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Effect of Prolonged Contralateral Acoustic Stimulation on TEOAE Suppression

By

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In fulfilment of the requirements for the degree

M. Communication Pathology

In the

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University of Pretoria

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November 2008

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Abstract

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Degree : M Communication Pathology (Audiology)

Although the suppressive effect of the medial olivocochlear system (MOCS) on peripheral auditory active mechanisms is well documented in humans, the effect of efferent inhibition over prolonged periods of acoustic stimulation is less well documented, especially as observed in suppression of transient evoked otoacoustic emissions (TEOAE's). The present study therefore evaluated the relationship between the duration of contralateral acoustic stimulation and the suppression of TEOAE's in ten adults with normal hearing. TEOAE recordings with linear clicks (60 dB sound pressure level) were measured at four intervals during 15 minutes of continuous contralateral white noise (45 dB sound pressure level), followed by two post-noise recordings. An identical within-subject control condition was recorded without contralateral noise. Experimental and control measurements were repeated three times, on separate days. Results revealed significant and sustained TEOAE amplitude reduction for the entire duration of contralateral stimulation. Suppression increased across the duration of contralateral noise, but not sufficiently to be statistically significant. After noise termination, TEOAE amplitudes increased to values significantly above control recordings. The sustained suppression of TEOAE's indicates continuous efferent inhibition over time in normal adults, with a significant increase in TEOAE amplitude after noise cessation possibly indicating increased outer hair cell responsiveness after prolonged contralateral noise.

Keywords: Transient evoked otoacoustic emissions; Contralateral stimulation; Medial olivocochlear efferent system; Prolonged stimulation

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Chapter 1: Orientation and Statement of the Problem

1.1 Introduction

Since David Kemp first described otoacoustic emissions (OAE's) in 1978, an extensive body of research has been produced, studying the many aspects of OAE's and their relation to auditory functioning. These studies have led to many new applications of this procedure towards more specific diagnoses of pathologies related to audition. A more recent area of interest that has started to enter clinical practice is the measurement and quantification of contralateral suppression of OAE's.

The purpose of this chapter is to present a brief overview of the ongoing development of OAE measurements with specific focus on contralateral suppression of OAE's, its clinical applications, advances and continued interests of research. It provides a brief explanation of the effect of contralateral acoustic stimulation (CAS) on the suppression of OAE's and the rationale for investigating the time course of this effect during continual CAS. This overview clearly indicates the need for investigations of the effect of prolonged excitation of the efferent system.

1.2 The Origin and Development of Otoacoustic Emission Measurements

The discovery of active cochlear mechanisms, in the form of OAE's (Kemp, 1978) contradicted established cochlear theories of the day. It was widely accepted that the cochlea was mechanically passive and functionally linear. These findings supposed that travelling waves along the cochlea moved without attenuation, that they could be reflected and reversed by non-linear processes and thereafter could reverberate along with distortions inside the cochlea for a notable period of time (Kemp, 1978).

Kemp discovered that sound could be recovered from the cochlea by means of an ear canal microphone following stimulation by either tones or clicks.

These low intensity sounds, referred to as "evoked acoustic emissions" (Kemp, 1978) were noticed for several milliseconds in the ear canal and were called "Kemps Echoes". They provided an indication of the cochlear response to acoustic stimulation. These echoes are today commonly known as otoacoustic emissions (Glattke & Kujawa, 1991).

It is generally believed that OAE's are the by-product of the amplification of sound in the cochlea (Kemp, 1978). These by-products of the preneural mechanisms of the cochlear amplifier are particularly linked to the normal functioning of the outer haircells (OHC) (Brownell and Kachar, 1985; Brownell, 1990). Of all the cells of the organ of Corti, only the OHC have been shown to produce active mechanical movements and may, therefore, generate sound (Folenkov, Belyatseva, Kurc, Mastroianni & Kachar, 1998). Thus OAE's are sounds generated by the motility of OHC in normal cochleae, either in response to acoustic stimulation or spontaneously. Different types of emissions can be distinguished by the relationship between the type of stimulation and the latency of the response after the stimulus onset.

Traditionally, OAE's have been classified into two types, namely Spontaneous OAE's (SOAE's) that are emitted from the ear in the absence of stimulation, and Evoked OAE's (EOAE's) that can be observed in response to a stimulus applied to the ear. SOAE's are believed to be caused by the active processes that occur in the cochlea (Pujol et al., 1994).The clinical value of SOAE's is restricted by their low prevalence in normal ears. These emissions occur in only 72% of healthy ears at frequencies that vary greatly among subjects (Talmadge, Long, Murphy & Tubis, 1993). While an absence of SOAE's does not imply outer hair cell dysfunction, their presence is evidence for the presence of an "active" element in the cochlea (Kim, 1986) and is a sign of normal cochlear function (Bright & Glattke, 1986).

The second type of OAE, EOAE's, can be subdivided into three subtypes. Stimulus Frequency OAE's (SFOAE's) are evoked by constant pure tone stimulation at low intensity levels and are normally swept gradually across a region of frequencies. More commonly researched and clinically applied, however, are the Transient Evoked OAE's (TEOAE's) and Distortion Product OAE's (DPOAE's). TEOAE's are low-level sounds emitted by the ear in response to brief stimuli, such as broadband clicks or tone bursts that can be measured with a low-noise, sensitive microphone in the external ear canal (Kemp, 1978). They have a high prevalence of nearly 100% in people with completely normal cochlear functioning (Bonfils, Uziel & Pujol, 1988b; Johnson & Elberling 1982; Kemp, 1978; Norton & Leely, 1987). DPOAE's are created by two slightly different pure tones closely spaced in frequency that activate the cochlea in the same region of the basilar membrane. The tow primary tones interact on the basilar membrane and create a family of distortion products that have a mathematical relationship to the primary tone frequencies. DPOAE's, like TEOAE's, can be measured in almost 100% of ears with normal hearing and normal middle ear function, and are stable within a given ear over time (Lonsbury-Martin et al., 1990a).

TEOAE's and DPOAE's are recognized to be very sensitive, clinically feasible measures of outer hair cell functioning and form an integral part of the basic test battery for evaluations of auditory functioning, therefore being commonly used in clinical practices. Although they are not tests of hearing, they complement the audiogram and provide sensitive measures of OHC integrity. Their role in the early identification and diagnosis of OHC dysfunction in paediatric and adult populations has become increasingly important and are applied in various forms of clinical application. Neonatal hearing screening (Bonfils et al., 1998) the assessment of suspected functional hearing loss (Musiek, Bornstein & Rintelmann, 1995), the monitoring of ototoxicity (Stavroulaki, Vossinakis, Dinopoulou, Doudounakis, Adamopoulos & Apostolopoulos, 2002), the diagnosis of tinnitus (Ceranic, Prasher & Luxon, 1995, 1998) and the differentiation between cochlear and retrocochlear dysfunction are among some of the clinical applications of OAE testing.

1.3 OAE suppression: a brief overview of the ongoing development in research and its clinical value

Apart from the clinical applications, advances in the field of OAE's are an area of continuing research interest. Recently numerous studies have been devoted to the suppression of OAE's by CAS (Collet, 1993; Veuillet, Collet & Morgon, 1992; Collet, Veuillet, Bene & Morgon, 1992; Berlin, Hood, Cecola, Jackson & Szabo (1993); Norman & Thornton, 1993; Morlet, Collet, Salle & Morgon, 1993; Froehlich, Collet & Morgon, 1993; Chery-Croze, Moulin & Collet, 1993; Moulin, Collet & Duclaux, 1993; Morlet, Collet, Salle & Morgon, 1993; Berlin, Hood, Hurley & Wen, 1994; Pujal, 1994; Collet & Grandori, 1994; Lind, 1994; Thornton, 1994; Graham & Hazel 1994; Prasher, Ryan & Luxon, 1994; Veuillet, Duverby-Bertholon & Collet, 1996; Maison, Micheyle & Collet, 1999; Hood et al., 1999). Contralateral suppression of OAE's is the phenomenon whereby the presentation of a sound ipsilateral or contralateral to a normal functioning ear from which OAE's are being recorded, reduces or suppresses the amplitude of the OAE (Berlin, Hood, Cecola, Jackson, & Szabo, 1993a; Berlin, Hood, Hurley, Wen & Kemp 1995b; Berlin, Hood, Hurley & Wen, 1994; Collet, Kemp & Veuillet, 1990b; Collet et al., 1992; Ryan, Kemp & Hichcliffe, 1991; Veuillet, Collet & Duclaux, 1991). This effect is attributed to alteration of cochlear micromechanics by the medial olivocochlear bundle (MOCB), activated by acoustic stimulation of the contralateral ear (Maison, Micheyl & Collet, 1995).

The MOCB innervates the organ of Corti and OHC's via efferent pathways (Rassmussen, 1946). This efferent or descending auditory system/reflex mediates sound-induced suppression of OAE's. Thus a reduction in the amplitude of OAE responses, in the presence of an acoustical signal in the contralateral ear, provides a non-invasive, objective approach for assessing MOCB efferent feedback activity in humans (Giraud, Collet, Chery-Croze, Magnan & Chays, 1995).

OAE's are the only objective and non-invasive method for the evaluation of the functional integrity of the medial efferent system and, therefore, for the evaluation of the structures lying along its course, at least up to the level of the inferior colliculi (VIII nerve, cerebellopontine angle and pons). Although contralateral acoustic suppression of OAE's is not yet completely understood and not widely used in clinical practice, some important information about the functioning of the medial efferent system and cochlear hair cells can be obtained from the presence, absence and amount of suppression.

Although data is rather limited in the literature, there is preliminary evidence that the efferent test could be useful in the diagnosis of pontine lesions either extrinsic (acoustic neuromas, meningiomas, congenital cholesteatomas) or intrinsic (multiple sclerosis, ischemic infarcts, tumours). Prasher et al., (1994) conducted a study in 18 patients suffering cerebellopontine angle (CPA) tumours and 11 patients with intrinsic pontine lesions. According to the results, 15 of the 18 patients with CPA tumours demonstrated abnormal TEOAE suppression ipsilateral to the lesion. The suppression was abnormal in all patients suffering intrinsic pontine lesions. The author performed the TEOAE suppression test in a group of 11 patients with CPA tumours (6 with acoustic neuroma, 1 congenital cholesteatoma, 3 meningioma, 1 lipoma) and a second group comprised of 21 patients suffering intrinsic pontine lesions (10 with multiple sclerosis, 7 ischemic infarct, 1 pontine haemorrhage and 3 tumours). A third group of 20 young healthy, normal hearing volunteers served as the control group for the TEOAE suppression test. Normal suppression in sound pressure level (≥1 dB SPL) was demonstrated in 18 out of the 20 controls (false positive rate 6.7%). All patients with CPA tumours showed abnormal suppression (<1 dB SPL), either ipsilaterally to the lesion or bilaterally (sensitivity 100%). Bilateral abnormal suppression was found whenever pressure was exerted on the pons due to the size of the tumour. Abnormal suppression was recorded in 17 out of the 21 patients with intrinsic pontine lesions (sensitivity 81%).

Auditory neuropathy is a clinical entity that has attracted the interest of audiologists and researchers in auditory function. It is characterized by sensorineural hearing loss in pure tone audiometry, speech discrimination difficulty, absence of acoustic reflexes, normal OAE's and absent or severely abnormal auditory brainstem responses (ABR's) without any radiologically evident retrocochlear lesion. The age of patients ranges from infancy to adulthood and it could present as a neuropathy of the VIII nerve alone or, most frequently, as a part of hereditary sensori-motor neuropathies (i.e. Charcot-Marie-Tooth syndrome, Friedreich's Ataxia syndrome) (Doyle, Sininger & Starr, 1998; Starr, Sininger, Hood & Berlin, 1996). Studies have demonstrated that patients with auditory neuropathy have absent efferent suppression of TEOAE's with binaural, contralateral or ipsilateral noise but usually have normal otoacoustic emissions (Berlin et al., 1993a; Hood, Berlin, Bordelon & Rose, 2003; Lalaki 2003; Abdala, Sininger & Starr 2000). In consideration, evidence exists that the assessment of the medial olivocochlear system by recording OAE's under CAS in a suspected lesion of the CNS could contribute to neuro-otological topographic - or site of lesion diagnostics. It could be performed to complement ABR's in cases with mean hearing thresholds worse than 60 dB HL, where the ABR test is of limited sensitivity (provided that TEOAE's could be recorded, due to the retrocochlear nature of the hearing loss).

It is important to know that efferent suppression of OAE's is difficult to study in patients with greater than mild cochlear hearing losses because emissions are absent when hearing thresholds exceed 30-40 dB HL. Liang, Liu & Lui, (1997), measured contralateral suppression of TEOAE's with broadband noise in 24 ears with cochlear hearing losses. They reported that TEOAE amplitude and suppression of emissions were significantly reduced in patients with cochlear hearing losses in comparison with normal ears.

Cases of tinnitus have also been linked to the efferent system and a possible link between the efferent system and the generation of tinnitus has been suggested by several authors. Veuillet, Collet and Duclaux (1991) observed a smaller suppression effect in the ear ipsilateral to the tinnitus in a patient with unilateral tinnitus. Chery-Croze, Collet and Morgon (1993) reported on 16 patients with bilateral tinnitus and 20 patients with unilateral tinnitus where suppression was measured using contralateral suppression with evoked otoacoustic emissions (EOAE's). Little suppression was observed in 10 of the

20 patients with unilateral and bilateral tinnitus. The majority of patients with unilateral tinnitus showed a decrease in the amount of suppression or an enhancement of emission amplitude on the side ipsilateral to the tinnitus, whereas a few patients showed an increase in emission amplitude under the suppression condition. Suppression of DPOAE's indicated medial olivocochlear (MOC) dysfunction in the frequency range of the tinnitus. Ceranic, Prasher, Raglan & Luxon (1998) studied efferent suppression in patients with tinnitus following head injury and difficulties listening in background noise despite normal peripheral hearing sensitivity. They also observed a reduction in suppression in the patients with tinnitus when compared with a control group of patients without tinnitus. In 19 subjects with unilateral tinnitus, Rita and de Azevedo (2005) found that the overall TEOAE response levels were significantly higher in the ear with no tinnitus and the medial olivocochlear system (MOCS) as measured with TEOAE suppression was significantly less efficient in the ear with tinnitus.

Berlin, Goforth-Barter, Hood and Bordelon (1999) reported that hyperacusis patients show abnormally large amounts of efferent suppression. They observed an increase in efferent suppression in a group of three patients with hyperacusis, two adults and one child, who complained that ordinary sounds were perceived as loud and frequently intolerable. These results suggested that efferent suppression may be a good tool to identify certain types of hyperacusis objectively.

Other studies in the field of contralateral suppression have focused on speech perception and the detection of sound in noise (Kumar & Vanaja, 2004; Micheyl et al., 1995). In addition to this, several studies have provided evidence suggesting that activation of the medial efferents serves a protective function against high-level auditory stimuli in the mammalian auditory periphery (Canlon, 1996; Subramanian, Henderson & Spongr, 1993).

1.4 Problem Statement

It is well documented that hearing deficits may result from exposures to relatively intense acoustic stimulation and, in addition, it has been shown that exposure to high intensity sounds results in various structural changes in the cochlea(Saunders, Dear & Schneider, 1985). Previous studies have shown that damage to, or abnormalities in, the efferent auditory system degrades perception of signals in noise (Muchnik et al., 2004) and may even make the cochlea more susceptible to damage from exposure to noise (Kujawa & Liberman, 1997; Maison & Liberman, 2000). Prasher et al. (1998) noted significant reductions in efferent suppression of TEOAE's with contralateral noise stimulation of up to one hour.

Industrial workers are commonly exposed to high noise levels for long durations. It is important to know if the protective function of the efferent system remains stable even when the cochlea is exposed to noise for prolonged durations. The fatiguing characteristics of sensory cells and auditory afferent neurons are well researched, but these characteristics are not as well-documented in efferent neurons. Sliwinska and Kotylo (2002) compared OAE suppression in subjects with normal hearing and subjects with occupational exposure to noise of up to five years. Their results showed that the amount of suppression was significantly decreased in the exposed group compared to non-exposed subjects (Sliwinska & Kotylo, 2002). This reduction in amplitude was ascribed to the damaged efferent auditory neurons in individuals exposed to noise. If this is the case, the protective characteristics of the efferent auditory neurons are expected to adapt or weaken over time, making the OHC's more susceptible to acoustic trauma and permanent damage. Another explanation for the noise induced hearing loss may be that the have a weak or poorly functioning MOCS to begin with and therefore might be susceptible to noise damage as a result of MOCS status.

From the existing literature it is clear that there is a need to study the relationship between outer hair cell integrity and the extent of efferent inhibition. An investigation of the effects of prolonged excitation of the efferent pathway in order to monitor changes in the amount of OAE suppression over a predetermined time of contralateral stimulation will provide better understanding of whether the mechanisms underlying these protective effects persist over longer periods of noise exposure. Thus the purpose of the present study is to evaluate the relationship between the duration of contralateral acoustic stimulus and suppression of evoked otoacoustic emissions.

1.5 Outline of the Thesis

Chapter One: Orientation and Statement of the problem

This chapter provides a brief overview of the development of OAE measurements with a specific focus on the development of research in contralateral suppression of OAE's. It formulates the need for knowledge regarding the effect of prolonged excitation of the efferent system and delineates the purpose of this study, which is to further investigate the initial time course of the suppressing effect during continual CAS.

Chapter two: Literature review

Chapter two primarily focuses on TEOAEs and suppression of TEOAES. It provides an in depth overview of the anatomy (the general afferent and efferent innervation fiber distribution) and physiology of the olivocochlear bundle, the feedback loop that involves OHC's, and the differenential characteristics of ipsilateral, bilateral and contralateral suppression of OAE's with specific focus on the literature on the effect of prolonged contralateral excitation on OHC's and the implications of this knowledge.

Chapter Three: Research Methodology

Chapter three will be a discussion of the methodology for data collection, preparation and analysis, apparatus, subjects, the research design and the procedures chosen for optimal contralateral suppression of TEOAE's.

Chapter Four: Results

Chapter four will present results of all experiments: Suppression of the overall TEOAE response and responses at each half-octave frequency over a predetermined period of separate TEOAE measurements.

Chapter Five: Discussion and Interpretation of Results

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

Chapter Six: 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.

1.6 Conclusion

Auditory efferent nerve fibres have an inhibitory influence on the auditory periphery, which in turn may serve as a protective reflex against acoustic overstimulation. Contralateral suppression of OAE's is known to be an objective, non-invasive clinical test for the exploration of the non-linear micromechanics of OHC's and the clinical evaluation of the descending efferent bundle in humans. Thus OAE's can be used to explore the duration of this protective reflex in order to determine whether it remains consistent over a long duration of acoustic stimulation, or adapts and weakens over time, making the OHC's more susceptible to acoustic injury.

1.7 Summary

This chapter provides a brief outline on the progress and advances in OAE measurements and in particular, suppression of OAE's. It briefly explains the effect of CAS on suppression of OAE’s and why a study of the duration of suppression during constant CAS will provide more information on the function of medial olivocochlear efferents and their ability, or lack thereof, to provide a sustained effect on OHC functioning.

Chapter 2: Functioning of the efferent medial olivocochlear system during prolonged stimulation.

2.1 Introduction

Efferent control of the OHC's and the cochlear efferent neurons has been investigated using studies of cochlear micromechanics, cochlear and eighth nerve electrophysiology and OAE's (Berlin, Hood, Hurley & Wen, 1996). Studies have used OAE recordings from subjects involving ipsilateral or contralateral competing stimuli, or artificial electrical stimulations of neurons in the efferent system in the case of animal subjects, to investigate the efferent influence on the OHC's and on cochlear efferent neurons. Through this, the anatomy and physiology of the olivocochlear bundle and its efferent control over the auditory periphery could be understood more thoroughly.

The purpose of this chapter is to describe the anatomy and physiology of the olivocochlear bundle, the feedback loop that involves OHC's and IHC afferents, the different characteristics of ipsilateral, bilateral and contralateral suppression of OAE's with a specific focus on the effect of prolonged contralateral excitation on OHC's and the implications of this knowledge. The existing literature provides evidence for ruling out the limitations on suppression duration studies, which emphasizes the need for further investigations, guidance in formulating the research methodology and assistance in the interpretation of the results.

The content of this chapter is organized in such a manner that the theoretical basis of the efferent system and its function are explained before elaborating on the use of OAE's to investigate certain properties of the efferent system and feedback loop, in particular the duration of the efferent effect on OAE's. The structure of concepts and theories clarified in this chapter is illustrated in figure 2.1 as a flow chart.

