance

The fact that OAEs require less time to administer than most behavioral tests is one aspect that makes it very economic (Danhauer, 1997). The ease in which it can be measured and interpreted influence the number of specialized personnel necessary to perform the test and therefore also the cost. OAEs are simple to measure and require no advanced technical training (Bonfils et al. 1990; Mauk & Behrens, 1993 Whitehead et al. 1996; Kim et al. 1997). According to Norton and Stover (1994) DPOAEs are technologically the easiest types of emission to measure, being relatively artifact free and requiring no post hoc processing.

2.5.8 Non-invasive, Comfortable for the Patient

DPOAEs are measured by the insertion of a probe tip into the ear canal and is painless and comfortable for the person being tested. It does not require extensive preparation and cleaning of the area where the electrode is placed such as in the case of ABR. The ear canal has to be free of excessive earwax however and the probe should be chosen in such a way that it fits snugly in the ear canal (Bright, 1994). This procedure is not more complex than the probe fitting for tympanometry.

2.5.9 Age Differences

There is some controversy regarding the effect of age on DPOAE levels. According to some researchers, DPOAEs are present at birth (Popelka, et al. 1998) and amplitudes of DPOAEs do not decrease significantly with age, when adjusted for PTTs (Karzon, Garcia, Peterein & Gates, 1994). He and Schmiedt (1996) confirmed these findings and found that differences in DPOAE measurements between neonates and adults are due to sensitivity changes and not due to aging itself. Lasky (1998b) found that I/O functions of newborns and adults were similar, it was only in the fine spectrum where differences could be observed such as a more linear I/O function in adults with saturation at higher primary levels. The amplitudes of DPOAE measurements in adults and neonates were within 1.5 dB of each other for all age groups (Lasky, 1998a). Abdala (1998) found that DPOAEs could even be measured in premature neonates although the fine structure characteristics at 1500 Hz and 6000 Hz were different than measured in adults and suspect that there may be an immaturity in cochlear frequency resolution prior to term birth. No differences were observed at 3000 Hz.

Other researchers attempting to predict PTTs with DPOAEs found that age was definitely a variable that influenced PTT prediction, and that a prediction scheme based on DPOAE level has to be adapted to incorporate subject age (Lonsbury-Martin et al. 1991; Kimberley et al. 1994a; Kimberley et al. 1994b; De Waal, 1998).

DPOAEs can be successfully measured and are present and in all age groups from birth onwards, but in the prediction of PTTs, age has to be included as a significant variable.

It seems that DPOAE measurement meets all the requirements for the development of an optimal PTT prediction procedure. The development of such a procedure also involves a data processing technique that is capable of handling the data sets in the prediction of pure tones from DPOAEs. The following section reviews the requirements for an optimal data processing technique.

2.6 Requirements for an Optimal Data Processing Procedure in the Prediction of PTTs with DPOAEs

The prediction of PTTs with DPOAEs is difficult because of the following attributes of DPOAE measurements:

2.6.1 DPOAEs are Nonlinear in Nature

There are two aspects regarding the nonlinearity of DPOAE measurements. First, the distortion evoked by two-tone stimulation is generated by nonlinear elements that deform the response by creating frequencies that are not in the input signal (Martin et al. 1990b). Second, the increase in amplitude of the distortion does not grow linearly with an increase of amplitude of the stimuli (Nakajima et al. 1998).

The procedure used to analyze DPOAE data, to first identify the correlation between DPOAEs and PTTs and then to apply the correlation to make predictions, should be able to handle nonlinear data sets well.

2.6.2 The Complex Data Set of DPOAEs

There are numerous factors contributing to a complex data set. There are measurement variables such as the choice of f1 and f2, the choice of the primary loudness levels L1 and L2, the ratio of f1 and f2, the definition of a present DPOAE as a certain dB level above the noise floor and the magnitude of the noise floor itself that influence the DPOAE response measured. There are subject variables such as hearing sensitivity, different cochlear impairment types and subject history aspects such as exposure to noise that changes DPOAE responses. Any measured DPOAE is a complex data set influenced by many factors.

A data processing technique is needed that can handle complex data sets by including many variables at a time to determine the correlation between DPOAEs and PTTs and determine the significance of selected variables.