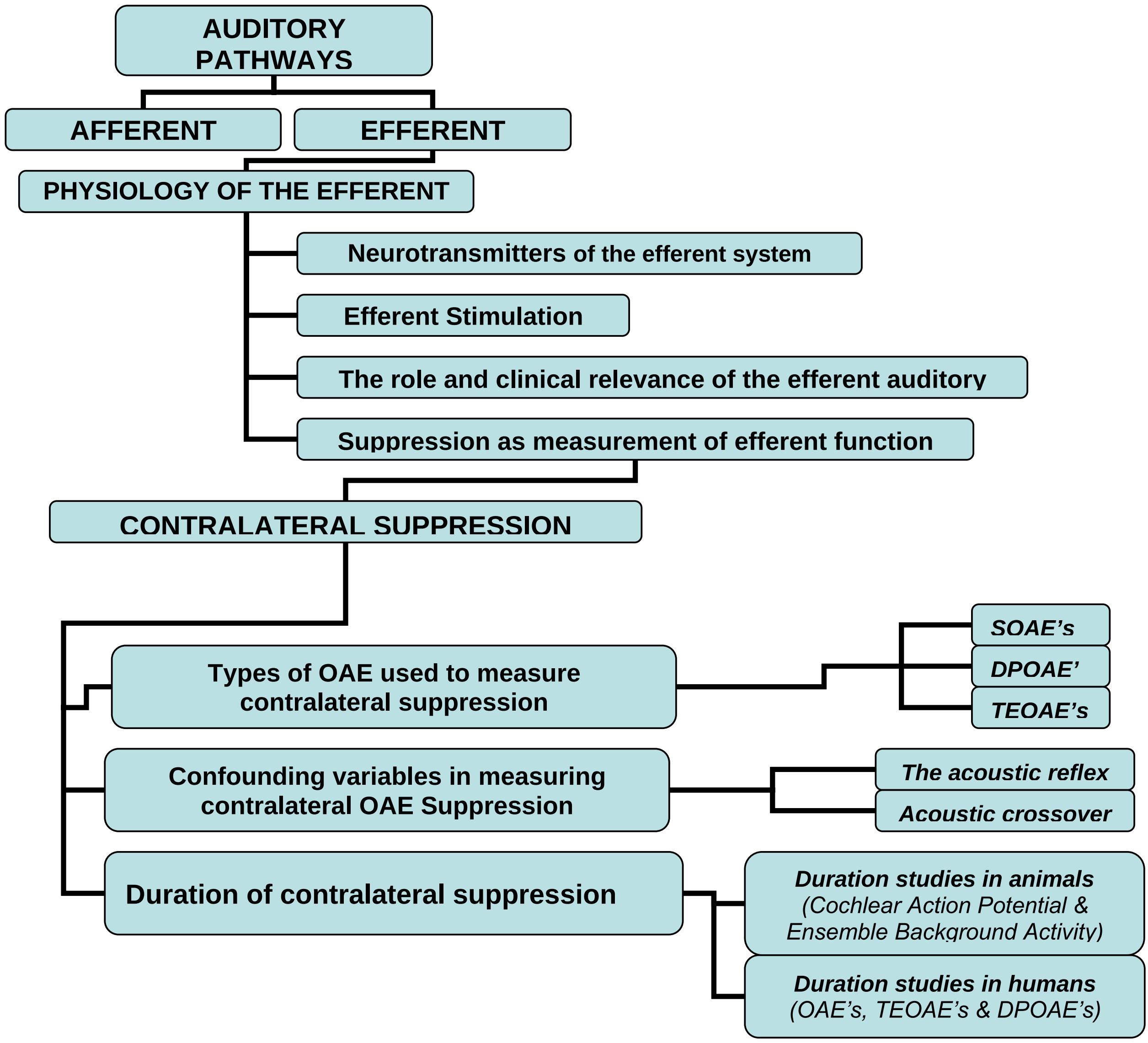


Figure 2.1 Concepts and theories discussed in chapter 2

It is well known that efferent suppression of OAE's is mediated by the olivocochlear bundle (OCB) (Berlin et al., 1996; Liberman, Puria & Guinan, 1996). Thus it is critical to discuss the neuroanatomy and physiology of this efferent system to better understand the mechanism and consequences of OAE suppression.

2.2 Anatomy of auditory pathways

The cochlear branch of cranial nerve VIII (vestibulocochlear nerve) is known as the auditory nerve. It contains afferent and efferent fibres. Auditory afferent fibres are mostly responsible for carrying incoming electrochemical signals that are transduced by sensory cells (hair cells) to the brainstem and auditory cortex. Efferent fibres in turn send information from the auditory cortex descending to the cochlea, forming the olivocochlear bundle, where they synapse with dendrites of ascending afferent fibres or directly with outer hair cells. Evidence confirms that the descending or efferent, auditory system plays a role in outer hair cell physiology and, therefore, influences OAE measures. It is difficult, however, to discuss the efferent system of the cochlea in isolation, since they are so closely integrated with the sensory cells. The following discussion will, therefore, explain both the afferent and efferent auditory pathways.

2.2.1 Afferent pathways

The innervations of OHC and IHC include both efferent and afferent connections. The afferent fibres leave the inner ear through the internal auditory canal (or meatus) located on the posterior surface of the petrous part of the temporal bone. They enter the brainstem at the level of the cerebellopontine angle (CPA) and terminate in the cochlear nucleus complex (CNC). The innervations of OHC and IHC include both afferent and efferent connection. Amongst a total of 30,000 eighth cranial nerve fibres in the human, two clear types of afferent neurons can be identified (Kiang, Rho, Northrop, Liberman & Ryugo, 1982), namely Type I and Type II afferent fibres. Table 2.1 delineate the differences between these two afferent fibres.

Table 2.1 Difference between Type I and Type II afferent fibres

Type I afferent fibres	Type II afferent fibres

Also known as	• *Radial afferents*	• *Outer spiral afferents*
Percentage of total afferent fibres	• *88%* *(Nandol et al., 1990)*	• *12 %* *(Nandol et al., 1990)*
Synapse with	• *Inner hair cells* *(Nandol et al., 1990)*	• *Outer hair cells* *(Nandol et al., 1990)*
Type of cell bodies	• *Bipolar cell bodies* *(Kiang et al., 1982)*	• *Monopolar or pseudomonopolar* *(Kiang et al., 1982; Brown et al., 1988)*
Amount of afferents connecting with hair cells	• *Form direct connections with inner hair cells, about 20 per hair cell (Kiang et al., 1982)*	• *Each outer hair cell may receive processes from up to 20 afferent fibres (Kiang et al., 1982)*
Neural pathway	• *Sends large myelinated axons to the cochlear nucleus in the brain stem (Brown et al., 1998)*	• *Sends small unmyelinated axons to neurons around the periphery of the cochlear nucleus (Brown et al., 1998)*
Function	• *Fibres convey sensory information from the cochlea to auditory regions of the central nervous system*	• *Difficult to document (Brown et al., 1998). Possible function of carrying information about the mechanical state of the cochlear duct. It is thought that these neurons possibly do not respond to sound (Robertson et al., 1999)*

2.2.1 Efferent pathways

Delineation of the efferent auditory pathways, and specifically the crossed and uncrossed olivocochlear bundles (OCB), dates back to the mid 1940’s (Rasmussen, 1945; 1960). Since then auditory physiologists have developed a specific interest in the OCB pathways and its function. Efferent innervation of the cochlea in mammals is provided by the OCB. Efferent fibres transmit impulses from the brain to the cochlea. These fibres arise from neurons whose cell bodies are located in the brain stem, mostly on the side opposite from the ear that they innervate. Once the efferent fibres reach the cochlea, they branch out to form a large number of nerve endings. Two distinct populations of efferents have been identified in the cochlea (Warr & Guinan, 1979). The two efferent divisions differ with respect to a number of morphological features, including the pattern of development, the size of their cell bodies, brainstem locus of origin, the preferred lateralization of projection to the periphery and the postsynaptic targets within the auditory periphery (Sahley et al., 1997a).

Hence the efferent olivocochlear system is divided into two subsystems, namely the lateral olivocochlear (LOC) system and the medial olivocochlear (MOC) system (Guinan, Warr & Norris, 1983). The pathways of both subsystems originate from the superior olivary complex (SOC), where their axons extend through the reticular formation (Warr, 1992) and join to form the olivocochlear bundle (OCB) close to the floor of the fourth ventricle (Rasmussen, 1947; Gacek, 1961). The OCB is made up of both fibers from LOC (63%) and from MOC neurons (37%) (Aschoff & Ostwald, 1987; Nakai & Igarashi, 1974; Warr, 1992). Table 2.2 summarizes the difference between LOC and MOC efferent subsystems.

Table 2.2 The difference between LOC and MOC efferent subsystems

	LOC efferents	MOC efferents
Arises from	• *Lateral superior olivary (LSO) nucleus complex in the upper pons*	• *The majority of MOC neurons are located in the medial periolivary region surrounding the medial superior olivary (MSO)*
Type of axons	• *Unmyelinated*	• *Myelinated*
Innervates	• *IHC's (89%-91%) of the ipsilateral cochlea (Warr, 1992). These efferents do not synapse directly at the basal surface of the IHC's but at specialized postsynaptic regions on afferent type I dendrites (Liberman, 1980; Pujol & Lenoir 1986)*	• *MOC fibres are unidirectional (Brown, 1987) and synapse with the base of the outer hair cells (OHC's) of the organ of Corti (Warr, 1975; Warr et al., 1986).* • *They innervate both cochleae (but mostly in the contralateral cochlea) and synapse with the OHC's*
Possible Function	• *The way the lateral efferents synapse with dendrites of the auditory ganglion neurons clearly points to a postsynaptic regulation of the IHC-auditory nerve synapses. Because lateral olivocochlear axons project to inner radial (type I) afferent fibres that communicate with IHC's, they do not directly influence hair cell activity (Spangler & Warr, 1991; Warr, 1992). However, they may affect neural activity resulting from IHC stimulation by virtue of their synapses with the inner radial fibres (Chen & Bobbin, 1997).*	• *MOC fibres play a significant role in altering and modulating the cochlear micromechanics that are discussed in depth elsewhere in this chapter. The MOC synaptic terminals at the hair cell body include innervation with a portion of the cistern structure of the OHC that is thought to enable the OHC to change length (Lim, 1986).*
Tonotopic organization	• *LOC neurons have the same tonotopic organization of the LSO neurons on the ipsilateral side and it is known that the LSO is the only nucleus in the SOC that receives a complete ipsilateral frequency representation from the ventral cochlear nucleus (Warr, 1992).*	• *Like the LOC fibres, the MOC fibres also have tonotopic organization by connecting areas with similar characteristic frequencies (Warr,1992).*

As mentioned in table 2.2, the MOC efferent pathway is mainly involved in OHC physiology. Thus the focus will be on the physiology of the efferent system. The physiology of the afferent system, which synapses with IHC, will not be discussed further in this chapter.

2.3 Physiology of the efferent system

Even though the physiologic role of each efferent system is not yet completely understood, much can be deduced by taking into account what is now quite clear about the function of each type of hair cell and the feedback loop of the efferent systems. To clearly comprehend the physiology of the efferent system in terms of efferent stimulation, it is critical to understand some neurochemical characteristics of the efferent system.

2.3.1 Neurotransmitters of the efferent system

Neurochemically, both the lateral and the medial efferent system have been found to be cholinergic, using acetylcholine as their neurotransmitter. The axodendritic synapses of the lateral efferents consist of several neurotransmitters, namely acetylcholine (ACh), dopamine and gama-amino-butyric-acid (GABA) and neuropeptides such as calcitonine gene related peptide (CGRP), dynorphins and enkephalins.

2.3.1.1 Neurotransmitter of the lateral efferent neurons

The lateral efferent neurons can synthesize and release different neurotransmitters depending on different physiological conditions. Enkephalins are negatively coupled to adenylate cyclase activity (Eybalin, Pujol & Bockaert, 1987a). Lateral efferents have an inhibitory function and may be related to the release of metaenkephalin during noise exposure (Eybalin, Rebillard, Jarry & Cupo, 1987b), or the increase in the perilymphatic enkephalin in noise-stimulated animals (Drescher, Drescher & Medina, 1983). It is thought that the enkephalinergic lateral efferent is responsible for the firing of auditory nerves or in protecting against abnormal spontaneous firing (tinnitus). The release of dopamine in noisy conditions has been observed (Vincent-Torres et al., 1993), indicating a protective effect against noise-induced toxicity. It also assists in the repair of auditory dendrites and their synapses with OHC's (Pujol, Zajic, Dulon, Rapheal, Altschuler & Schacht, 1991; Pujol et al., 1993).

2.3.1.2 Neurotransmitter of the medial efferent neurons

The axo-dendritic synapses between the medial efferents and outer hair cells are known to contain ACh, CGRP and GABA. Although GABA and CGRP may play some role, most of the protective effects of the system seem to be ACh-dependent. When applying ACh at efferent synaptic terminals, it mimics the effects of electrical stimulation of the olivocochlear bundle (Bobbin & Konishi, 1971). It reduces the compound action potential and alters cochlear micromechanics (Kujawa, Glattke, Fallon & Bobbin, 1992). Neuromodulation is regulated by the presence and release of ACh, and the presence of synthetic and degradative enzymes (Altschuler, Kachar, Rubia, Parakkal & Flex, 1985). ACh has a rapid synaptic effect, whereas neuroactive peptides show a more slow and sustained action (Musiek & Hoffman, 1990).

2.3.2 Efferent Stimulation

Most of the earlier studies defining the physiology of the efferents of the LOC and MOC pathways was performed on animals. Although much is understood about the neuroanatomy of the LOC efferents, the influence of the LOC on the auditory system still remains unclear. The possibility of a postsynaptic control over type I afferents of the IHC's has been suggested (Liberman, 1980). Sahley et al. (1997) proposed a model of lateral efferent action wherein LOC efferents release ACh, which causes hyperpolarization of the type I radial afferents. Chen et al. (1997) suggested that the LOC efferents release afferent neurotransmitters that depolarize the type I fibres. The enkephalins and dopamine from the lateral efferents were thought to protect the auditory nerve dendrites from acoustic trauma damage and excitotoxity (Pujol, 1994). Much more is understood about the physiology of the MOC efferent functioning, however, and this section will focus more on the function of this system.

To better understand the effect of efferent auditory stimulation, and ultimately its effect on OAE's, it is necessary to understand what happens when the OCB is stimulated (electrically or acoustically) and the response of OHC's to olivocochlear (OC) stimulation. Galambos (1956) first described the effect of electrical stimulation on efferent fibres that project to the cochlea. He reported a reduction of auditory nerve responses to acoustic stimulation on concurrent electrical activation of these fibres by comparing the compound action potentials (N1) stimulated acoustically with a click to those elicited under similar conditions in the presence of recurring electrical shocks to efferent fibres. Reduction in N1 amplitude was observed in the presence of electrical stimulation and thus signified an inhibitory role of the OCB (Galambos, 1956).

It is now clear that olivocochlear stimulation of the inner ear results in two different efferent effects, namely slow and fast effects of OHC innervation. OHC's move when electrically stimulated by shortening when depolarized and lengthening when hyperpolarized (Brownell, 1983). This OHC movement is extremely fast effect and is known as the fast effect of OHC innervation (Reuter & Liberman, 1995). The change in electromotility is ascribed to changes in voltage across the OHC membrane (Santos-Sacchi, 1991; Kalinec, Khanna, Ulfedahl & Teich, 1992) and appears to be produced by molecular "motors" along the length of the cell (Dallos, Evans & Hallworth, 1991). Single hair cell studies have observed nonlinearities in the electromotility of OHC's (Evans, 1990; Santos-Sacchi, 1993). These nonlinearities originate in the electromotile response inherent in the transducer channel that provides the voltage changes that drive motility (Santos-Sacchi, 1993). Slow motility effects of OHC efferent innervation can be described as gradual changes in length that occur over the course of several seconds (Ohnishi et al., 1992). Zenner et al., (1989) suggested that activation of the efferents at the bases of the OHC's might produce this response and that molecular mechanisms different from those of fast motility may produce this slow effect (Zenner, 1988). Both the slow and fast effects of OHC innervation are discussed more thoroughly later in this chapter.

Acoustical stimulation of OHC's via the travelling wave to the cochlea is believed to ultimately depolarize and hyperpolarize the ionic current in OHC's by way of K+ and CA2+ regulation (Ashmore, 1988). Cell depolarization results in OHC contraction and an enhancement of the upward movement of the basilar membrane (Evans & Dallos, 1993). Hyperpolarization results in an increase of OHC length and decrease in width that restores the cell to its resting length (Ashmore, 1987). It is believed that medial efferent induced hyperpolarization counteracts the amplifying effect of OHC activity (Szikai et al., 1993). Stimulation of MOC efferents results in a release of ACh at OHC synapses that is responsible for K+ efflux from the OHC's, thus hyperpolarizing them (Ashmore, 1998). Hyperpolarization of OHC's therefore causes the cells to lengthen (Evans & Dallos, 1993) and reduce the gain that could result from OHC electromotility. It is known that medial efferent stimulation also has an inhibitory effect on IHC's. It reduces IHC sensitivity and broadens IHC tuning (Brown, Nuttal & Masta, 1983).

2.4 The role and clinical relevance of the efferent auditory system

As described above, the MOCS has an inhibitory effect on the OHC's, but this effect depends on the stimulus conditions and in some cases actually modulates the OHC electromotility. The result can be described as either inhibitory or enhancing. In quiet backgrounds, MOC activation by noise or electrical stimulation at the midline results in the suppression of N1 action potential and TOAE's (Galambos, 1956; Collet, Gartner, Moulin & Morgon, 1990a). In noisy listening environments, MOC activation decreases physiological thresholds and increases the response amplitudes to transient signals (Nieder & Nieder, 1970; Winslow & Sachs, 1987, 1988; Dolan & Nattall, 1998; Kawase, Delguette & Liberman, 1993; Kawase & Liberman, 1993). Whether suppressive or enhancing, it is now generally presumed that the MOC acts by reducing the motility of the OHC's (i.e. it acts as a cochlear amplifier). In situations where the effects are enhancing, the result is an inhibition of the OHC response to the concurrent, sustained masking noise, resulting in an unmasking of the response to the transient target stimulus (Winslow & Sachs, 1987, 1988; Kawase et al., 1993; Kawase & Liberman, 1993).

Although the physiological function of the efferent auditory system is well documented, its specific biological role remains uncertain. In view of the preferential innervation of the OHC's by MOC fibres, it has been hypothesized that the stimulation of the medial efferents alters IHC sensitivity indirectly by altering the micromechanical properties of the OHC's. It is well established that the length, tension and the stiffness of the OHC's are under the control of the MOC bundle. The MOC bundle enhances the auditory sensitivity, especially for low-level stimuli at 30 to 40 dB sensation level (SL) (Brownell 1990; Guinan 1986; Kim 1986).

There is also increasing evidence suggesting that the MOCS enhances frequency resolving capacity (Micheyl & Collet, 1996) and vowel discrimination, especially in noisy background environments (Muchnik et al., 2004; Sahley , Nodar & Musiek, 1997c). The presentation of contralateral noise has been found to enhance speech-in-noise intelligibility in subjects with normal hearing. This improvement was minimal in patients with de-efferented ears (Giraud, Collet, Chery-Croze, Magnan & Chays, 1995) A relationship has been found between the improvement in perceptual performance on speech-in-noise intelligibility tasks (brought about by contralateral noise) and the effectiveness of the MOCS feedback (as assessed by strength of contralateral suppression of TOAE's) (Giraud, Collet & Chery-Croze, 1997; Micheyl, Morlet, Giraud, Collet & Morgon, 1995). In addition to this, a correlation has been established between contralateral suppression of OAE's and detection-in-noise thresholds (Micheyl & Collet, 1995). These correlations suggested that normal-hearing subjects with the strongest improvement in speech-in-noise intelligibility with contralateral noise were those with the most robust MOCS feedback (Micheyl & Collet, 1996). It has been suggested that this improvement in speech intelligibility in noise, when the MOCS is activated, is the result of suppression in the response of fibres to continuous noise, which in turn become more responsive to transient stimuli such as speech (Kawase, Delgutte, & Liberman, 1993; Kawase & Liberman, 1993). Tolbert et al. (1982) suggested that the olivocochlear bundle (OCB) optimizes the detection of interaural intensity differences for higher frequency signals by increasing, within the cochlea, the interaural difference, reaching the lateral superior olive (LSO). Thus it is supposed that a better comprehension of the medial efferent system and its pharmacological manipulation may be beneficial for subjects struggling with speech discrimination difficulties in noisy environment, despite normal pure tone audiometric thresholds.

A number of research reports have suggested that medial efferent stimulation also serves as a protective function against high levels of acoustic stimulation (Canlon, 1996; Subramanian et al., 1993; Liberman, 1991). The long-standing observation that electrical stimulation of the olivocochlear (OC) efferents to the OHC's raises acoustic thresholds in the cochlea (Galambos, 1956) has led to speculation that activation of this pathway might protect the ear from acoustic overstimulation (Thrahiotis & Elliot, 1969). Studies in animals have shown that the crossed olivocochlear efferent system can reduce the cochlear neural desensitization caused by loud sounds. Several authors in the past have indicated that a hearing loss produced by loud sound in one ear of a guinea pig can be reduced by simultaneously presenting a non-traumatising sound to the other ear (Cody and Johnstone, 1982; Rajan and Johnstone, 1983, 1989). According to these authors, it was highly unlikely that this effect was due to the action of middle ear muscles, since their experiments were carried out in paralysed animals and at high frequencies where contraction of the middle ear muscle has very little effect (Moller, 1962). This reducing effect was also abolished by systemic administration of strychnine, a pharmacological blocker of the olivocochlear pathway, (Cody and Johnstone, 1982; Rajan and Johnstone, 1983), or by lesioning these neurons at the floor of the fourth ventricle (Rajan and Johnstone, 1989). These findings led authors to believe that a "contralateral protective effect" may be mediated within the cochlea by the MOCS of efferent neurons, which cross the brain at the floor of the fourth ventricle.

It is thought that forces generated by the OHC’s act to partially cancel friction within the organ of Corti, and that these forces are generated by an electro-mechanical transduction process which relies on the receptor current through the OHC’s, and that any disruption of the mechano-electrical transduction process producing these receptor currents should reduce vibration and produce elevation of neural thresholds. Patuzzi, Yates and Johnstone (1989b) studied the link between disruption of the mechano-electrical transduction of OHC’s and the elevation of neural thresholds and found that the amount of noise-induced hearing loss is highly correlated with the amount of disruption of OHC mechano-electrical transduction. These authors suggest that it is possible that the efferent neurons of the MOCS act to protect the cochlea from acoustic trauma by reducing the disruption of the mechano-electrical transduction at the apex of the OHC’s. Based on these observations, Patuzzi and Thompson (1991) monitored the influence of simultaneous contralateral sound on the changes in the neural response and low-frequency microphonic response produced by acoustic trauma in the first turn on the guinea pig cochlea. They reported that the MOCS may operate to protect the ipsilateral ear by reducing the inactivation of these channels. This was indicated by a smaller decrease in the low-frequency microphonic by reducing the loss of electrical drive to the active process within the cochlea caused by acoustic trauma (Patuzzi & Thompson, 1991).

Rajan (1991) found that activation of the olivocochlear (OC) efferent system in anaesthetised animals minimized the acute and temporary threshold shifts (TTS’s) seen with hazardous noise exposure. The role of olivocochlear activation in protecting the ear in animals or humans from the damaging effects of acoustic overexposure is much less understood, although some research has been done in attempt to explain the protective role of the OC efferent system (Handrock and Zeisberg, 1989; Liberman and Gao, 1995; Zeng et al., 1997a). These studies all found that chronically de-efferented animals can show greater permanent threshold shifts (PTS’s) than identically exposed animals without sectioning of the efferents. This protective role of the OC bundle has led authors to speculate that the MOCS may also play a role in the reduction of threshold shifts seen with noise exposure. This protective effect has been referred to as “conditioning” or “toughening” of the ear (Canlon 1996; Subramaniam, Henderson & Henselman, 1996). The toughening effect of the ear has been studied by conditioning animals with a daily exposure to moderate-level, non-damaging acoustic stimuli for several days and then exposing them to a traumatic acoustic stimulus of a shorter duration (Canlon, 1996). Canlon (1996) found that when the animals were conditioned before the traumatic acoustic exposure, less severe PTS’s could be observed than in the animals that were not conditioned previously.

A form of protection is also demonstrable in a very different paradigm, the repeated-exposure paradigm, in which animals are exposed to a mildly traumatic acoustic stimulus on a daily basis. In the repeated-exposure paradigm, protection is seen as a daily decrease in the acute threshold shifts measured immediately after each day’s noise exposure. As the daily exposures continue, the animals develop a slowly growing residual threshold, as seen from the deterioration of thresholds measured before each daily exposure, which ultimately becomes a PTS (Boettcher, Sprongr & Salvi, 1992). Thus the protection measured in the repeated-exposure paradigm appears to be a compound threshold shift, consisting of relatively large TTS and smaller accumulating PTS. Boettcher et al. (1992) suggested that this slow progression in PTS may involve slowly progressing damage to the stereocilia on IHC’s and/or OHC’s, causing a decrease in ion fluxes during daily noise exposure and decreasing the TTS each day.

Zeng et al. (1997) explored the possible OC system’s role in protection by using a combination of the repeated-exposure and condition/trauma approaches. The animals were exposed daily to a mildly traumatic stimulus, and DPOAE’s were measured before and after each exposure. Then, after the last of these daily exposures, the animals were exposed to the same stimulus at a much higher SPL, and the final PTS was measured several days later. The OCB was cut in the inferior vestibular nerve of one group of these animals, but there were only three successful de-efferentations, of which only two completed the whole protocol. Zeng et al. (1997) observed that, in the repeated-exposure, control animals showed reducing compound threshold shifts (CTS's) (i.e., protection). In contrast, the three de-efferented animals showed less reduction of CTS (less protection), but protection was not abolished, even though the de-efferentation was essentially complete. As for the final PTS after the high-level traumatic exposure, the two de-efferented animals that completed the protocol showed significantly higher PTS's than the control animals with the same noise exposure. These studies have all provided promising evidence suggesting that activation of the MOCS serves a protective function in the mammalian auditory periphery against high-level auditory stimuli and that de-efferented animals are more vulnerable to acoustic injury, regardless of their noise-exposure history.

To add support to this theory, Maison and Liberman (2000) examined inter-subject variability of vulnerability to acoustic injury in relation to differences in olivocochlear reflex strength. They used DPOAE suppression to measure MOC reflex strength in normal hearing awake guinea pigs two days before exposing them to 109 dB SPL noise for four hours. They then measured compound action potentials one week after the exposure, allowing recovery from temporary noise-induced hearing loss (Maison & Liberman; 2000). From their results, they suggested that the strength of the MOC reflex is a major contributor to the differences in vulnerability to acoustic overexposure.

The discovery of slow effects of OC activation on the inner ear (Sridhar, Liberman, Brown & Sewell, 1995) led researchers to believe that there might be a direct relationship between this slow effect and the efferent protection from acoustic injury. Pharmacological and physiological evidence suggests that both the slow and fast effects that involve conductance changes in the OHC's are affected by the interaction of acetylcholine with the same receptor on the OHC's, and both are mediated by the MOCS (Sridhar et al., 1995). The classical fast effects of OC activation are known with an onset and offset of suppression in the order of 50 to 100 ms (Wiederhold & Kiang; 1970). Slow effects of OC activation (slow suppression of cochlear response) appears with a time constant of 30 to 70s and can last for 1 to 2 minutes after the termination of the OC activation. There are two differences between fast and slow effects. Slow effects are largest for cochlear regions tuned to 14 kHz and are minimal below 10 kHz, whereas fast effects peak from 6 to 10 kHz. Slow effects are maximal for OC stimulation of 1 to 2 minutes and are virtually extinguished when duration exceeds 4 minutes, whereas fast effects remain essentially undiminished by OC stimulation in excess of 10 minutes (Sridhar et al., 1995).

Reiter and Liberman (1995) examined the effects of exposure frequency and duration on the OC-mediated protection from acoustic exposure in guinea pigs in order to examine the relation between this protective phenomenon and the slow effect of OC stimulation. From their results they observed that TTS protection from brainstem electrical stimulation was only demonstrable for exposure frequencies above 8 kHz and for exposure durations of less than 2 minutes, which proved that cochlear protection arises from the slow effects of OC stimulation rather than from the classic fast effect of OC action on the auditory periphery (Reiter & Liberman, 1995). If cochlear protection is mainly contributed to by the slow rather than the fast effect of OC stimulation, protection from acoustic overexposures would be predicted for exposure duration of 1 to 2 minutes and not for longer exposure durations of more than 4 minutes.

2.5 OAE suppression as a measurement of efferent function

Because descending medial efferent fibres preferentially terminate on OHC's, the prevailing view is that the micromechanical properties of the OHC's are under direct control of efferent innervation. Since OAE's are thought to reflect these dynamic properties, it has been hypothesized that activating the medial efferents would produce alterations to cochlear micromechanics and, hence, to OAE's. Indeed, there is now a great body of evidence that auditory stimulation, presented ipsilaterally, bilaterally or contralaterally (Warr, Guinan & White,1986; Warr & Guinan, 1978; Peul & Rebillard, 1990; Liberman, 1989

Kujawa, Glattke, Fallon & Bobbin, 1993; Kujawa, Glattke, Fallon & Bobbin, 1994; Tavartkiladge et al., 1993;1997; Wilson, 1980; Liberman et al., 1996; Berlin, Hood, Hurley, Kemp & Wen,1995a;1995b) results in the reduction of the amplitude of both spontaneous and evoked OAE's (TEOAE's and DPOAE's) (Ryan et al., 1991; Collet et al., 1990). This phenomenon is called suppression of OAE's and there is evidence that it is mediated through the medial efferent system (Kujawa, Glattke, Fallon & Bobbin, 1992; Veuillet et al., 1991; Warren & Liberman 1989). Thus, it has been suggested that the suppression of OAE's could serve as an objective, non-invasive clinical test for the exploration of the non-linear micromechanics of OHC's and the clinical neurological evaluation of the auditory brainstem in general, and descending efferent bundle specifically.

As mentioned before OAE's, can be suppressed when auditory stimuli are applied ipsilaterally, contralaterally or bilaterally. In relation to contralateral stimulation, ipsilateral masking can result in more pronounced suppression of evoked OAE's (Kemp & Chum, 1980; Tavartkiladge, Frolenkov, Kruglov & Artamasov, 1994; Wilson, 1980). The mechanisms underlying this effect seem to be twofold. One perspective is that the suppression results from intracochlear masking processes, whereas from another perspective it appears to be mediated through the olivocochlear system. There are two approaches for assessing the effect of ipsilateral suppressors on OAE's. The first approach, known as the ipsilateral simultaneous masking paradigm, uses a suppressor of one or more tones that is presented simultaneously with an OAE-evoking stimulus, at nearby frequencies. The simultaneous masking experiments are recorded with custom-designed acoustic probes, consisting of a microphone and two electroacoustic transducers, which provide the same ear with the suppressor signal and the recording-evoked OAE. With the second approach, the ipsilateral forward masking paradigm, a suppressor signal (ranging from a click to a relatively extended duration noise band), is presented to an ear prior to the presentation of an OAE–evoking stimulus (Tavartkiladge et al., 1994; Berlin et al., 1995).

Contralateral suppression is more commonly used in both clinical and experimental projects than ipsilateral suppression. The reason for this is that ipsilateral suppression measurements require special equipment (probe) and, as stated by the authors, suppression of TEOAE's could not be attributed only to the MOC bundle but also to intracochlear processes.

The mechanism underlining binaural suppression is similar to that of contralateral suppression. In addition, the full effect of the MOCS is brought to bear on the OAE elicited by bilateral acoustic stimulation. The approach typically used for bilateral suppression of TEOAE's uses a short-duration burst of noise that precedes a click stimulus, with a duration that is sufficient to elicit an efferent response. The typical latency for eliciting MOC effects is approximately 100 ms from the onset of an acoustic stimulus (Liberman et al., 1996). Berlin et al. (1995b) studied the effect of binaural noise on TEOAE's. They used a technique of presenting one ear with linear clicks that were preceded by binaural, ipsilateral, or contralateral noise bursts with a duration of 408 ms. In their experiment they found that the greatest amount of suppression was measured using binaural noise busts with the click train onset no later than 5 ms after the noise burst ended, and no suppression was observed when the time period between the end of the noise and the click onset was 1000 ms or longer. Ipsilateral noise in the same time frame showed less suppression than noise presented bilaterally and the least amount of suppression was observed with contralateral noise bursts (Berlin et al., 1995b)

Though the use of bilateral suppressors elicits more OAE suppression than contralateral suppressors and has been proved to measure the effect of the medial efferents on OHC's (acoustic stimulation of MOCS) effectively, the specific techniques used in measuring bilateral suppression with TEOAE's (binaural noise bursts with a click onset 5 ms after the noise burst ceases) can not be used when measuring the time course of the medial efferent effects with the use of prolonged continual noise stimulation. Binaural stimulation also has the same limitation as ipsilateral stimulation, namely intracochlear processes which contribute to the suppressive response. Thus this chapter will focus more on the different characteristics of contralateral suppression of OAE's.

2.5.1 Contralateral suppression

Since the fundamental paper by Buno (1978), first described auditory nerve activity influenced by contralateral sound stimulation, contralateral auditory stimulation and the effect on peripheral auditory responses have been extensively studied. Through the use of animal (Buno, 1978) and human studies (Folsom & Owsley, 1987), it became evident that contralateral auditory stimulation alters the afferent nerve fibre response of the opposite ear. More recently, researchers discovered changes in OAE's of humans (Mott, Norton, Neely & Warr, 1989) and in animals (Puel & Rebillard, 1990; Kujawa et al., 1992). In numerous studies of the effect of contralateral stimuli on various parameters of OAE's in human and in animals, it was evident that the stimulation of the ear opposite the one in which emissions are being measured reduces the amplitude of the OAE (Berlin et al., 1993a; Berlin, Hood, Wen, et al., 1993b; 1994; Collet et al., 1990b; Collet, Veuillet, Bene & Morgon, 1992; Harrison & Burns, 1993; Kujawa et al., 1993; Peul et al., 1990; Ryan et al., 1991; Veuillet et al., 1991). Contralateral suppression of OAE's was thought to be an ideal tool for studying the effect of contralateral auditory stimulation, because the medial olivocochlear bundle synapses directly with OHC's of the organ of Corti and OHC's are directly involved in the generation of OAE's (Collet, 1993; Giraud, Collet, Chery-Croze, Magnan & Chays, 1995).

2.5.1.1 Types of OAE used to measure contralateral suppression

Three types of OAE's have been used to study the effect of contralateral auditory stimulation, namely SOAE's (Mott, Norton, Neely & Warr, 1989; Moulin, 1993; Harrison et al., 1993; Irby, 1998), TEOAE's with linear clicks (Collet et al., 1990; 1992a, 1993; Veuillet et al., 1991; Veuillet, Collet & Morgon,1992), non-linear clicks (Veuillet et al., 1991: Berlin et al., 1993a, b), tone pips (Berlin et al., 1993b) and DPOAE's (Moulin, Collet & Morgon, 1992; Moulin, Collet & Duclaux, 1993; Chery-Croze et al., 1993).

Contralateral suppression of SOAE's

Harrison et al. (1993), Irby (1998) and Mott et al. (1989) found that introducing acoustic stimulation to the contralateral ear alters the frequency and amplitude of SOAE's. It has been reported that an upward shift of SOAE frequency can be observed in the presence of a contralateral tonal stimulus (Mott et al., 1989; Harrison and Burns, 1993; Irby, 1998). When Mott et al. (1989) used contralateral stimulation with continuous pure tones of various frequencies and sound pressure levels (SPL's), they observed an upward shift in SOAE frequency, with the greatest frequency shift when the suppressor tone was one-half to three-eights of an octave below the SOAE frequency. SOAE amplitudes increased, decreased or remained unchanged in the presence of contralateral tones that elicited these frequency shifts (Mott et al., 1989). The researchers noted that no suppression effects could be recorded with contralateral stimuli below 60 dB SPL and that the suppression remained stable for up to 4 minutes of contralateral stimulation (Mott et al., 1989). With the onset of the contralateral stimulus, an abrupt shift in SOAE frequency could be observed, followed by a gradual decrease over the stimulus duration and returning to the pre-stimulus SOAE frequency when the contralateral stimulus ceased (Harrison & Burns, 1993; Irby, 1998). No consistent relationship between the frequency of the contralateral stimulus and frequency shifts of SOAE's could be found (Irby, 1998). The SOAE amplitude effects of contralateral stimulation proved to be variable (Harrison & Burns, 1993; Irby, 1998). Although contralateral effects on SOAE's have been observed to vary between subjects, they are repeatable and reliable (Harrison and Burns, 1993; Irby, 1998; Mott et al., 1989).

Contralateral suppression of DPOAE's

Brown (1988) was the first to describe the effects of continuous contralateral low-level auditory stimulation on DPOAE's and suggested that an efferent effect may exist. Since then other researchers also investigated the effect of contralateral sound stimulation on DPOAE's and supported Brown's (1998) hypothesis that the suppressive effect of contralateral sound stimulation of DPOAE's is mediated by the medial efferent system (Peul & Rebillard, 1990). The suppression of DPOAE's is now clearly understood to be controlled by the medial efferents (Chery-Croze et al., 1993; Moulin et al., 1993). The overall decrease in DPOAE amplitude in the presence of a contralateral acoustic stimulus is reported to be between 1 and 4 dB (Chery-Croze et al., 1993; Moulin et al., 1993).

Broadband and narrowband noise have been found to be effective contralateral stimuli in the suppression of DPOAE's. Narrowband noise with a centre frequency of the noise band close to that of the DPOAE is most effective in suppressing DPOAE's, especially when the DPOAE'S are in a range of 1 to 2 kHz (Chery-Croze et al., 1993). Chery-Croze et al., (1993) observed that a 3 kHz noise band showed effective suppression of DPOAE's in the area of 3 KHz. Contralateral noise band stimuli with centre frequencies between 250 and 750 Hz were found to be less effective in suppression (Chery-Croze et al., 1993). Broadband noise appears to have the greatest effect on DPOAE's between 1 and 3 kHz (Moulin et al., 1993; Santaolalla Montoya et al., 1997; Williams & Brown, 1997).

An inverse relation between DPOAE amplitude and the level of contralateral stimulus can be seen (Peul & Rebillard, 1990). Peul and Rebillard (1990) reported that DP amplitudes decreased as the SPL's of contralateral stimuli increased. This increase in contralateral level showed a greater suppressive effect when the DP primary levels were 60 dB SPL (Peul & Rebillard, 1990). When a contralateral broadband noise of 80 dB SPL was used to suppress DPOAE's from 35 to 65 dB primary levels, it was noted that suppression was most effective with primary levels of 55 dB SPL and the effectiveness thereof decreased after 55 dB SPL, to negligible suppression at primary levels of 70 dB and greater (Puria, Guinian & Liberman,1996).

Contralateral suppression of TEOAE's

Like SOAE's and DPOAE's, certain properties of TEOAE's are altered in the presence of contralateral auditory stimulation (CAS). The main effect of contralateral stimuli on TEOAE's, is the attenuation of the TEOAE amplitude of about 1 to 4 dB (Berlin et al., 1993b; 1994; Collet et al., 1990b; 1992; Ryan et al., 1991; Veuillet et al., 1991). Alterations in phase shifts can also be observed in TEOAE's in the presence of CAS (Veuillet et al., 1991). The suppression of TEOAE's in normal hearing adults shows great intra-individual variability, but, according to several studies, 1 dB SPL is considered to be the cut-off point for normal suppression(Prasher et al., 1994; Collet, 1993; Micheyl & Collet, 1995). Considering 1 dB SPL as the lowest "normal" level, the method shows a false positive rate of 6% in normal hearing subjects (Prasher et al, 1994).

Researchers have studied the effectiveness of different types of contralateral stimuli, such as clicks, pure tones, narrowband noise and white noise, in suppressing TEOAE's (Berlin et al., 1993b; Norman & Thornton, 1993). Only low-frequency pure tones have enough energy to elicit contralateral TEOAE suppression (Berlin et al. 1993b). This may be because low frequency pure-tones stimulate a larger area on the basilar membrane than higher frequencies and activate more efferents. Using narrowband noise, suppression has been observed at hearing levels (HL's) as low as 20 dB (Berlin et al., 1993b). White noise, consisting of energy from 20 to 20,000 Hz (the frequency response range of the human ear), stimulates the whole contralateral cochlear partition and activates the largest number of MOC efferents, thus making it the most effective stimulus in suppressing TEOAE's (Berlin et al., 1993b; Norman and Thornton, 1993).

Several authors have found an inverse relationship between the level of the contralateral stimulus and the amount of TEOAE amplitude reduction (Collet et al., 1990b; Ryan et al., 1991; Berlin et al., 1993b). These findings concluded that the TEOAE amplitude decreases as the level of contralateral stimuli increased, regardless of the type of contralateral stimuli. Collet et al. (1990) used contralateral white noise stimuli with intensities ranging from 0 to 80 dB SPL and found that the TEOAE amplitude decreases are observed from as low as 30 dB SPL. As the contralateral stimulus level increased in intensity, a decrease in TEOAE amplitude was observed. Berlin et al. (1993b) used narrowband stimuli at SPL's of up to 80 dB and found a relationship between contralateral stimulus level and TEOAE amplitudes. Norman and Thornton (1993) measured emission with 75 dB SPL nonlinear clicks and narrowband noises with intensity levels ranging from 40 dB to 60 dB sensation level (SL). It was reported that decreases in emission amplitude only became significant when the intensity of the narrowband noise exceeded 40 dB SL. Ryan et al. (1991) used recordings with and without broadband noise (BBN) from 0 dB to 70 dB SL and noticed a reduction in TEOAE amplitude from as low as 20 dB SL, but better perceived from 50 dB SL BBN. However, when the contralateral noise level was held constant and the stimulus level was varied, the amount of suppression was reported to be relatively constant (Veuillet et al., 1991)

These results were inconsistent with other findings of greater suppression of auditory nerve responses by lower intensity electrical or acoustic stimuli, with either saturation or lesser effect at higher intensity levels (e.g. Nieder & Nieder, 1970; Gifford & Guinan, 1987; Warren & Liberman, 1989). In order to address the discrepancies between previous reports of intensity effects on suppression of emissions versus auditory nerve responses, Hood, Berlin, Hurley, Cecola & Bell (1996), examined suppression of TEOAE's in human subjects whilst systematically varying both the emission-eliciting stimulus and the suppressor noise over a wide range of click and suppressor noise levels. This was done to determine the appropriate click and noise levels of TEOAE suppression studies. In their study the authors reported that greater amplitude suppression for emissions was found with lower intensity level clicks when the intensity of the contralateral noise was at or near 60 dB SPL (Hood, Berlin, Hurley, Cecola & Bell, 1996a). The sound pressure level of the click used to evoke TEOAE's can also affect the amount of suppression resulting from a contralateral stimulus. Click stimulus intensities of below 65 dB SPL have been found to be the most effective when recording TEOAE suppression amplitudes with contralateral white noise stimuli (Hood et al., 1996a). Hood et al. (1996a) suggested using 55 or 60 dB peak SPL with the overall intensity level of the noise set at, or 5 dB higher than, the click intensity. Regardless of the intensity selected for measuring decreases in TEOAE amplitude, it is imperative to avoid using high click intensities (e.g. 70 dB SPL), in order to minimize the risk of major participation of the middle ear muscle reflexes, as discussed elsewhere in this chapter.