2.6.3 DPOAE Measurements are Often "Noisy"

In the DPOAE spectrum, some of the measurements in the frequency sweep may be absent where others may be preset and some subjects have a higher noise floor measured in the low frequencies. A data processing technique is needed that can make a definite correlation between two data sets even when dealing with absent or noisy data.

2.7 Artificial Neural Networks (ANNs) as a Data Processing Procedure for the Prediction of PTTs with DPOAEs

In the prediction of PTTs with DPOAEs it has been proved that multivariate techniques such as discriminant analysis work better than the more traditional single-variable applications of decision theory (Dorn, Piskorski, Gorga, Neely & Keefe, 1999). It has also been proved that the multivariate technique of a neural network approach is more accurate than discriminant analysis in the prediction of PTTs with DPOAEs (Kimberley et al. 1994a). ANNs have been proven to predict better than discriminant analysis in other field as well, such as bankruptcy prediction (Raghupathi, Schkade & Raju, 1993; Rahimian, Singh, Odom & Shara, 1993) and prediction of the US-$ and DM exchange (Hann & Steurer, 1996).

ANNs excel for a number of reasons: There is less need to determine relevant factors a priori: irrelevant data has such low connection strength that it has no effect on the outcome. Neural networks excel at determining what data is relevant and can cope with numerous factors at the same time. When hundreds of factors are at play, even if some only have a very small effect, neural network models are much more likely to be more accurate for difficult problems than any statistical model (Rahimian, Singh, Thammachote & Virmani, 1993). Neural networks are extremely fault tolerant and can learn from and make decisions based on incomplete data (Nelson & Illingworth, 1991). Even if some of the hardware fails, the neural network system will not be considerably changed. Blum (1992) even suggests training on noisy data to possibly enhance post-training performance. Furthermore, ANNs can deal with nonlinear correlations and has little difficulty outlying data points (Kimberley, et al. 1997).

When it comes to the prediction of PTTs with DPOAEs, a neural network approach is clearly the superior data processing technique to choose (Kimberley et al. 1994a).

2.8 Rationale

Progress in modern technology enabled audiologists to measure the exact degree, configuration, and site of hearing loss and to confirm these findings with a series of objective physiologic procedures, such as tympanometry, the acoustic reflex, ABR, and OAEs in adults and older children. It is in the evaluation of pure tone sensitivity in difficult-to-test populations such as neonates, infants, malingerers and the crucially ill that certain limitations arise and the need for another objective diagnostic evaluation tool was identified. The quest to predict pure tone thresholds accurately with DPOAEs arises therefore not from the need to replace existing conventional behavioral evaluation procedures, but to aid in the assessment of special populations.

An overview of current objective measurements available in audiology indicated that DPOAEs seem to be the most applicable measurement to predict pure tone thresholds objectively, rapidly and over a broad frequency range. Unfortunately, that is only half the case won due to the nonlinear, complex and noisy nature of DPOAE measurements and the inability of conventional statistics to correlate that to pure tone thresholds and make accurate frequency specific predictions. Artificial neural networks were identified as a possible data processing technique to attempt accurate frequency specific predictions.

The study preceding this one (De Waal, 1998) attempted to predict pure tone thresholds with DPOAEs and artificial neural networks. First, PTTs were categorized as normal or impaired (normal defined as < 20 dB HL) with DPOAEs and ANNs and correct classification of normal hearing was 92 % at 500, 87% at 1000, 84% at 2000 and 91% at 4000 Hz. Predictions of impaired hearing was less satisfactory partly due to insufficient data for the ANN to train on and also for similar reasons experienced in all the other studies described in the literature overview of studies attempting to predict hearing sensitivity with DPOAEs (see 2.3.4. PTT prediction with DPOAEs in perspective).

The rationale for this study is to improve prediction accuracy of pure tone thresholds at 500, 1000, 2000 and 4000 Hz in normal and hearing-impaired ears with DPOAEs and artificial neural networks.

It is anticipated that the prediction of PTTs with DPOAEs and ANNs will improve if the amplitude of the distortion product is included as a variable to determine correlations and make predictions. In the previous study, the amplitude of the distortion product was not included as a variable. Furthermore, more extensive experimentation of optimal neural network topologies will be experimented with, such as the optimal number of middle neurons and the structure of input data. Different types of networks will be investigated with as well as different types of network topologies and error tolerance levels. All these aspects that influence prediction accuracy of neural networks will be discussed in chapter three.