Studies by Berlin et al., (1993) revealed that narrowband noise with different frequency centres all have the same effect on the TEOAE spectrum This implies that contralateral suppression of TEOAE's is not frequency specific. Although the contralateral suppression effect of TEOAE's does not seem to be tuned, the greatest effects occur between 1000 and 4000 Hz in the TEOAE spectrum (Berlin et al., 1993b; Collet et al., 1990b; Norman & Thornton, 1993). This may be due to greater density of MOC efferent innervation of OHC's in the area of the cochlea that responds to this frequency range, which implies that more efferent control may exist in this area (Guinan, Warr & Norris, 1983; Liberman & Guinan 1998; Warr et al., 1986). The second reason why this frequency range seems to create a greater contralateral suppression effect may be because a greater efferent response may be generated from the area of the cochlea that has the greatest sensitivity, which is the cochlear portion between 1000 and 4000 Hz (Fletcher and Munson, 1933).

Normally nonlinear click stimuli are used to evoke emissions when measuring TEOAE's. Clicks are presented in sets of four with the first three at the same SPL and phase and the last click, 180 degrees out of phase with the preceding clicks and at an SPL 10 dB greater than the first three clicks. The reason for the use of this mode is because the nonlinear stimulus has the advantage of largely eliminating the stimulus artifact in the recording(Berlin et al., 1993). The last click of the linear mode evokes a larger response than the first three, resulting in some growth in the emission between the third and the fourth clicks. This effect of growth can affect suppression in the presence of contralateral stimuli(Berlin et al., 1993). Another disadvantage with nonlinear clicks is the higher level of residual noise (Moleti et al, 2002) which leads to lower response reproducibility and a lower signal-to-noise ratio (SNR). Hoth et al. (2007) investigated TEOAE's at stimulus levels ranging from 83 dB SPL down to individual response thresholds, using linear and nonlinear recording methods. They found that, when using stimulus levels above 70 dB SPL, the TEOAEs recorded in linear mode were contaminated with stimulus artefacts. They suggested that when lower stimulus levels are used, the linear mode proves to be better suited for signal detection due to inherent lower noise levels. When using linear clicks at lower stimulus levels (65 dB peak SPL or less) in the evaluation of contralateral suppression effects, fewer contaminated responses were generated (Berlin et al., 1993b).

2.6 Confounding variables in measuring contralateral OAE Suppression

Considering that OAE's are measured in the ear opposite to the stimulus, it is imperative to acknowledge the confounding variables, namely the acoustic reflex and transcranial acoustic crossover, both of which may influence suppression measurement.

Elicitation of the middle ear acoustic reflex

The acoustic reflex can also be described as an efferent feedback loop that may affect the response of the auditory system by reducing energy transmission through the middle ear (Borg, 1973). Several researchers were initially concerned that the acoustic reflex may be responsible for the reduction in OAE amplitude resulting from contralateral stimulation (Berlin et al., 1993; Veuillet et al., 1991; Harrison & Burns, 1993). The acoustic reflex results in a reduction in the transmission power of the ossicular chain and may be responsible for the attenuation of OAE amplitude observed as a result of contralateral stimulation, because OAE's travel backwards through the middle ear. Numerous studies have proven the possibility of the acoustic reflex playing a significant role in contralateral suppression of OAE's to be doubtful. The stimuli necessary to produce OAE suppression are presented at sound pressure levels below the level required to elicit acoustic reflexes (Berlin et al., 1993b; Collet et al., 1990; Hood et al., 1996a; Norman & Thornton, 1993; Veuillet et al., 1991). In addition to this, several researchers have observed contralateral suppression of OAE's in subjects with paralyzed or severed stapedius muscles (Giraud et al., 1995; Veuillet et al., 1991). Guinan et al. (2003) used stimulus SFOAEs in humans to distinguish medial efferent from acoustic reflex effects by relying on group-delay differences in their respective latencies. The results of these investigators indicated that efferent effects were mixed in terms of MOC efferent and acoustic reflex contributions and that the acoustic reflex dominated the effects for MOC noise elicitors of 55 dB

SPL or above. If CAS of 55dB SPL or above will result in acoustic reflex elicitation, lower CAS intensities may be more useful in the investigation of the MOC efferent effects.

Acoustic crossover

Another confounding problem that has concerned researchers was that contralateral suppression of OAE's may be due in part to masking from the acoustic crossover. However, many animal studies have provided evidence that the contralateral suppression effect on OAE's results from OCB activation and is not the result of acoustic crossover (Peul & Rebillard, 1990; Kujawa et al., 1993). Acoustic crossover has also been investigated using unilateral totally deaf patients where the EOAE's were recorded in the healthy ear with contralateral stimulation of the deaf ear. No effects on the ipsilateral OAE were found with CAS of up to 80 dB SPL intensity white noise, thus ruling out any crossover influences (Collet, 1993). Velonovsky (1998) found no significant acoustic crossover for contralateral noise up to 85 dB. In addition to this, it has been shown that insert earphones can also reduce the influence of acoustic crossover. If standard ear phones such as TDH-39 with MX 41-AR cushions are used, crossover by bone conduction or even partly by air conduction could conceivably take place at levels as low as 40 dB HL. When insert earphones are used, the amount of interaural attenuation increases to 80 to 82dB HL thus minimizing leakage of air-conducted noise to the opposite ear due to the seal in the ear canal, but more importantly there is less opportunity for bone-conducted sound transmission due to material differences and surface area contact difference between supra-aural and insert earphones.

2.7 Duration of contralateral suppression

Amongst the previously described factors that influence the OAE suppression effects when stimulated contralaterally, one can include contralateral stimulus duration effects. Before describing these characteristic in OAE's, it is necessary to review existing literature on the duration of MOCS efferent effects when the MOCS are electrically or acoustically stimulated for different durations.

Since Wiederhold and Kiang (1970) reported that the decrease in the discharge rate of auditory neurons under electrical stimulation of the crossed olivocochlear bundle persisted for the duration of the delivery of the electrical shocks (350 seconds), some authors developed an interest in the duration characteristics of the olivocochlear efferent effects, whether this suppression effect has the same temporal characteristics when the OCB is stimulated acoustically, and if this effect is prone to response adaptation over time. Attempts had been made in the past to study the duration characteristics of the MOCS efferent effects (suppression) in animals and humans using different recording methods, ranging from cochlear compound action potential (CAP) measurements (Puria, Guinan & Liberman, 1996), ensemble background activity (EBA) measurements of the VIII nerve from an electrode implanted on the round window (Da Costa, Chibios, Erre, Blanchet, De Suauvage & Aran, 1997) and EOAE's (DPOAE and TEOAE) (Giraud, Collet & Chery-Croze, 1997; Moulin & Carrier, 1998) while delivering constant CAS. These methods were used to gain insight into the response adaptation properties of olivocochlear neurons during ongoing stimuli of long duration.

2.7.1 Duration of contralateral suppression: measured with electrophysiological recordings (electrical stimulation)

Puria et al. (1996) studied the suppression of cochlear CAP during 12 seconds of contralateral broadband noise in anaesthetized cats and found that suppression reached a constant, steady state after two seconds of the onset of contralateral noise. When the contralateral noise was turned off, the suppression disappeared in less than 0.62 seconds (Puria et al., 1996). In contrast to this supposed steady state effect, it has been suggested that suppression increases during the first 60 to 80 seconds after contralateral broadband noise onset and then decreases, as measured during 500 seconds of CAS in guinea pigs (Kujawa, Glattke & Fallon, 1993). Studies of duration properties were further influenced by the discovery of two different effects, namely the fast and slow effects on the MOCS when electrically stimulated and measured on the CAP (Shridar et al., 1995). These fast and slow effects of OC stimulation in guinea pigs are illustrated in figure 2.2.

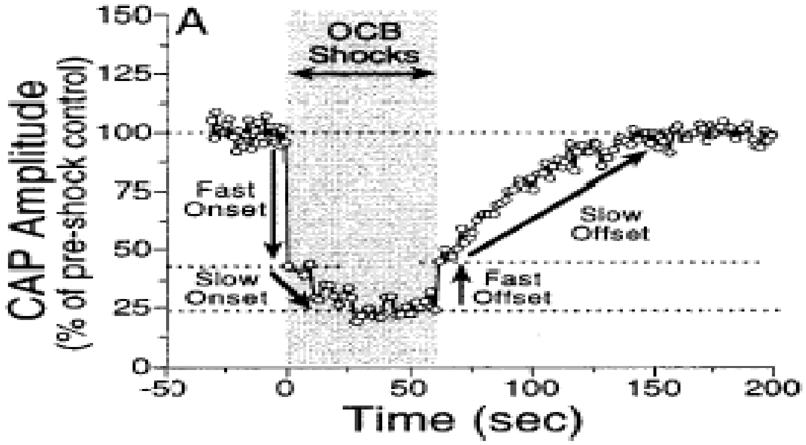


Figure 2.2 Slow and fast effects on CAP amplitude when the OCB is electically stimulated. Figure taken from Shridhar et al. (1995)

As illustrated in figure 2.2, the CAP amplitude was reduced to less than 50% of the control values ('fast' effect onset) almost immediately after the electrical stimulation onset. From there on the CAP amplitude continued to decline slowly by a further 20% ('slow' effect onset). The CAP amplitude remained depressed for up to two minutes after the cessation of electrical stimulation. The fast effect of OCB stimulation reached its maximum within 100 ms (fast effect offset) of efferent electrical stimulation onset and persisted during the efferent electrical stimulation. At the efferent electrical stimulation offset, the fast effect was extinguished within 100 ms, whereas the slow effect did not return to preshock control values until almost 100 seconds later (slow effect offset) (Shridhar, Liberman, Brown & Sewel, 1995).

Da Costa et al. (1997) further studied these slow and fast components of OC stimulation by measuring ensemble background activity (EBA) of the VIII nerve from electrodes at the round window of guinea pigs and comparing EBA measurements with and without a contralateral low-level broadband noise. They observed a rapid decrease in EBA value with a latency of less than ten milliseconds after the onset of the contralateral noise stimulation (fast effect onset). At the offset of contralateral noise stimulation, EBA rapidly returned to the control values at a similar latency. With longer contralateral broadband noise stimulation (one minute or longer), EBA presented, after the fast decrease, an additional slower decrease (slow effect onset) and remained constant for more than two hours (steady state effect) of contralateral stimulation. At the offset of contralateral noise stimulation, EBA returned to control values with fast and slow phases (Da Costa et al., 1997). If these findings are true and an efferent suppressive effect is considered to persist for the entire duration of electrical and acoustical OC stimulation, even over prolonged stimulation (Da Costa et al., 1997), it may mean that the MOC neurons do not adapt to ongoing stimuli, but exert their effect throughout stimulation.

Adaptation is known as a neuropsychological process whereby neurons are able to produce small responses to constant ongoing stimuli and larger responses to transient stimuli. It is generally accepted that most sensory neurons adapt their responses to constant stimuli. Several researchers have found that auditory neurons adapt to ongoing stimulation with tone bursts (Chimento & Schreiner 1991; Delgutte 1980; Javel, 1996; Kiang, Watanabe, Thomas & Clark, 1965; Muller & Robertson, 1991; Nomoto, Suga & Katsuki, 1964; Rhode & Smith, 1985; Smith, 1979; Smith & Zwislocki, 1975; Westerman & Smith, 1984). Long-term adaptation over several minutes in nerve fibres may be the result from synaptic processes which involve depletion of neurotransmitters at the hair cell/nerve fibre synapse (Javel, 1996; Furakawa, Hayashida & Matsuura, 1978; Norris et al., 1977).

Although the adaptation characteristics of the auditory nerve are well established, Brown (2001) found that they differ in several ways from the adaptation characteristics of the MOC neurons. He noted that there was almost no adaptation in the single MOC neuron responses for more than several seconds of sound stimulation in guinea pigs. Even though the auditory nerve fibres provide input to the MOC reflex, the difference in adaptation was ascribed to compensation for the decline in auditory nerve input by elements within the MOC reflex at more central locations, or as a result of changes at the level of the MOC neurons themselves (Brown, 2001). In addition to this, Brown (2001) sometimes observed suppression and a slow recovery after the acoustic stimulation ended. In his report he suggested the investigation of MOC adaptation to longer stimulation durations (longer than ten seconds), although he doubted that there would be any change in the MOC firing rate (Brown, 2001).

2.7.2 Duration of contralateral suppression: measured using OAE's

Though several studies describe the duration characteristics of the MOCS efferent effects arising from continual stimulation (electric or acoustic) in animals, only a few focused on these properties in humans (Giraud et al., 1997; Moulin and Carrier, 1998). These studies investigated efferent effect duration by examining the influence of CAS duration on suppression of EOAE's, which can be considered as a good physiological indicator of efferent activation. The following section will provide a literature overview of the few attempts to describe the effect of contralateral stimulus duration on the amplitude of TEOAE's and DPOAE's

Giraud et al. (1997) used stimulus durations ranging from ten to 180 seconds prior to the onset of TEOAE recordings, and continued throughout the recording time of 60 seconds. The authors used broadband noises of various durations on twenty human subjects. TEOAE's were recorded in responses to a 63 dB SPL stimulus in the presence and absence of a 35 dB SL (sensation level) noise, preceding the onset of TEOAE recordings by a variable time (10, 20, 40, 80 or 180 seconds). The study concluded that, within four minutes of low-level continuous acoustic stimulation, there is no appearance of significant efferent fatigue, because suppression remained constant throughout the measurement. The focus was placed on shorter durations of one to four minutes of CAS duration, because click-evoked TOAE clinical protocols usually do not require more than four minutes on average. However, these short durations of contralateral stimulation are possibly not long enough to cause efferent fatigue. Giraud et al. (1997) observed a slight tendency towards reduction of suppression after three minutes of CAS, which may suggest that amplitude reductions due to OAE suppression may be observable in TEOAE's with increasing duration of contralateral broadband noise beyond three minutes. Since these findings no other attempts have been made in using TEOAE's to explore the duration of contralateral suppression.

Duration characteristics of contralateral stimulation have also been investigated using DPOAE's. Moulin and Carrier (1998) studied the time course of the medial olivocochlear efferent effect on DPOAE's in 20 normal hearing humans. 2f1-f2 DPOAE's were recorded in the one ear of each subject, while a 40 dB SL contralateral broadband noise was applied to the other ear with DPOAE primary levels set at 45 dB SPL and 50 dB SPL respectively for f1 and f2. F2 was fixed at frequency 1501 Hz. This made it possible to measure DPOAE's every minute during continuous contralateral stimulation, because the responses could be collected in a rapid manner. Moulin and Carrier (1998) recorded DPOAE's for two minutes without contralateral broadband noise, followed by 20 minutes with contralateral broadband noise and ten minutes without contralateral broadband noise. Figure 2.3 displays the relative amplitude of DPOAE's before, during and after the contralateral broadband noise (CBBN)

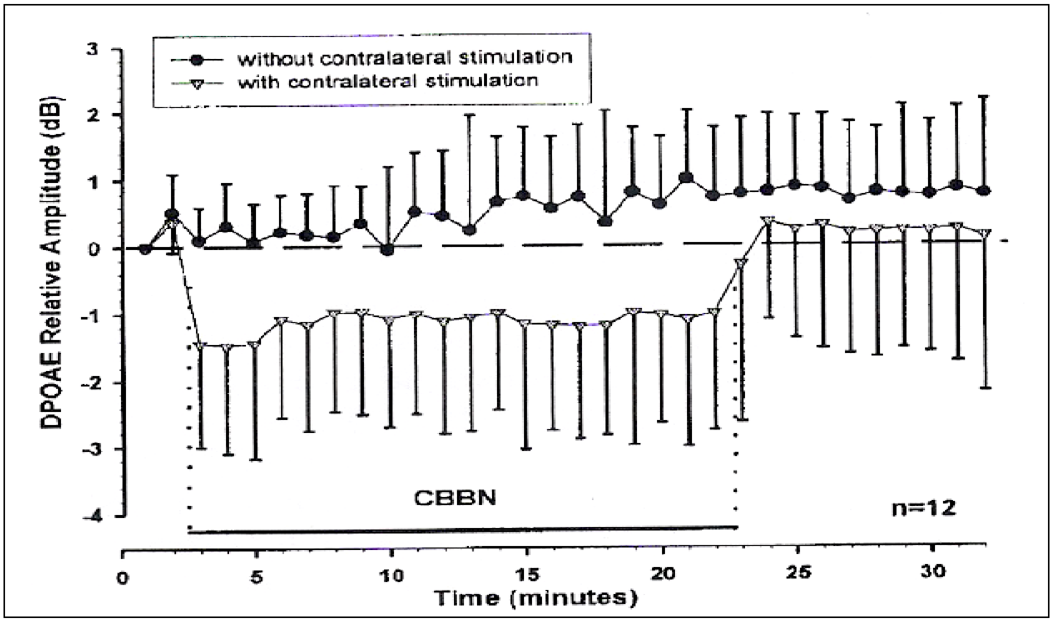


Figure 2.3 Relative DPOAE amplitude over 32 min without (black dots) and with (triangles) CBBN applied for 20 min (from 3-22min) as measured by Moulin and Carrier, (1998)

Moulin and Carrier (1998) found that the suppressive response on DPOAE amplitude with contralateral stimulus offset, increased for more than one minute, then reached a constant effect of no change in suppression amplitudes for the duration of 20 minutes and lasted more than two minutes after the contralateral stimulation was ended. The persistence of the effect after the stimulation ceased, indicated that the efferent effect can outlast the CBBN by more than one minute.

Table 2.3 Summary of existing studies to date, investigating the duration of contralateral suppression

Study (Year)	Subjects	Stimulus duration	Measurement with	MOCS suppressor	Duration of efferent effect
Wiederhold and Kiang (1970)	• *Animal*	• *350 s*	• *Electrical stimulation of crossed olivocochlear bundle*	• *Electrical stimulation*	• *Entire duration of stimulus 5 min 48 s*
Puria et al. (1996)	• *Animal*	• *12 s*	• *Cochlear CAP*	• *Contralateral broadband noise*	• *Entire duration of stimulus 12 s*
Kujawa, Glattke & Fallon (1993)	• *Animal*	• *500 s*	• *Cochlear CAP*	• *Contralateral broadband noise*	• *Increases during the first 60 – 80 s*
Shridar et al. (1995)	• *Animal*	• *50 s*	• *Cochlear CAP (Slow and fast effects)*	• *Electrical stimulation*	• *Entire duration of stimulus 50 s*
Da Costa et al. (1997)	• *Animal*	• *2 h*	• *Ensemble background activity (EBA)*	• *Contralateral broadband noise*	• *Entire duration of stimulus 2 h*
Giraud et al. (1997)	• *Human*	• *4 min*	• *TEOAE's*	• *Contralateral broadband noise*	• *Entire duration of stimulus 4 min (Slight tendency towards reduction after 3 min)*
Moulin and Carrier (1998)	• *Human*	• *20 min*	• *DPOAE's*	• *Contralateral broadband noise*	• *Entire duration of stimulus 20 min*

Collectively, the results of the majority of these studies lead to the impression that suppression that results from MOCS stimulation (electrical or acoustic), exerts its effect for the entire duration of efferent CAS. Most of these studies focused on shorter stimulus durations of seconds to a few minutes and were possibly not long enough to cause efferent fatigue or sensory adaptation. To add to this, many were conducted only on animal subjects, due to the invasive nature of measurements. Minimal research has been done describing prolonged contralateral acoustic stimulation on OAE suppression in humans. The generalization that the MOCS is capable of sustaining the suppressive response on OAE amplitudes for prolonged durations and the assumption that contralateral suppression of OAE's is not affected by fatigue, based on limited findings, can be questioned. It may prove to be valuable to use different measuring techniques to examine the same duration properties. TEOAE's, measured as a function of prolonged contralateral stimulation (more than four minutes) could support or contradict previous findings of suppression to prolonged durations of CAS.

Knowledge of the duration characteristics of contralateral suppression would be useful in the prediction of exposure durations for which MOC protection is most effective and the durations for which the MOCS plays a role in adjusting the dynamic range of the cochlea and in reducing the effects of noise masking.

Not only will this study attempt to explain the relationship between OHC integrity and the extent of efferent inhibition in a attempt to understand the medial olivocochlear feedback loop more thoroughly, it will also seek possible explanations for why the amount of suppression is significantly decreased in individuals exposed to noise for long durations, even though they show normal hearing thresholds (Sliwinska & Kotylo, 2002). Can the damage to efferent auditory neurons in these individuals be ascribed to neural adaptation, weakening the protective function of the medial efferent system and making the OHC's more susceptible to noise damage? Or does the MOCS produce a sustained effect in the auditory periphery, providing a protective and speech-in-noise-enhancing role during ongoing stimuli of long durations?

2.8 Conclusion

It has been suggested that the medial efferent system is involved in protection against acoustic overstimulation (Canlon 1996; Subramanian et al., 1993; Liberman, 1991) or in different auditory perception properties, such as speech-in-noise intelligibility (Muchnik et al., 2004; Sahley et al., 1997c). The suppressive effect of the MOCS on the peripheral auditory system is still under active exploration and very little has been documented about the duration of its effect on efferents in humans. An overview of different studies of MOCS efferent stimulation, in particular OAE suppression, revealed limited research describing the effect of prolonged contralateral stimulation. Since little literature exists describing prolonged (e.g. >4 minutes) acoustic stimulation effects on OAE amplitude in humans, it would be interesting to investigate these properties with broadband click TEOAE's.

2.9 Summary

The purpose of this chapter was to explain the anatomy and physiology of auditory pathways, to serve as a platform for understanding the efferent feedback loop and its clinical relevance and value to auditory neurophysiologists and audiologists. This chapter also served to identify and discuss all the different aspects of CAS in suppression of OAE's. This aids in identifying an optimal set of parameters for the measurement of TEOAE suppression, which was applied in the testing procedures in the following chapter. These parameters were also adjusted to suit the purpose of the study, in an attempt to describe the effect on TEOAE's of a prolonged duration of contralateral stimulation. The need for research on the duration properties of contralateral suppression of TEOAE's was emphasized, because there is currently a lack of available studies describing these properties in humans.

Chapter 3: Research Methodology

3.1 Introduction

One interesting viewpoint on the essence of research methodology was given by Leedy (1993) "The process of research is largely circular in configuration: It begins with a problem; it ends with that problem solved. Between crude prehistoric attempts to resolve problems and the refinements of modern research methodology the road has not always been smooth, nor has the researcher's zeal remained unimpeded." According to Leedy (2003) research originates with a question or problem, it requires clear articulation of a goal and a specific plan for proceeding, it divides the principal problem into more manageable sub-problems and it is guided by the specific research problem. The researcher accepts certain critical assumptions that require the collection and interpretation of data in an attempt to resolve the problem that initiated the research.

The problem inspiring this research project has already been extensively stated in Chapters 1 and 2. In short, many researchers studied the different contralateral stimulus characteristics that have an impact on OAE suppression amplitudes in an attempt to understand the effects of the medial olivocochlear efferent system on OHC's. Few of them focused on longer stimulus durations of several minutes and whether these neurons adapt to ongoing stimuli (Giraud et al., 1997; Brown, 2001; Moulin & Carrier, 1998). This study attempted to explain the relationship between OHC integrity and the extent of efferent inhibition in an attempt to understand the medial olivocochlear feedback loop more thoroughly. By investigating TEOAE suppression as a result of prolonged CAS, the researcher was able to understand the extent of prolonged MOCS inhibition on OHC's. Is the MOCS capable of a sustained suppressive response on TEOAE amplitudes over several minutes of contralateral noise or does TEOAE amplitudes increase as a result of efferent adaptation to ongoing stimuli?

The aim of this chapter is to describe the research aims, methods and apparatus that were used in order to describe the relationship between the prolonged CAS and the amount of efferent suppression measured with TEOAE's.

3.2 Research Aims

One essential step in the process of creating a clearly articulated primary aim, generated from the specific research problem, is to divide the principal aim or problem into more manageable sub-aims. By addressing these sub-aims, the researcher can more easily address the main problem. The research study aims were divided into a primary aim and underlying sub-aims.

Primary Aim

To investigate TEOAE suppression as a function of prolonged CAS

Sub-Aims

- To compare recordings of TEOAE amplitudes obtained over an identical time period divided into identical intervals in a controlled condition (20 minutes without CAS) and in an experimental condition (16 minutes with and four minutes without CAS).

- To describe the relationship between the duration of CAS and TEOAE suppression amplitude

3.3 Research Design

This study follows an experimental design that is quantitative in nature. Experimental research involves formulating a hypothesis, modifying something in a situation and comparing the outcomes with and without the modification (Neuman, 1997). OAE amplitudes were measured in normal-hearing subjects at predetermined time intervals in the absence (controlled condition) and presence (experimental condition) of contralateral acoustic noise (CAS). The amplitudes found in both conditions were then compared to investigate the possible effects of prolonged CAS. According to Leedy & Ormrod (2005) “quantitative research is used to answer questions about relationships among measured variables with the purpose of explaining, predicting and controlling phenomena”. The study is focused, with known variables, using predetermined methods and standardized instruments to collect numeric data (OAE amplitudes) that represent a larger sample. A few participants who could best shed light on the phenomenon under investigation were selected, using a purposive sampling method. This sampling technique was selected because subjects had to adhere to specific criteria of normal hearing. Deductive reasoning, beginning with aims and sub-aims, was used to draw logical conclusions. Objectivity in data analysis was retained by conducting predetermined statistical procedures and using objective criteria to evaluate the outcomes of those procedures (Leedy & Ormrod, 2005). In this case, OAE amplitude measurements were used as objective measurements (in the sense that they require no behavioural response from the subject).

3.4 Research Subjects

In this section the population, sampling technique, subject selection criteria and subject selection apparatus and procedures are discussed.

3.4.1 Population

Ten normal-hearing subjects between the ages of 20 and 29 were recruited for TEOAE suppression measurements.

3.4.2 Sampling technique

The selection process can be described as convenience sampling (Maxwell & Satake, 2006), as the sample consisted mainly of students and other people living in and around Pretoria. This technique was followed because subjects had to adhere to certain selection criteria to ensure assure the opportunity to record TEOAE suppression in a healthy human ear.

3.4.3 Criteria for subject selection

Subjects were selected according to set criteria as discussed below. Should the criteria not have been met, the results of the study would have been negatively impacted upon.

Normal hearing acuity

According to Kemp (1978) otoacoustic emissions are absent in ears with a sensorineural hearing loss greater than 30 dB HL. For this reason it was critical for the subjects to have normal hearing ability. Clark (1981) described normal hearing as having hearing sensitivity between 0 and 15 dB HL across 250 to 8000 Hz. Thus subjects underwent pure tone testing to verify their hearing ability. It has been found that some subjects may exhibit abnormal OAE's, despite having despite having normal pure tone thresholds. In a study by Attias, Bresloff and Furman (1996), it was found that in some cases, subjects with normal pure tone thresholds of 0 dB HL exhibit abnormal otoacoustic emissions, due to noise exposure. The physiological effects of noise exposure can clearly be seen long before the actual hearing loss occurs. This is also true for ototoxic medication (Danhauer, 1997). A short interview collecting information regarding hearing history such as exposure to noise or ototoxic medication was conducted in order to exclude these subjects from the research project. Subjects who reported being exposed to ototoxic medications or to hazardous sound environments and did not show normal hearing sensitivity (thresholds between 0-15 dB) were referred for a diagnostic hearing assessment at the University of Pretoria and were excluded from the study.

Normal external and middle ear functioning

Because OAE's are transmitted from the cochlea to the ear canal via the middle ear, the transmission properties of the middle ear directly influences OAE characteristics [Margolis, 1999 (cited in Robinette & Glattke, 2000)]. An otoscopic examination of the external auditory meatus was conducted on all subjects. If any foreign objects, impacted cerumen, growths, abnormal tissue or redness of the tympanic membrane were observed, the subjects were excluded from the study and referred for further medical intervention.

The second criterion was that all the subjects who were selected to participate in the study had to have normal middle ear functioning. Otoacoustic emissions can be recorded only in subjects with normal middle ear function. Only a very small amount of energy is released by the cochlea to be transmitted backwards through the oval window and ossicular chain to vibrate the tympanic membrane. Normal middle ear function is crucial to this transmission process (Norton, 1993; Osterhammel, Nielsen & Rasmussen, 1993; Zhang & Abbas, 1997). To ensure that all subjects who participated in the study had normal middle ear functioning, immittance measures was performed. Only subjects with Type A tympanograms with a middle ear compliance of 1.68 to 1.75 ml, volume of 0.65 to 1.57 ml and middle ear pressure of +50 to -50 daPa were included in the study. The subjects who had abnormal tympanograms or any external abnormalities were referred for further medical intervention.

No broadband acoustic reflexes below 70dB SPL

Numerous studies have established that normal ART's (acoustic reflex thresholds) range from about 85 to 100 dB SPL for pure tone stimuli and are roughly 20 dB lower for BBN (Gelfand, 1984) Low threshold broadband acoustic reflexes are problematic, in that they may trigger the contraction of the contralateral stapedius muscle in some subjects. CAS can be contaminated and the effect on OAE's invalidated by contraction of the stapedial muscle and the resulting alteration of middle ear transmission. Acoustic reflex-induced changes in middle ear transmission can greatly affect the inward/outward propagation of energy in OAE measurement and totally obscure the relatively slight true efferent effects. Thus it is imperative to use an adequately low suppressor intensity level to minimize the effect of acoustic reflex involvement. This problem can be overcome, as in other studies, by first determining the contralateral acoustic reflex threshold for subjects (Williams, Brookes & Prasher, 1994). In comparing the threshold of this contralateral acoustic reflex with the intended maximum amount of contralateral noise the researcher would be able to determine whether the contralateral acoustic reflex would negatively impact upon the OAE elicited in the presence of contralateral broadband noise. For this reason all subjects had to undergo a contralateral acoustic reflex test elicited at a minimum intensity of 70 dB. If subjects did not fit these predetermined criteria they were not allowed to participate in this study.

Age (20-29 years)

Age appears to affect contralateral suppression of OAE's. Several authors have revealed that efferent suppression effects decline with age (Castor, Veuillet, Morgon & Collet, 1994; Hood, Hurley, Goforth, Bordelon & Berlin, 1997; Parhasarathy, 2001). According to Parhasarathy (2001) age does not play a significant role in the amount of amplitude measured with OAE's between the ages of 20 and 29. For this reason, subjects between these ages were selected to ensure that age-related factors did not have any impact on research results. Another reason was that this population are more likely to have normal hearing ability, because they have not had the potential for more years of noise exposure as compared to older participants would.

3.4.4 Subject selection apparatus

Table 3.1 contains the subject selection apparatus that was used to ensure that subjects met the criteria (as discussed in section 3.4.3) and could be included in the study.

Table 3.1 Subject selection apparatus

Selection apparatus	Apparatus	Rationale
Short Interview	• *Appendix A, reviewing the aspects that were addressed in the short interview*	• *Collection of information regarding hearing status, such as the amount of noise or ototoxic exposure and complaints of middle ear problems*
Otoscopic Examination	• *Heine Mini 2000*	• *Visual inspection of the external ear to identify possible abnormalities*
Pure Tone Audiometry	• *GSI 61 Clinical Audiometer with TDH 39 – supra-aural earphones.* *Test was performed in a soundproof booth*	• *To determine hearing thresholds for audiometric test frequencies at octave intervals from 250 Hz to 8000 Hz*
Tympanometry	• *GSI Tympstar, with a 226 Hz probe tone*	• *To determine if middle ear functioning was normal*
Contralateral Acoustic Reflexes	• *GSI Tympstar, with BBN signal*	• *To determine the ART and whether stapedius reflexes would have an effect on TEOAE suppression*

3.4.5 Subject selection procedures

The procedure in which subjects were selected started with a brief interview, followed by an otoscopic examination of the external meatus, immitance testing, acoustic reflex measurements and pure tone audiometry bilaterally.

Case history and personal information

A short interview was performed prior to testing to obtain a limited case history and some biographical details. The research project was also discussed with the subject briefly and any questions were answered. The purpose of the case history was firstly to obtain sufficient biographical detail to open a new subject file and to determine the subject's age and gender. Secondly, information regarding hearing status factors, such as exposure to noise or ototoxic medication and a history of middle ear problems, was obtained. Appendix A reviews the aspects that were addressed in the short interview.

Subject selection testing prosedures

Table3.2 provides a summary of the testing procedures that were followed for the selection of participants. These procedures were followed when selecting subjects to ensure that all subjects adhered to the selection criteria discussed in 3.4.3.

Table 3.2 Subject selection testing procedures

Test	Instructions	Test Procedure	References	Pass criteria
Otoscopic Examination	• *The subjects were instructed to remain still. An explanation of the procedure was given.*	• *A speculum was selected according to the size of the entrance of the ear canal. Observation of the pinna, external ear meatus and tympanic membrane.*	• Hall III & Chandler (1994)	• *Normal amounts of cerumen with no occlusion of the ear canal. Observation of pearl-colour tympanic membrane with visible light reflex.*
Pure Tone Audiometry	• *The subjects were informed that different tones of varying intensities would be presented and that they should react to all audible tones by pressing the button*	• *The stimulus was presented at 30 dB HL. Lower intensity tones in intervals of 10 dB were presented until the subject reacted 50% of the time*	• Clark (1981)	• *Hearing sensitivity of 15 dB or less at octave intervals between 125 Hz and 8000 Hz.*
Tympanometry	• *Subjects were seated and instructed not to talk or swallow*	• *A tight seal was obtained by choosing the appropriate size probe. The compliance of the tympanic membrane, volume and pressure of middle ear were measured*	• Block & Wiley (1994)	• *Compliance: 0.3-1.9 ml Volume: 0.65-1.75 ml Pressure: +100 daPa to -100 daPa. Type A tympanograms*
Contralateral acoustic reflexes (CAR)	• *The subjects were asked to remain still. The procedure was explained before hand*	• *A contralateral BBN signal was measured in each ear. The ART was obtained by decreasing the stimulus intensity in 5 dB SPL steps*	• Williams et al.(1994)	• *Contralateral BBN reflex threshold of ≤ 70 dB HL*

3.4.6 Description of the sample

Ten adults (5 females and 5 males, ranging in age from 20 to 26 years) were evaluated in this study. All subjects met the following inclusion criteria based on the subject interview: (1) negative family history of hearing loss, (2) no history of ototoxic drug use, (3) no history of excessive noise exposure and (4) no history of middle ear disease. All subjects presented with no external ears abnormalities on otoscopic inspection, with external auditory canals free from obstruction. Individual thresholds were less than 10 dB HL for frequencies 0.25 to 8 kHz and normal results were obtained for their immitance audiometry. All subjects had contralateral broadband acoustic reflex thresholds above 70 dB SPL and perception thresholds for contralateral white noise of less than 10 dB, excluding middle ear responses to experimental TEOAE's conducted. All subjects had normal, measurable TEOAE's. These tests were conducted bilaterally on each subject.

3.5 Preliminary Study

The preliminary study was done to determine whether any changes to the series of tests were necessary and what amount of time would be needed to complete all the tests. The reasons for the preliminary study were: firstly, to confirm subject selection criteria and secondly, to determine which stimulus parameters and procedures to use in the measurements of TEOAE suppression.

3.5.1 Confirmation of subject selection criteria

A large part of the determination of subject selection criteria was based on an extensive overview of related literature. The subjects on whom the preliminary study was performed were two students of the University of Pretoria. They had no history of being exposed to noise or ototoxic medications and no family history of hearing loss. During otoscopic examination normal external ear canals and tympanic membranes could be observed bilaterally. Normal Type A tympanograms that met the criterion were obtained. During pure tone testing, normal hearing thresholds were obtained.

When contralateral broadband acoustic reflexes were measured one subject had reflex thresholds at stimulus levels as low as 70 dB SPL. This correlates with the finding of Wiley, Oviatt and Block (1987) in which he described BBN reflex thresholds being almost 20 dB lower than pure tone acoustic reflex thresholds. The criteria were changed in order to exclude subjects with BBN reflexes at thresholds < 65 dB SPL from further data collection. A second series of tests was conducted to determine optimal stimulus and suppressor parameters and the best procedure to follow to provide an opportunity to collect measurements.

3.5.2 Determination of optimal stimulus and suppressor parameters

Most of the stimulus parameters for this study were derived from an in-depth literature study. Parameters such as the loudness levels of the TEOAE stimulus and the optimal contralateral suppressor parameters were selected according to recommendations made in previous studies. The rationale for these stimulus and suppressor parameters is described in 3.4.2 “Data collection protocols”. After the completion of the second series of tests, it was evident that the contralaterally suppressed TEOAE’s were successfully elicited within the selected parameters, enabling the comparison of the responses with other findings. During the TEOAE recordings, the amount of contralateral suppression found was between 1 and 3 dB, which correlates with published norms (Morlet, Collet, Salle, Morgon, 1993; Veuillet et al., 1991; Collet et al, 1990). It was thus not necessary to make further modifications.

3.5.3 Confirmation of data collection procedures

The data collection procedure was developed in such a way as to investigate the relationship between the duration of CAS and the amplitude of suppression of TEOAE’s. The selected procedures are described in 3.4.3 “Data collection procedures”. After the preliminary study, it was decided to include an additional post-noise TEOAE measurement, three minutes after the contralateral suppressor was ceased, in order to investigate a longer time course of possible persistence of a suppression effect after prolonged contralateral noise stimulation ceased.

3.6 Data Collection

The following procedures and instruments were used during the collection of all data:

3.6.1 Apparatus

TEOAE's were recorded and analysed using the Otodynamics V6 Analyzer hardware and software (Otodynamics Ltd.) The probe was calibrated for a quiet room before testing and all measurements took place in a soundproof booth. The masking of the ear contralateral to the one in which the OAE's were evoked, was done using a GSI 61 clinical Audiometer. Insert earphones were used to increase the amount of interaural attenuation and prevent acoustic crossover to the test ear (Ryan et al., 1991).

3.6.2 Data Collection Protocols

There are many stimulus parameters that must be specified to enable the repetition of this research project. The following section summarizes and discusses the protocols that were used when measuring TEOAE recordings and the contralateral stimulus used to suppress these recordings. The "stimulus" refers to the signal used to elicit the OAE and the "suppressor" refers to the signal presented to the contralateral ear to elicit the suppression effect. The TEOAE protocol, summarized in table 3.3, includes the test parameters that are most effective when using CAS in suppressing TEOAE's. The stimulus parameters are discussed according to the specific settings and ranges selected for TEOAE recordings and the rationale supporting this selection.

Table 3.3 Test protocol for TEOAE stimuli parameters

TEOAE stimulus parameters	***Settings and Range***	***Rationale***	***References***
Stimulus type	- *Broadband 80 µs clicks*	- *The use of broadband clicks ensures that the components of the TEOAE across a broad frequency range can be elicited*	- *Berlin et al. (1993b)* - *Kemp (1978)*
Stimulus polarity	- *Linear stimulus with a set of four clicks of the same phase and SPL*	- *A constant stimulus polarity can be used, because lower click intensity levels are used in the evaluation of contralateral suppression effects*	- *Berlin et al. (1993)*
Stimulus intensity	- *60 dB SPL*	- *A contralateral BBN stimulus is most effective in suppressing TEOAE's when the intensity of the click stimulus used to evoke an emission is between 55 and 65 dB SPL*	- *Hood et al. (1996)* - *Veuillet et al. (1996)* - *Veuillet et al.(1991)*
Click repetition rate	- *50/s*	- *Significant reduction in amplitude occurs as the stimulus rate increases from 50/s up to over 1000/s*	- *Granade and Collet (1995,1997)*
Stimulus presentation ear	- *right*	- *OAE's show more suppression in the right ear when compared with the left. The MOCS appears to be more efficient in the right ear than in the left ear*	- *Kumar & Vanaja (2004)*

The suppressor parameters are summarized in table 3.4.

Table 3.4 Test protocol for TEOAE suppressor parameters

Suppressor parameters	Settings and Range	Rationale	References
Suppressor type	- *White noise*	- *Suppressors with broadband spectrums are more effective than narrowband noise or tonal suppressors*	- *Berlin et al. (1993b)*
Suppressor frequency bandwidth	- *100 to 4000 Hz*	- *The GSI 61 Clinical Diagnostic Audiometer produces a White (Broadband) noise spectrum of between 100 Hz to 4000 Hz ± 5dB.*	
Suppressor intensity	- *45 dB SL*	- *Sensation level intensities of 30-50 dB SL are low enough to prevent any crossover and contraction of the contralateral stapedius muscle.*	- *Berlin et al. (1994); Ryan et al. (1991)*

3.6.3 Data Collection Procedures

OAE measurements were performed directly after the subject selection procedure. Subjects were instructed to sit, not to talk and to remain as still as possible. Subjects were allowed to read as long as they kept their heads as still as possible. A new file was initiated for the subject. An appropriately sized probe was selected by examining the size of the subject's external auditory meatus and was inserted into the right external meatus such that an airtight seal was obtained. A foam tip probe, connected to the audiometer stimulus transducer, was selected according to the size of the ear canal and inserted in the left ear, ensuring that there was no cords noise that can interfere with the OAE recordings. The probe tip was inserted deeply into the ear canal to insure an airtight pressure seal instead of flush with the ear canal opening. Before and during TEOAE measurements, stimulus stability was monitored. Stimulus ringing was prevented by adjusting the probe in the ear, if necessary.

TEOAE recordings were measured in two conditions:

a. Controlled condition*: OAE measurements at specific intervals over a period of 20 min without CAS (white noise) to establish a baseline.*

b. Experimental condition*: OAE measurements at specific intervals over a period of 16 min with CAS (white noise) and 4 min without contralateral noise.*

TEOAE amplitudes were first recorded in the control condition followed by the same recordings in the experimental condition. Both conditions were subdivided into individual OAE amplitude recordings with specific time intervals of five minutes between each recording. In the experimental condition a continuous white noise was introduced in the contralateral ear for a period of 16 minutes while four OAE measurements were recorded in the ipsilateral ear. OAE amplitudes were measured directly after the CAS was introduced, a second time after CAS for five minutes, a third time after ten minutes of CAS, and a fourth time, after CAS for 15 minutes. A schematic representation of the research procedures is illustrated in figure 3.1. Thereafter, a post-noise period of one minute and three minutes (without CAS) were allowed, followed by OAE amplitude measurements after each quiet period respectively to determine if the suppression effect persisted after prolonged exposure to CAS ceased and if this effect still existed after three minutes post-stimulation. The controlled condition followed the same pattern, only without the presence of CAS. Measurements of both conditions were repeated three times, each on separate days, in all the subjects, to increase the reliability of the results.