2.9 Summary

An overview of pure tone prediction with current objective diagnostic procedures revealed limitations in the evaluation of difficult-to-test populations. It seemed that, despite all the strengths and positive attributes of ABR, tympanometry, MLR, and LLR, a few weaknesses in these procedures made it difficult to measure exact hearing ability and site-of-lesion in populations such as neonates, infants, malingerers, the crucially ill and foreign speakers. ABR is currently the preferred method for diagnostic audiology in special populations (Hall III & Mueller III, 1997) but demonstrates weaknesses such as a limited frequency area in which hearing ability can be determined, lengthy test times, the possibility of sedation and the level of expertise and expense required (Ferraro & Durrant, 1994; Musiek et al. 1994; Robinette, 1994; Weber, 1994). It is therefore with much hope that many researchers turned their investigations to otoacoustic emissions.

Kemp (1978) identified different classes of otoacoustic emissions, depending on the stimuli used to evoke them. Spontaneous otoacoustic emissions (SOAEs) are only prevalent in half of normal hearing persons and can therefore not be implemented as a screening test or diagnostically (Lonsbury-Martin, 1994; Norton & Stover, 1994). Stimulus frequency otoacoustic emissions (SFOAEs) are not currently clinically used due to difficulties in separating in-going stimuli and out-going emitted responses (Lonsbury-Martin & Martin, 1990). Transient evoked otoacoustic emissions (TEOAEs) have been proven as a clinical acceptable hearing screening procedure, but the fact that they are only recordable in normal ears limited their diagnostic hearing testing applications (Kemp & Ryan, 1993; Lonsbury-Martin et al. 1992; Stevens et al. 1990). Distortion product otoacoustic emissions (DPOAEs) on the other hand, revealed many possibilities as a potential test of auditory functioning. First, it has been proven useful in both clinical and research settings, for it is the only emission type that can easily be recorded in many laboratory animals, allowing for experimental control of certain factors (Mills, 1997). Second, it can be measured in ears with a hearing loss of up to 65dB HL, therefore revealing information regarding outer hair cell functioning of hearing-impaired populations as well (Moulin et al. 1994). Third, it is the emission type that can be most easily compared to the conventional audiogram, due to the pure tone frequency nature of the stimuli that can be chosen to stimulate any specific region on the basilar membrane (Durrant, 1992; Lonsbury-Martin & Martin, 1990). Fourth, DPOAEs correlate well with pure tone thresholds and the configuration of the hearing loss (Durrant, 1992; Kimberly & Nelson, 1989; Stover et al. 1996a). Fifth, DPOAEs are not influenced by aspects such as gender and state of consciousness (Cacace et al. 1996; Karzon et al. 1994, Kemp, 1997). Of all the emission types, DPOAEs meet the most requirements for an optimal pure tone prediction procedure.

Many studies described the relationship between DPOAEs and pure tone thresholds (Avan & Bonfils, 1993; Bonfils et al.; 1991; Gaskill & Brown, 1990; Gorga et al. 1993; Kimberley et al. 1994b; Probst & Hauser, 1990; Stover et al. 1996a). Statistical methods used to date, such as multivariate (discriminant) analysis in the case of the study of Kimberley et al. (1994b), but also in all the other studies previously named, indicated a correlation between DPOAE measurements and behavioral pure tones. These studies however, could not predict the actual pure tone thresholds given only the distortion product responses (Lee et al. 1993, Kemp, 1997). The complexity of the data, the numerous variables involved and the possibility of a nonlinear correlation have been some of the reasons why conventional statistical methods could not predict pure tone thresholds given only DPOAEs, but only distinguish between normal hearing and hearing-impaired ears. There are also factors contributing to PTTs that do not contribute to the measurement of OAEs. It is clear that the emission field is still in the early stages of information gathering and that there are many aspects not yet fully understood or agreed upon. Regardless, major expectations concerning clinical applicability of DPOAEs is that DPOAEs will eventually be understood and developed to such an extent that DPOAEs can predict PTTs (Kemp, 1997; Lonsbury-Martin et al. 1997).

The complexities of the measurement, analysis and interpretation of distortion product emissions will be discussed in the following chapter.