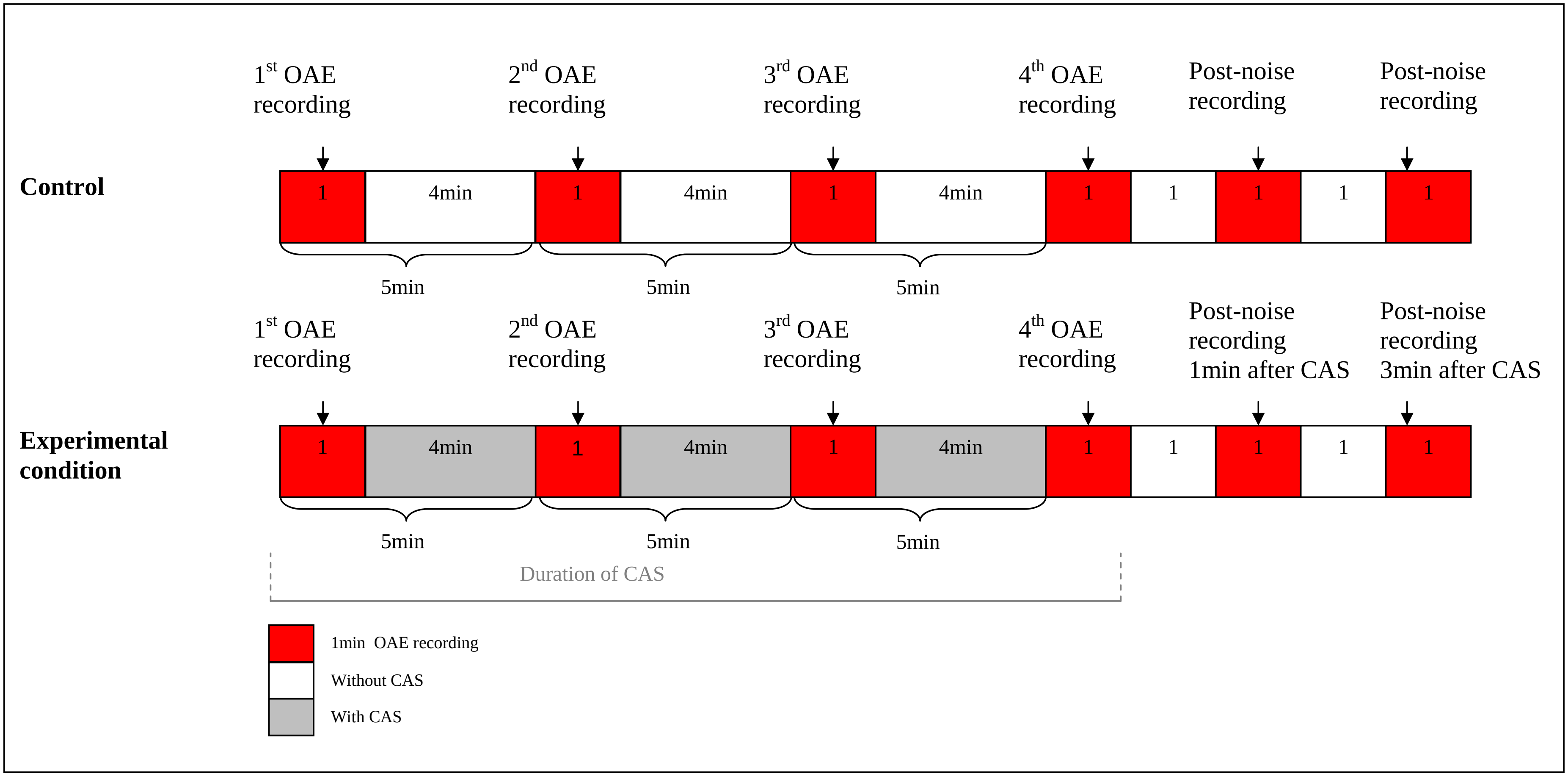


Figure 3.1 Schematic representation of the test procedure in the controlled and experimental conditions

The red areas represent the single OAE recordings that were measured without contralateral noise (white areas) in the controlled condition and without contralateral noise (grey areas) in the experimental condition. A post-noise period of one minute without noise was given after the fourth recording to determine if the suppression effect persisted after the noise had ceased.

3.6.4 The Criteria for acceptable TEOAE amplitudes measured with contralateral white noise.

In order to set criteria to differentiate the presence from the absence of an acceptable TEOAE response, several factors related to the stimulus and recording parameters should be considered. TEOAE response measures include the overall correlation of the two waveforms obtained from time averaging (reproducibility), the overall level of the response in relation to noise in the measurement, the reproducibility within specific frequency bands and the stimulus stability. In earlier TEOAE studies, the analysis of TOAE responses was almost limited to a description of overall reproducibility (in %) and overall amplitude level (in dB SPL). These response measures do not take advantage of the frequency-specific information available in TEOAE's. Thus it is important to not only investigate the whole reproducibility, but also the band reproducibility from 1.0 to 4 KHz. In general the TEOAE's may be considered as always present when reproducibility is 60% or greater or the response level minus the level of the noise is 2.4 dB or greater (Welzl-Muller and Stephan, 1994). Several investigators have determined that percentage reproducibility values from 50% to 70% would separate normal from impaired ears (Gorga, Neely, Bergman, Beauchaine, Kamisnski, Peters & Jesteadt, 1993; Prieve, Gorga, Schimidt, Neely, Peters, Schultes & Jesteadt, 1993). Thus a signal to noise ratio of ≥ 6 dB SPL and reproducibility greater than 70% was required to accept the TEOAE as being present (significant) in any frequency band. Only those ears which had significant TEOAE responses meeting these creteria at half octave frequencies between 1000 Hz and 4000 Hz were considered for further analysis. Responses to stimulus sweeps in which the intensity of ambient noise exceed 48.8 dB peak SPL 9 (default settings on the equipment) were rejected . The stimulus stability was monitored throughout the sampling duration and only responses generated with stimuli at a stability of 80% and greater were included in the data analysis. If TEOAE date did not meet the criteria (e.g. a stimulus stability of less than 80% or reproducibility less than 70 %), it was excluded from statistical analysis, by not including the data to the averaging of the three separate trials and using only the remaining two trial recordings.

Data organization and calculation of suppression amplitude

TEOAE amplitude values for both controlled and experimental conditions were extracted from the specified time interval recordings and tabulated into Microsoft Excel 2007 spreadsheets for further analysis. TEOAE overall amplitudes as well as the amplitude at each half-octave frequency (1.0 to 4 kHz) following averaging of 260 sweeps were noted and included in the spreadsheets. Thereafter, the suppression amplitude was derived by subtracting the three trials of emission amplitudes with contralateral noise (controlled condition) from the three trails of emission amplitudes without contralateral broadband noise (experimental condition) at each specified time recording. This was done for each individual.

3.6.5 Analysis

The mean contralateral broadband acoustic reflex threshold for the sample was 85.3 dB SPL (SD = 5.3) Individual subjective thresholds for detection for contralateral white noise were measured using insert earphones for each subject and found to be equal to or less than 10 dB SPL with a mean threshold of 5.2 dB SL (SD = 5.4). The mean OAE amplitudes of the control condition stayed relatively stable over the course of measurement, with no statistically significant differences ($p>0.05$) between the mean amplitude of the different time intervals recordings. TEOAE amplitude was reduced with contralateral stimulation at 45 dB SL compared to that found without contralateral stimulation.

The analysis process consisted of a series calculation of descriptive values for amplitude and noise floors for each time recording in both the control and experimental condition separately, including the post-noise periods. Comparisons of these values were done to evaluate consistency and/or change over time and between conditions. Thereafter suppression values (at each time recording) were derived from subtracting the with-noise (experimental condition) TEOAE amplitude from the without-trace in the corresponding time recording of the controlled condition. Suppression values between different time recordings were compared to assess the change or sustainability over the duration of CAS. All calculations were done for the overall TEOAE response and filtered frequencies (1kHz, 1.5kHz, 2kHz, 3kHz and 4kHz). Suppression for half-octave frequencies over time was then compared for corresponding time recordings between frequencies. The analysis procedures are discussed according to sub-aims.

Sub-aim 1: To compare replicated recordings of TEOAE amplitudes obtained over an identical time period divided into identical intervals in the control condition and in the experimental condition

The Otodynamic V6 provided both a TEOAE signal (amplitude in dB SPL) and noise level in the form of an overall response and half-octave frequencies (1kHz, 1.5kHz, 2kHz, 3kHz and 4kHz) for each TEOAE recording. The data collection procedure was repeated over three different days for each subject and the mean TEOAE amplitude and noise level for all specified recordings were therefore calculated for each subject over the three trials. Descriptive analysis (means, standard deviations and ranges) of both the signal (TEOAE amplitude) and noise levels were done for the overall response and filtered frequencies measurements at each time recording in both conditions. Thereafter two different comparisons were made. Firstly, comparisons were made between the different recordings (amplitude and noise levels) for each condition. This was done by using the Wilcoxon matched-pair signed rank test. These comparisons provided information about the stability of noise levels in both conditions and the stability of TEOAE amplitudes in the control condition in order to insure validation of consistent noise floor levels across trials. Statistical comparisons also provided information about the changes in ipsilateral TEOAE amplitudes over time with contralateral stimuli and the post-noise period (experimental condition). Secondly, comparisons were made between corresponding recordings of conditions (also with the Wilcoxon tests of significance). This was done to evaluate the significance of the reducing effect of contralateral stimuli on TEOAE amplitudes and after the cessation of the stimuli. TEOAE amplitudes in both conditions were used to calculate suppression values.

Sub-aim 2: To describe the relationship between the duration of CAS and TEOAE suppression amplitude

After suppression values were calculated, (for overall response and filtered frequencies) descriptive analyses for TEAOE suppression at each specified time recording were done. Thereafter, amplitude comparisons between recordings over time were made using the Wilcoxen test of significance. These comparisons were done for the overall response and half-octave frequencies. Differences between amplitudes of the first OAE recording and the OAE recording after five minutes, the OAE recording after five minutes and recording after ten minutes, the OAE recording after ten minutes and recording after 15 minutes and finally the initial OAE recording and recording after 15 minutes, were calculated to determine whether there were any significant differences amongst these time intervals. Figure 3.2 illustrates the comparisons between different time intervals of OAE recordings that were done.

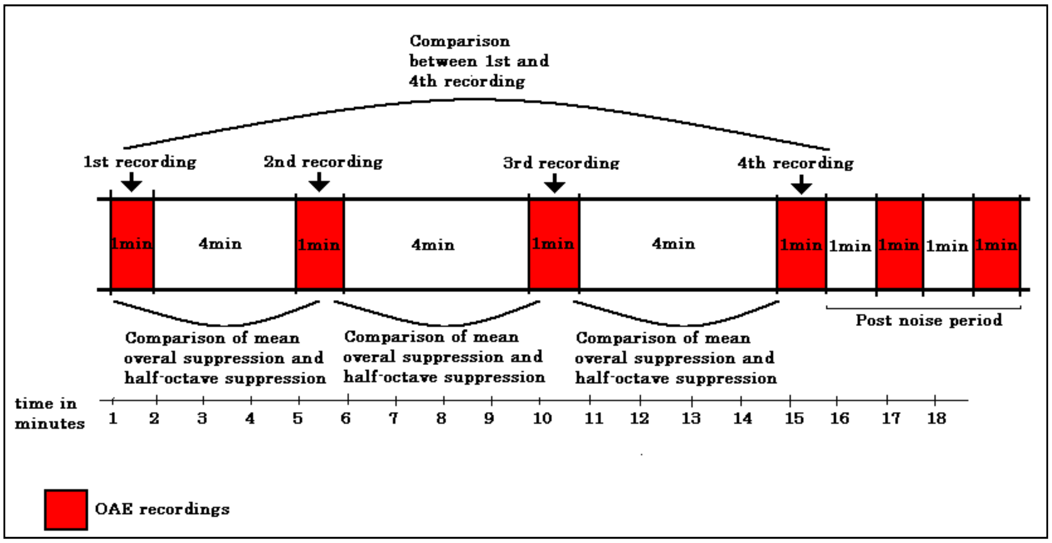


Figure 3.2 Analyses of the differences amongst the mean suppression amplitudes in the various time intervals.

This provided information about change or sustainability of suppression amplitudes as a function of contralateral noise duration. Additionally, TEOAE suppression amplitudes amongst half-octave frequencies for each specified time recording were compared (Wilcoxen signed rank test) to evaluate differences between frequencies.

3.7 Ethical Considerations

Responsible ethical conduct in research is fundamental to the quality of science in any discipline, and ultimately to the advancement of knowledge (Ingham, 2003). The following ethical aspects were therefore taken into account in the planning of this research project:

3.7.1 Respect for the privacy of research participants

In order to ensure the privacy of all the participants (Huysamen, 1994; Hegde, 2003), no individuals were named in the research report. This was achieved by assigning a code to each subject, and noting it in the name section on the questionnaire (Appendix A). No names were used during the study and all personal information remained confidential. Data was processed, analysed and discussed according to these codes to make the best possible effort to maintain confidentiality. This was clearly explained in the informed consent letter.

3.7.2 Informed consent

According to Hegde (2003), informed consent is a crucial ethical principle, which consists of the following components – the participants should fully comprehend the nature of the study and research procedures that will be undergone and they should be given the choice to participate or not. Consequently, the present study acquired written informed consent from each participant by their signing the appropriate form (attached as Appendix B). This form was signed by each participant after they had read a letter explaining the goal of the study and what was expected of them. The letter provided a brief description of the nature of the study, including the rationale and time it would take for each measurement. It clearly stated that participation was strictly voluntary and participants could withdraw from the study at any time. The letter guaranteed participants of the confidentiality of their personal particulars.

3.7.3 Beneficence and non- malfeasance

None of the test procedures caused physical, social or emotional harm to the participants. The potential inconvenience of participating in the study (the time and effort required to undergo the test) was indicated in the letter of consent. The letter also explained that the information gathered would provide useful data to the field of Audiology through publication of the results upon conclusion of the study. The letter also informed subjects that all data obtained in the study would be stored for a minimum of fifteen years for record-keeping purposes. An offer was made to provide detailed information about the study and individual results of the test procedure upon its completion. However, there were no incentives or rewards (financial or other) offered for participation in the study.

3.8 Validity and reliability of research methodology

To measure the validity of the present study in terms of instruments and data collection procedures, the researcher had to re-evaluate the chosen approach and evaluate the extent to which the apparatus and procedures measured what they were supposed to measure (Leedy & Ormrod, 2005). The main objective for the selection of subjects was to ensure that all had normal hearing, which implied that subjects had no symptoms associated with hearing loss, the absence of any ear pathology, and had normal cochlear function. The validity of the subject selection apparatus (measuring normal hearing) was affirmed by a multi-method (Campbell & Fiske, 1959) approach. Various measuring methods (both subjective and objective) were included, all with the intention to screen subjects with normal hearing. The use of objective measurements in the subject selection protocol further validates findings, because it does not require subjects to participate actively, thus excluding subject input bias. Subject selection criteria ensured a somewhat homogenous (all had normal hearing) group, decreasing limitations of convenience sampling and serving as a good representative population. Data collection followed an experimental design which made it possible to carefully control for influential factors, except those whose possible effects are the focus of investigation. Because of the fact that all TEOAE measurements followed a strict protocol, environmental factors could be controlled. TEOAE measurements are relatively objective (not requiring subject's active participation/ based on physiological rather than behavioural responses), so other factors or possible explanations for the results were greatly eliminated.

The reliability of the research methodology was considered in order to assess the consistency with which the recording apparatus and method yielded a specific (similar) result when the characteristic being measured had not changed (Leedy & Ormrod, 2005). Two forms of reliability in the data collection procedures were confirmed when raw data was viewed. The first, formally known as "Interrater reliability", was observed when TEOAE amplitudes were compared in different subjects, using the same test procedures (Leedy & Ormrod, 2005). Although there is a degree of variability in TEOAE amplitude amongst the subjects, all obtained TEOAE amplitudes within the normal range, and the same effect from prolonged contralateral stimulation was observed in all subjects. The whole data collection procedure was repeated on three different days and revealed similar results for each subject across the three days. This ensured the second form of reliability, known as "Test-retest reliability" (Leedy & Ormrod, 2005).

3.9 Summary

The need for investigating TEOAE suppression during continual CAS in order to understand the extent of prolonged MOCS inhibition on OHC's inspired this research project. The aim of this study was to investigate TEOAE suppression as a function of prolonged CAS. Ten healthy normal-hearing volunteers between the ages of 20 and 26 were selected. Their hearing thresholds were less than 15 dB HL at standard audiometric frequencies (250Hz – 8000Hz). 60 dB SPL (±3 dB) linear clicks were presented to record TEOAEs in the right ear using the Otodynamics V6 Analyzer hardware and software in the presence and then the absence of a 45 dB SL contralateral broadband noise, using a GSI 61 clinical Audiometer and insert earphones. TEOAE recordings were measured in the two conditions, namely the control and experimental conditions. The control condition comprised of a series of TEOAE recordings without the presentation to the non-test ear, four with a time interval of five minutes between the on- and offset of recordings, followed by two recordings, one and three minutes after the fourth recording. This was done to establish a baseline. The experimental condition consisted of four TEOAE recordings (with the same time intervals as in control condition) in the presence of contralateral broadband noise, followed by two recordings, one and three minutes after noise termination, to determine if the suppressive effect persisted after stimulus offset. Final averages were accepted when the reproducibility was 70% or more and the stimulus stability was maintained at greater than 80%. The whole procedure was repeated thee time on each subject. Noise levels, as well as averaged amplitudes of the TEOAE overall response and half-octave frequency (1.0 to 4 kHz) for each recording, were noted and included in spreadsheets. Data analysis determined descriptive values and compared TEOAE over time and between conditions, in an attempt to describe the significance in amplitude reduction at each recording and the change/sustainability over prolonged CAS and in the two recordings after noise offset. Suppression values were calculated by subtracting the without-noise recordings from the with-noise recordings and further manipulated in Excel for Windows 2007 to create visual representations.

Chapter 4: Results

The results of the current study are discussed according to the research aims that were described in Chapter t3. In order to achieve the primary aim of this study, that is, to investigate the relationship between the duration of CAS and the degree of TEOAE suppression, subjects had to adhere to strict selection criteria, also discussed in Chapter 3. TEOAE suppression was used to explore the time course of the efferent reflex in order to determine if it remains consistent over a long duration of CAS, or if it adapts and weakens over time. Ten subjects were repeatedly tested over three different days. Tests followed a strict protocol with little inter-subject and test-parameter variance, to minimize the possibility of bias in the recordings The results were presented according to each sub-aim, as described in the methodology.

The aim of this chapter is to present all the collected and processed data (in displays and summaries - graphs, charts and tables) and to describe these results according to the sub-aims that were discussed in chapter three.

4.1 Sub-aim 1: TEOAE amplitudes over time for control and experimental conditions

As described in chapter three, a control (without contralateral noise stimulation) and an experimental (with contralateral noise) condition were used to calculate TEOAE suppression over a predetermined time. These conditions were subdivided into individual TEOAE amplitude recordings with specific time intervals of five minutes between each recording. Thus TEOAE amplitudes were recorded four times with a five minute period between the onsets of each recording in both the conditions. Two additional TEOAE recordings were taken after the period of contralateral noise. These recordings took place at one and three minutes after the CAS ended (post-noise periods).

This results section presents the distribution of overall and half-octave frequency TEOAE amplitudes elicited in both with and without contralateral noise conditions and in the two additional post-noise periods of normal hearing subjects. It also describes the noise levels during the period of measurement in terms of consistency over time and between conditions.

4.1.1 Consistency of noise levels in control and experimental conditions over time

In both conditions the noise levels (average SPL detected by the microphone during the samples that were not rejected by the software algorithm) were monitored for each of the recordings over the duration of measurement. Noise levels were then noted and analyzed to examine stability over the duration of the measurements. This was necessary to determine whether variability in the average noise levels of TEOAE's elicited across the course of measurements existed within or between conditions. The descriptive analyses (means, standard deviations, range) of the noise levels (in SPL) of the overall and half-octave frequencies for all subjects are summarized and presented in Table 4.1.

Table 4.1 Descriptive analysis of overall and half-octave frequency noise levels as calculated for both conditions

	Mean Noise level in amplitude (dB SPL)	Standard deviation (dB)	Range (dB SPL)
Overall Response	*-2.7*	*2.12*	*-6.2 - 5.4*
1 kHz	*-12.5*	*4.72*	*-22.1 - 3.6*
1.5 kHz	*-13.9*	*3.2*	*-20.6 - -2.8*
2 kHz	*-11.8*	*1.9*	*-16.5 - -4.3*
3 kHz	*-11.7*	*1.3*	*-14.9 - -6.8*
4 kHz	*-11.4*	*1.1*	*-14.7 - -7.6*

In terms of stability between recordings over time, no significant differences (p-value <0.05; Friedman test statistic) between recordings in the control conditions were found. This was also true for all the recordings over time in the experimental conditions. Thus the noise levels were stable during the entire course of measurement within each condition.

A comparison of noise levels between recordings measured in the control (without contralateral stimulation) and the corresponding time interval recording in the experimental condition (with contralateral stimulation) was also conducted to determine the variability between corresponding noise levels across both conditions. From these results we can construe that the mean values of the noise levels for TEOAE's without contralateral stimulation did not differ from the mean values of noise levels for TEOAE's elicited in the presence of CAS and that this noise variable did not influence results. The results of a valid Wilcoxon test with the level of significant difference set to 5% indicated no significant differences in the means of the TEOAE noise levels for the overall response across the duration of measurement between both conditions. All noise levels measured at half-octave intervals were also not significantly different, except for two half-octave measurements at 1.5 kHz and 2 kHz recorded at the initial recording, where a significant difference was present. Here the noise levels in the experimental condition showed significantly higher noise levels than in the control. These two frequencies showed no further significant differences (p-value < 0.05: Wilcoxen test of Significance) between conditions for all recordings after the initial recording for the entire duration of measurement. Taking into consideration the total noise level in this initial recording also demonstrates that the significant differences at the half-octave frequencies do not result in a significant difference in the total noise levels. It is necessary to consider that this small difference found only at two half-frequencies during the initial measurements may be the result of the patient's initial restlessness. With minimal differences between noise levels between the recordings with and without noise, comparisons of TEOAE amplitudes across conditions could, therefore, be considered valid and reliable.

4.1.2 TEOAE amplitudes for control and experimental conditions over time

TEOAE's were present in 100% of subjects. The overall and half-octave frequency (1 kHz, 1.5 kHz, 2 kHz, 3 kHz and 4 kHz) TEOAE amplitudes for both the control and experimental conditions at each specified time period over the duration of measurement (20 minutes) were recorded in all subjects. This procedure was repeated over three different days of one week. The mean TEOAE amplitudes of the three trials of control and experimental conditions for each subject were calculated and processed for descriptive and comparative statistical analyses.

The descriptive analyses (means, standard deviations, range) of the overall and half octave frequency TEOAE amplitudes at specified recording periods for all subjects are summarized and presented in Table 4.2.

Table 4.2 Descriptive analysis of TEOAE amplitudes in control and experimental condition

		Initial recording		5 min		10 min		15 min		1 min post-noise		3 min post-noise	
		Mean (SD)	**Range**	**Mean (SD)**	**Range**	**Mean (SD)**	**Range**	**Mean (SD)**	**Range**	**Mean (SD)**	**Range**	**Mean (SD)**	**Range**
1 kHz	***C**	*-0.4 (4.1)*	*-5.1 - 7.3*	*0.1 (4)*	*-3.8 – 8.2*	*0.5 (3.7)*	*-4 – 8.8*	*0.4 (4.2)*	*-5.6 – 9.2*	*0.5 (3.7)*	*-2 – 9*	*0.2 (4.3)*	*-4.7 – 9*
	***E**	*-1.9 (4.2)*	*-6.2 - 5.3*	*-1.3 (3.7)*	*-5.7 – 8.2*	*-1.3 (3.8)*	*-6.7 – 5.5*	*-1.7 (4)*	*-8.6 – 5.2*	*0 (4.2)*	*-4 – 8.7*	*0.1 (4)*	*-3.4 – 8*
1.5 kHz	**C**	*0.5 (3,5)*	*-7 - 4.4*	*0.3 (4)*	*-7.8 – 5*	*0.6 (3.7)*	*-6.9 – 5.5*	*0.9 (3.7)*	*-6.7 – 6*	*0.9 (3.8)*	*-7.2 – 5.9*	*0.6 (4.3)*	*-8.3 – 5.9*
	E	*-1 (4.3)*	*-11.7 - 2.3*	*-0.8 (4.2)*	*-11.3 – 2.8*	*-0.5 (3.7)*	*-9.3 -3.6*	*-0.9 (4)*	*-10.5 – 2.9*	*0.9 (4.2)*	*-9 – 6.1*	*0.8 (4.1)*	*-9.1 – 5.3*
2 kHz	**C**	*4.4 (4)*	*-2.6 - 10.5*	*3.1 (4.1)*	*-2.9 – 11.1*	*3.3 (3.9)*	*-2 – 11.3*	*3.6 (4.2)*	*-2.4 – 11.9*	*3.3 (4)*	*-1.8 – 11.6*	*3 (4.4)*	*-3.2 – 11.5*
	E	*2.2 (3.8)*	*-2.7 - 9.3*	*2.3 (3.9)*	*-2.1 – 9.8*	*2.3 (3.8)*	*-1.5 – 9.4*	*2.3 (3.9)*	*-1.8 – 9.2*	*3.7 (4)*	*-1.2 – 12.2*	*3.7 (3.8)*	*-0.8 – 11.8*
3 kHz	**C**	*-0.4 (3.6)*	*-5.2 - 5.8*	*-0.7 (3.3)*	*-5.9 – 5.1*	*-0.4 (3.2)*	*-5.2 – 5.2*	*-0.3 (3.4)*	*-6 – 5.4*	*-0.4 (3.4)*	*-6.3 – 5.4*	*-0.4 (3.3)*	*-6.2 – 5.2*
	E	*-1.7 (3.6)*	*-6.8 – 4.8*	*-1 (3.2)*	*-5.7 – 5.3*	*-0.9 (3.4)*	*-5.3 – 5.1*	*-0.8 (3.3)*	*-5.6 – 5.1*	*0.6 (2.9)*	*-3.9 – 5.4*	*0.5 (2.8)*	*-3.7 – 5.3*
4 kHz	**C**	*-9 (6)*	*-15.8-1.9*	*-9 (6.2)*	*-16.6 – 1.7*	*-8.9 (5.9)*	*-14.6 – 1.7*	*-8.5 (5.9)*	*-15.9 – 1.6*	*-8.9 (5.9)*	*-16.4 – 0.9*	*-8.9 (6.5)*	*-18.4 – 1.4*
	E	*-9.4 (5.3)*	*-16.5 – 0.4*	*-9.6 (6.2)*	*-18.3 – 0.6*	*-9.2 (5.9)*	*-14.7 – 1.7*	*-9.2 (6)*	*-15.9 – 1.3*	*-8.6 (6.1)*	*-15 – 2.5*	*-7.9 (5.8)*	*-14.3 – 2.9*
Overall	**C**	*7.9 (3.1)*	*4.1-13.2*	*7.7 (3.2)*	*3.7 – 13.8*	*7.9 (3)*	*4.4 – 14.2*	*8.3 (3.2)*	*3.8 – 14.7*	*8.1 (3)*	*4.2 – 14.5*	*7.8 (3.5)*	*3.1 – 14.4*
	E	*6.7 (3.2)*	*2.6 – 11.7*	*6.6 (3.5)*	*3.4 – 11.8*	*6.8 (3)*	*2.8 – 11.5*	*6.8 (3)*	*2.4 – 11*	*8.3 (3)*	*4.6 – 14.7*	*8.4 (2.9)*	*5.1 – 14.4*

***E = Experimental condition**
***C = Control**

The results of the TEOAE amplitude differences between the control and experimental condition in the overall and half-octave frequency measurements were analyzed separately. Comparisons between conditions furthermore focused on two different recording aspects. The first comparisons between the two conditions were between the first four recordings to ascertain the effect of contralateral noise over time. The second set of comparisons was between OAE amplitudes in the post-noise periods for the experimental and control conditions, to determine if any residual suppression was evident in the post-noise timeframe.

TEOAE amplitude for overall response

Figure 4.1 illustrates the mean overall TEOAE amplitude elicited at each specified time interval in both the control and experimental condition.

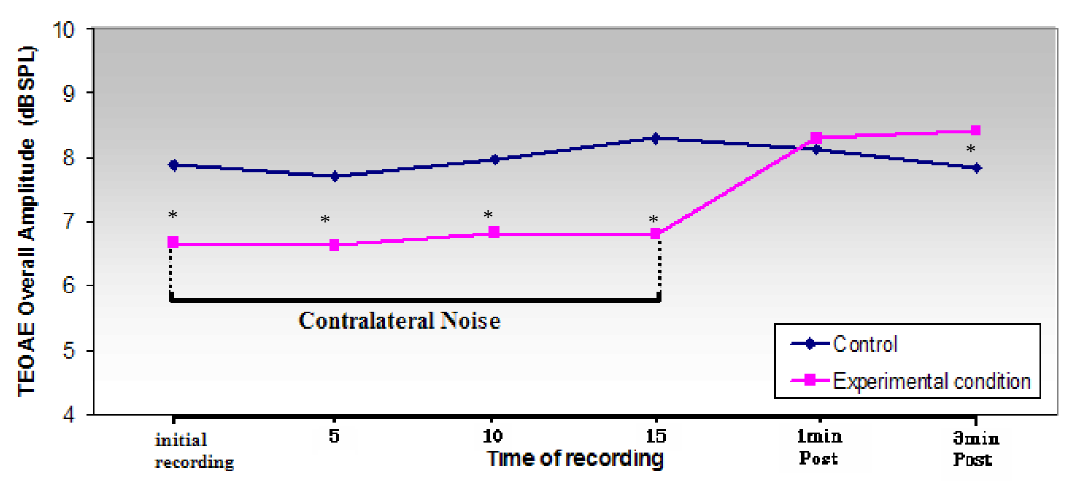


Figure 4.1 Mean overall OAE amplitudes over time across conditions.

***significant difference between conditions**

As seen in figure 4.1 a decrease in mean overall TEOAE amplitude is evident in the experimental condition with the onset of the contralateral stimulation. This reduction in TEOAE amplitude with contralateral stimuli was observed in all subjects. The difference in mean TEOAE amplitude between the control and experimental condition was significant (p>0.05) for all recordings from the onset of CAS up to 15 minutes of contralateral noise stimulation. In the initial recording, the mean overall TEOAE amplitude significantly reduced from 7.9 to 6.7 dB SPL when contralateral noise was introduced. At five, ten and 15 minutes of contralateral noise, the experimental mean TEOAE amplitude reduced from 7.7 to 6.6, 7.9 to 6.8 and 8.3 to 6.8 dB SPL, respectively.

One minute after the contralateral stimulus was terminated (post noise period), the mean TEOAE amplitude in the experimental condition rapidly increased to a value that does not significantly differ ($p<0.05$) from the corresponding TEOAE recording in the control condition (difference=0.18 dB SPL+-0.4). Thereafter the mean amplitude in the experimental condition continued to increase to 8.4 dB SPL three minutes after the offset of contralateral noise (three minutes post-noise period) above its initial value (7.8 dB SPL) in the corresponding time recording of the control condition (difference = 1.58 dB SPL ±0.82). This increase in OAE amplitude in the experimental condition at three minutes post noise was significantly ($p>0.05$) higher than the control condition. The amplitude in the experimental condition exceeding the corresponding condition in the recording three minutes after noise termination was observed in 90% of subjects (9/10).

TEOAE amplitude at half-octave frequency intervals

Figure 4.2 shows the mean TEOAE amplitude over time in both the control and experimental conditions plotted against bandwidth for each of the five half-octave frequencies.

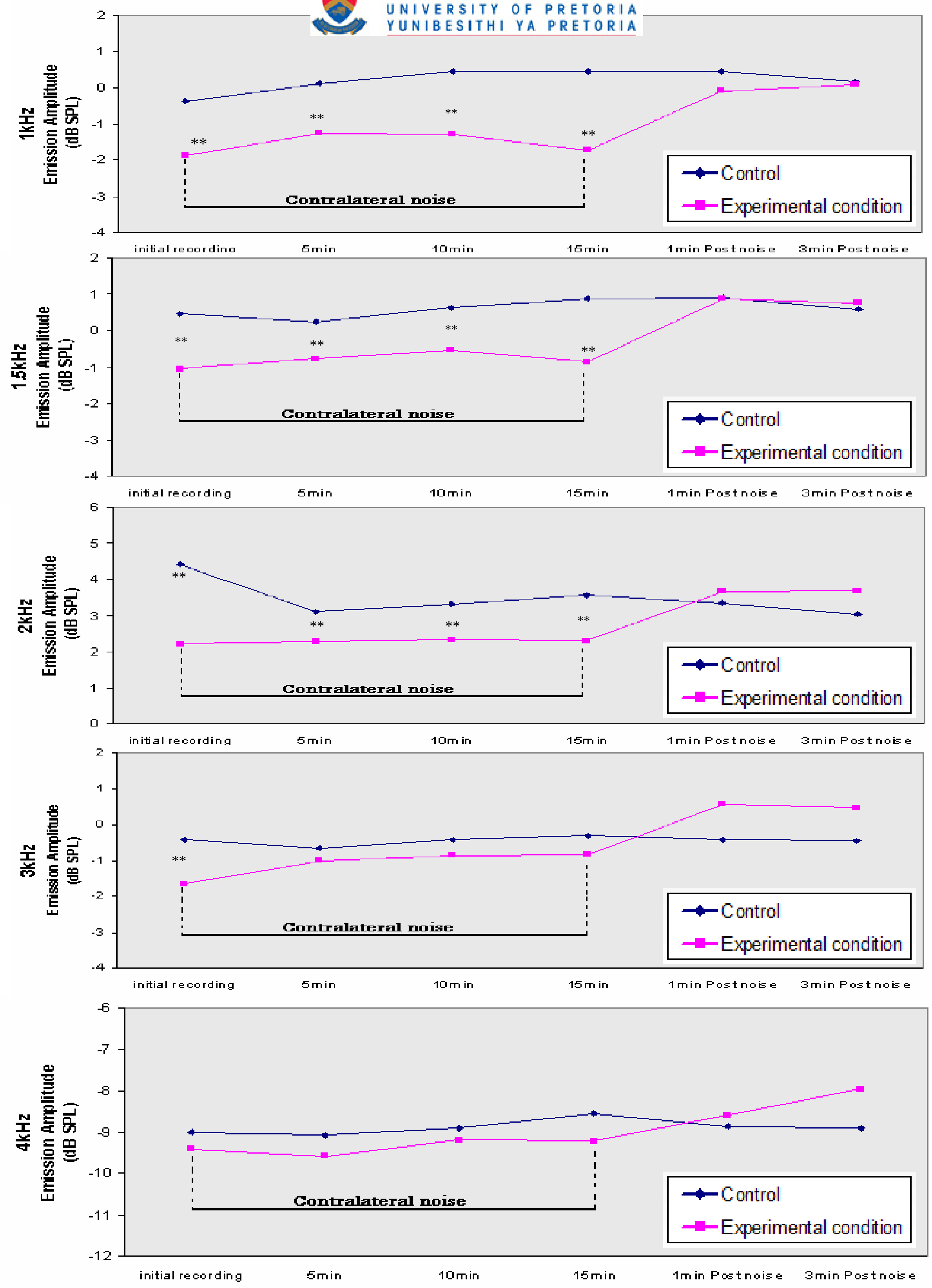
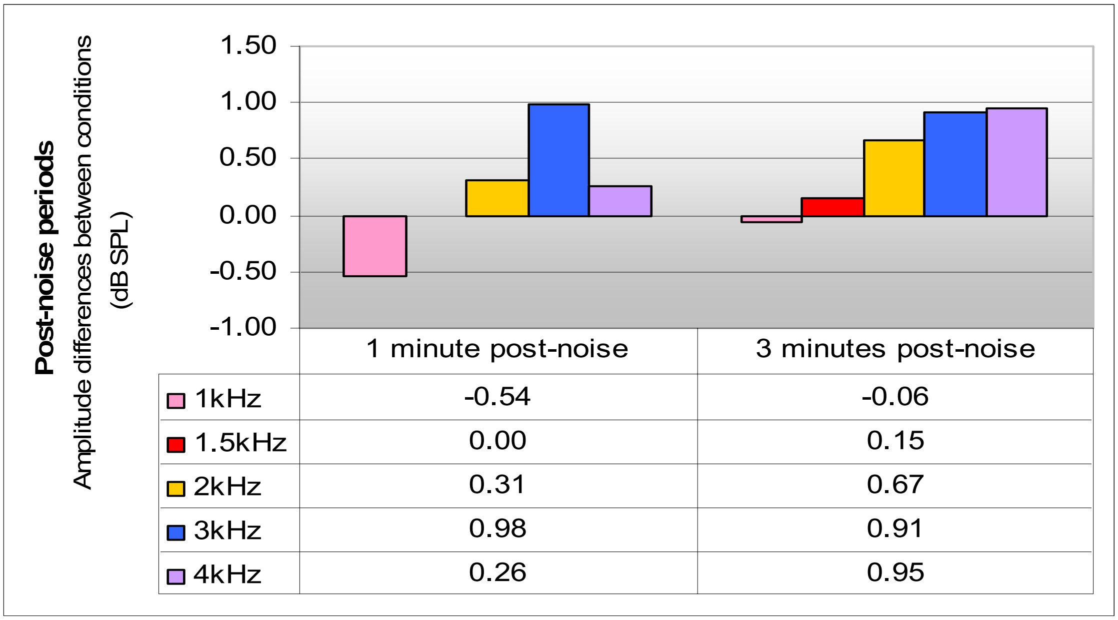


Figure 4.2 Mean OAE amplitudes at half-octave frequency intervals for control and experimental conditions over time
**** significant differences between conditions**

Like the overall TEOAE, the presentation of CAS decreased TEOAE amplitudes over all half-octave frequency bands for the entire duration of stimulation. For lower frequency bands such as 1 kHz, 1.5 kHz and 2 kHz this decrease in mean TEOAE amplitude was significant ($p>0.05$) at all intervals measured over time. The smallest differences between the amplitude of the experimental and control conditions was for the higher frequencies (3 and 4 kHz) with no significant ($p<0.05$) differences over time, except for the first recording in the 3 kHz bandwidth, which was significantly reduced. The differences between mean OAE amplitudes elicited in the control and experimental conditions decreased with an increase in frequency, with the largest difference at 1 kHz and the smallest difference at 3 kHz and 4 kHz measurements. These differences are illustrated and discussed in more depth elsewhere in this chapter.

All TEOAE amplitudes at half-octave frequency intervals in the experimental condition significantly ($p<0.05$) increased from the last recording with contralateral noise to one minute after noise termination. The TEOAE amplitude in the experimental condition was larger at three minutes post-noise compared to one minute post-noise in four of the five half-octave frequency bands (3 kHz demonstrated a decrease). In three out of four half-octave frequencies (higher frequencies), the TEOAE amplitude in the experimental condition exceeded the initial value in the corresponding control recording), one minute after noise termination. There was an exceptionally difference between conditions at 3 kHz. Four of the five half-octaves had amplitudes in the experimental condition that exceeded those in the control, three minutes after the cessation of contralateral noise.

Figure 4.3 illustrates the mean amplitude differences between the control and experimental conditions in the post-noise recordings for each half-octave frequency band.



	1 minute post-noise	3 minutes post-noise
1kHz	-0.54	-0.06
1.5kHz	0.00	0.15
2kHz	0.31	0.67
3kHz	0.98	0.91
4kHz	0.26	0.95

Figure 4.3 Mean amplitude differences between control and experimental conditions in the post-noise period.

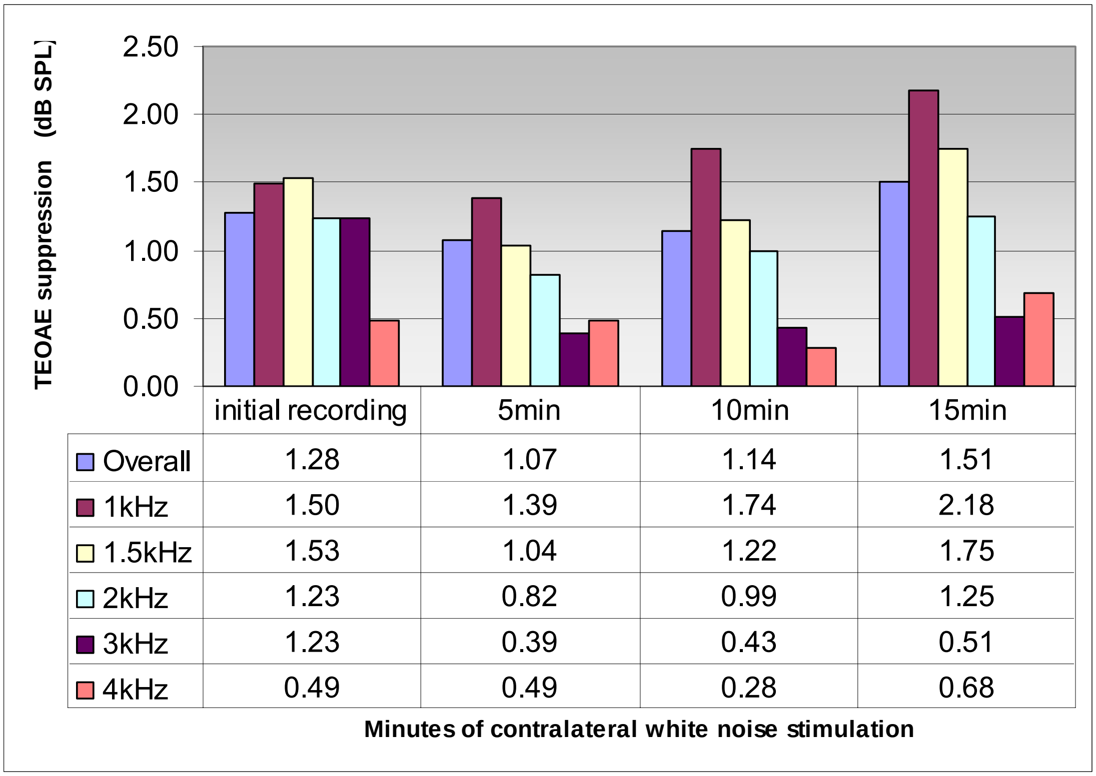
Although not significant ($p<0.05$), amplitudes of the 1 kHz band demonstrated a mean decrease in the experimental compared to the control condition, which is evident in the negative values (inversion) in figure 4.3 For the recording one minute after contralateral noise, 3 kHz showed the largest difference (which was also the only significant difference between conditions). The recording at 1.5 kHz one minute after contralateral noise, revealed almost no differences between conditions. Differences between conditions at 3 kHz slightly decreased at the three minute post-noise period, whereas the other frequencies increased, leaving 4 kHz with the biggest difference.

4.2 Sub-aim 2: Relationship between the duration of CAS and TEOAE suppression

Suppression amplitudes (overall and half-octave frequencies) were calculated by subtracting the average OAE amplitudes elicited in the three trials with CAS from the average OAE amplitudes elicited in the corresponding three trials without CAS. These calculations were done for the initial recording (recorded at the onset of the CAS) and the recordings after five, ten and fifteen minutes of contralateral stimulation. As significant reductions of TEOAE amplitudes in the experimental conditions were not observed in the recordings after contralateral noise was terminated, these are not further discussed in this section.

This section presents the result of TEOAE suppression over a 15 minute time interval in the presence of sustained CAS to describe suppression characteristics over prolonged periods.

A descriptive analysis is provided for suppression amplitude (overall and half-octave frequencies) at each recording interval over the period of sustained contralateral noise stimulation. Figure 4.4 illustrates these average suppression values.



	initial recording	5min	10min	15min
■ Overall	1.28	1.07	1.14	1.51
■ 1kHz	1.50	1.39	1.74	2.18
□ 1.5kHz	1.53	1.04	1.22	1.75
□ 2kHz	1.23	0.82	0.99	1.25
■ 3kHz	1.23	0.39	0.43	0.51
■ 4kHz	0.49	0.49	0.28	0.68

Figure 4.4 Mean TEOAE (overall & half-octave frequencies) suppression as a function of CAS

Suppression values plotted in figure 4.4 correspond to the difference in magnitude between TEOAE's recorded in the presence and absence of CAS and are consistent with those obtained by the Euclidean distance calculation method (Chery-Croze et al., 1994). Generally the largest mean suppression at each recording time interval was observed at lower half-octave frequency, 1 kHz, except for the initial time interval of 1.5 kHz showing larger suppression values. In the initial recording, the higher frequencies (3 kHz and 4 kHz) revealed the least suppression over all time recordings, except in the initial time interval recording of 3 kHz, which showed a significant difference between conditions. Descriptive illustrations of overall and half-octave frequencies over time, including the standard deviation, are presented in figures 4.6 and 4.7.

4.2.1 Overall suppression

Figure 4.5 demonstrates the mean and standard deviation of overall TEOAE suppression at the four recording intervals as a result of sustained CAS.

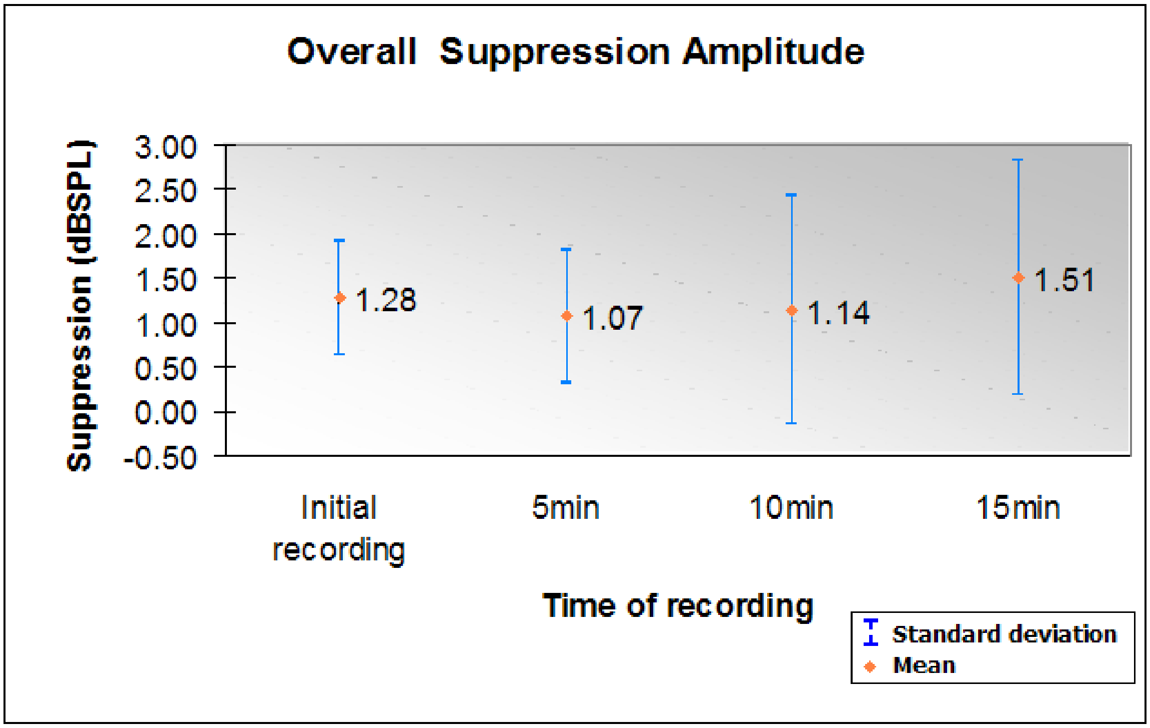


Figure 4.5 Overall TEOAE suppression as a function of contralateral noise duration (Mean ± SD)

The first recording with CAS revealed suppression within the ranges of 0.66 to 2.8 dB SPL with a mean of 1.28 dB SPL (SD ± 0.63). In this time interval recording only two of the 10 subjects had overall suppression below 1.0 dB SPL, while the majority had normal suppression values of between 1.0 and 3 dB SPL. At the five minute time interval recording suppression ranged from 0 dB to 2.1 dB SPL with a mean of 1.0 dB SPL (SD ± 0.74) and three of the ten subjects showed suppression of less than 1.0 dB SPL. Although not significant ($p<0.05$), a slight reduction in mean suppression was observed from the initial time interval recording to the recording of five minutes contralateral noise stimulation. At the ten minute time interval recording the mean suppression was 1.14 dB SPL (SD ± 1.28) and ranged from -1 dB SPL (no suppression) to 3.33 dB SPL with two subjects presenting with suppression below 1.0 dB SPL. From the 10 minute recording, overall mean suppression at the 15 minute time interval recording slightly increased (though not statistically significantly) to 1.51 dB SPL (SD = 1.31), ranging from 0.42 to 4.1 dB SPL. Only 2 subjects presented with suppression of less than 1.0 dB in this time interval recording. In conclusion, statistical analysis revealed no significant differences in suppression values between recordings over time, as a result of small values and low subject numbers, but a small increase in mean suppression was observed from the time interval recordings of five minutes to 15 minutes of contralateral stimulation.

4.2.2 Suppression at half-octave frequency bands

Figure 4.7 illustrates the mean and standard deviation of TEOAE suppression in frequency bands over the duration of CAS on a relative scale.

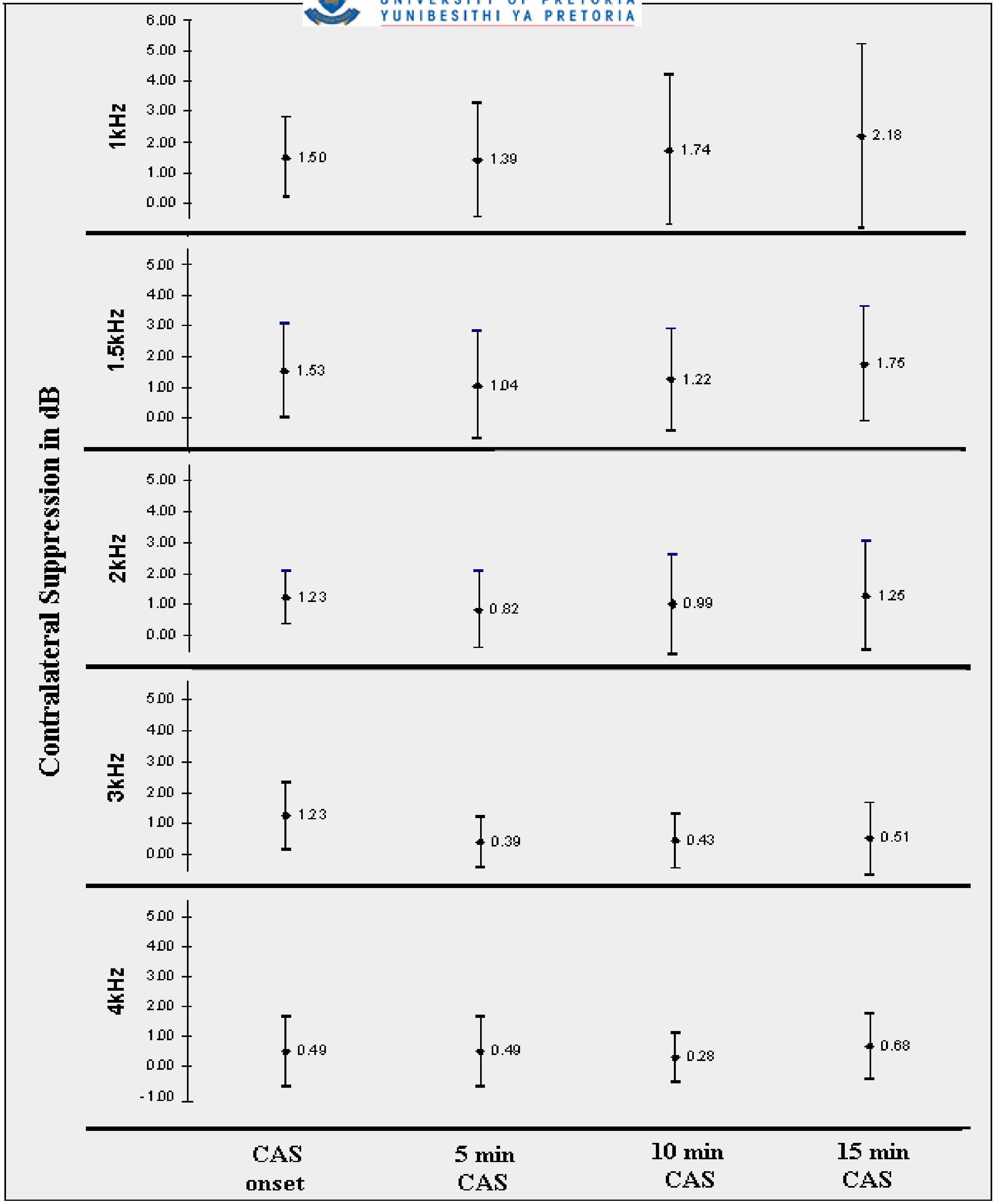


Figure 4.6 TEOAE suppression as a function of CAS duration at half-octave frequencies (Mean ± SD)

4.2.3 Frequency suppression differences over time

Figure 4.7 illustrates the mean suppression values at half-octave frequencies over a sustained period of contralateral noise stimulation.

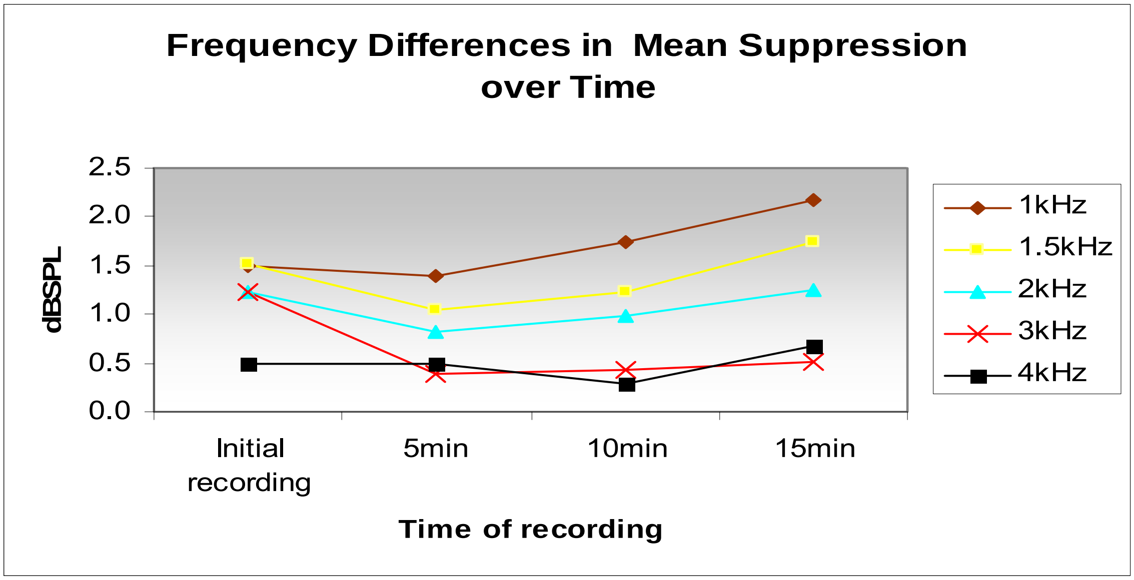


Figure 4.7 Mean suppression across frequency bands as a function of CAS duration

Clear suppression could be observed in the frequency bands where the effect was the greatest (1-2 kHz). As the frequency increased, mean suppression was decreased, with the least suppression in 3 and 4 kHz half-octave frequencies. However, because mean suppression values differ minimally and have widely overlapping standard deviations, no statistically significant differences were found between frequencies at each time interval recording. Among these half-octave frequencies, it was also found that there was no significant change in suppression over time as the CAS duration increased, indicating a stable suppressive effect over prolonged stimulation. With the exception of 4 kHz, an upward tendency was observed in the mean suppression values from five minutes of CAS to 15 minutes of CAS and in the mean overall suppression, as seen in figure 5.7.

4.3 Conclusion

From the results it could be concluded that a contralateral 45 dB SL white noise significantly reduces ipsilateral TEOAE's over a time period of 15 minutes, except for the high frequencies of 3 to 4 kHz). Suppression was observed for the entire duration of CAS. The amount of suppression stayed relatively stable for over 15 minutes and did not significantly reduce as a result of prolonged contralateral stimulation. However, a slight increase in mean suppression was observed from five to 15 minutes of stimulation in the overall and half-octave frequency measurements. After the offset of CAS, TEOAE amplitudes rapidly increased to values above those seen in the control condition, and no traces of suppression were observed after one minute of noise termination, except at 1 kHz, although suppression was minor and not significant ($p<0.05$). The amplitude in the experimental condition at 3 min after the CAS termination indicated a significant increase in overall TEOAE and some frequency band (2, 3 and 4 kHz) amplitudes compared to the control condition. The average overshoot was largest at 4 kHz (0.95 dB) followed by 3 kHz (0.91 dB) and 2 kHz (0.69 dB). The average overshoot (0.58 dB) of the overall TEOAE amplitude in the experimental condition was statistically significant ($p > 0.05$) at the 3 min post-noise recording interval compared to the control condition. This overshoot, or amplitude enhancement, above control values was observed in 7 out of the 10 subjects with only one individual showing the same amplitudes and two individuals showing control amplitudes slightly higher than experimental amplitudes in the recording 3 min post-CAS termination.

4.4 Summary

In the TEOAE (overall and filtered frequencies), the noise levels were low and stable during the entire course of measurement within each condition. This suggested that all TEOAE's elicited during the control and experimental conditions were valid and reliable and allowed the researcher to confidently investigate the distribution of OAE amplitudes over the duration of measurement. The mean OAE amplitudes of the control condition stayed relatively stable over the course of measurement with no statistically significant differences between the amplitude of the different time interval recordings, thus serving as a valid control to compare with amplitudes in the experimental condition and the calculation of suppression. TEOAE amplitudes (overall and half-octave frequencies) were reduced under contralateral stimulation at 45 dB SL compared to those found without contralateral stimulation. This reduction with CAS was significant for all recordings within the overall TEOAE measurement and half octave frequencies of 1 to 2 kHz. The loss of suppression (not significant) in higher frequencies (3 and 4 kHz). Only the initial recording of 3 kHz showed a significant reduction. The overall and all half-octave mean TEOAE amplitudes in the experimental condition significantly increased from the last recording with contralateral noise to one minute after noise termination. From there mean TEOAE amplitudes continued to increase up to three minutes post noise offset. A reduction in amplitude after stimulus offset was present only in 1 kHz and the overall TEOAE measurement and the majority of filtered frequencies showed amplitudes in the experimental condition greater than in the corresponding control condition. 1 kHz revealed the largest mean suppression for all recordings during the measurement and the higher frequencies (3 kHz and 4 KHz) the least. No significant change in suppression was found over time as the CAS duration increased, indicating a stable suppressive effect over prolonged stimulation. However, an upward trend from five minutes of CAS to 15 minutes of CAS was observed in the mean suppression values in overall suppression and the majority of half-octave frequencies.

Chapter 5: Discussion

5.1 Introduction

Suppression of otoacoustic emissions (OAE's) is a relatively new and exciting research area in the field of audiology. It has a great future with possible applications in such areas as the diagnosis of eighth cranial nerve tumours and Meniere's disease. Clinical audiologists may be surprised to learn that the literature describing investigations of OAE suppression by acoustic stimulation is quite extensive, although the majority of the studies were conducted using animal subjects. These studies all agree on the general conclusions, namely: a) efferent suppression of OAE's results in a reduction of emission amplitude, occurring immediately after the onset of the suppression stimulus and being reversed moments after its cessation; b) there is an inverse relationship between the intensity of the contralateral stimulus and the amount of OAE amplitude reduction, and c) broadband noise is the most effective suppressor. Although extensive research has been done to reveal these properties in OAE suppression, limited research exists describing the effect of prolonged contralateral stimulation on OAE suppression.

The aim of this chapter is to discuss all findings and interpret the significance thereof. These findings will be discussed according to sub-aims. Firstly, TEOAE amplitudes will be discussed as a function of duration of CAS for both the control and experimental conditions. This section will also discuss noise levels during the period of measurement, the differences in TEOAE amplitude between conditions at corresponding time interval recordings and after the termination of CAS (post noise periods). Secondly, the correlation between the different durations of CAS and TEOAE suppression will be interpreted and discussed.

5.2 Sub-aim 1: TEOAE amplitudes over time for control and experimental conditions

TEOAE amplitudes were monitored for the duration of 15 minutes with and without CAS in five minute interval recordings, with the first recording (in the experimental condition) directly at the onset of CAS. Thereafter amplitudes were observed in the post-noise periods of one and three minutes after CAS offset. To investigate TEOAE amplitudes for both conditions over the duration of measurement it was necessary to exclude any influences of noise levels related to the subject or ambient noise.

5.2.1 Consistency of noise levels within and between conditions

Noise levels in both the control and experimental condition were noted and found to be stable, with no significant differences ($p<0.05$) between recordings over time in the both conditions and no significant differences ($p<0.05$) between corresponding time recordings of the control and experimental condition.

All noise levels measured at half-octave intervals were also not significantly different, except for two half-octave frequencies (1.5 kHz and 2 kHz) recorded at the initial recording, where a significant difference was present. Noise levels in the experimental condition were found to be significantly higher than in the control at these frequencies. With the majority of half-octave frequency and the overall measurement showing no significant variability between average noise levels of TEOAE's elicited across the duration of measurements within or between conditions, the researcher could infer that all TEOAE's elicited during the control and experimental condition were valid and reliable. The knowledge that there was no significant variability present in the noise levels in recordings over time and between conditions allowed the researcher to investigate the distribution of OAE amplitudes over the duration of measurement.

5.2.2 TEOAE amplitude reduction as a function of CAS

Comparisons were made between the first four recordings of the two conditions in order to study the differences in TEOAE amplitudes over time in the with-noise and without-noise traces.

Results showed that there was a significant reduction ($p>0.05$) in the mean amplitude of the overall TEOAE when contralateral noise was introduced for the duration of the CAS. As can be seen in figure 4.1, amplitude reduction in the experimental condition was observed from the first recording (which lasted 60 s), directly after CAS onset and at the recordings of five, ten and fifteen minutes of CAS. Thus it can be assumed that amplitude reduction lasted for the entire duration of contralateral stimulation. The time required for contralateral sound suppression to reach maximal effect is in the order of 100 ms (Warren & Liberman, 1989). This reduction may be the result of activation of medial efferent neurons, as has been reported earlier (Norman & Thornton, 1993). Activation of medial efferent neurons results in the release of acetylcholine at the synapse, which in turn induces alteration in the shape and/ or compliance of outer hair cells. These alterations can damp the micro-mechanical activity, reduce the sensitivity of the basilar membrane (Neely & Kim, 1986), and thus reduce the amplitude of TEOAE's.

As was found for overall TEOAE, the presentation of a CAS decreased TEOAE amplitudes over all half-octave frequency bands for each recording with CAS. As can been seen in figure 4.2, it is evident that TEOAE amplitude reduction was more pronounced in the lower half-octave frequency bands. Lower frequencies (1, 1.5, & 2 kHz) revealed significant ($p<0.05$) amplitude reduction, which persisted for each recording during the 15 minutes of CAS (excluding the last recording at 2 kHz), whereas higher (3 and 4 kHz) half-octave frequencies showed much less TEOAE amplitude reduction (not significantly reduced; $p<0.05$). This observation is in agreement with other studies (Berlin et al., 1993; Collet et al. 1992; Norman & Thornton, 1993). These investigators all reported that the largest reduction of TEOAE amplitudes occurs in the range of 1 to 4 kHz and that it tends to be greatest within the 1 to 2 kHz region, with a broadband noise suppressor or when narrow band suppressors are compared (Veuillet et al 1991). The reason for more reduction in this area may be ascribed to the greater density of MOC efferent innervations and more efferent control of OHC's in the area of the cochlea that responds to this frequency range (Guinan et al., 1983; Liberman & Guinan, 1998; Warr et al., 1986).

5.2.3 TEOAE amplitude characteristics after noise termination

In the first recording, one minute after the CAS offset, no significant reduction ($p<0.05$) in TEOAE amplitude was present in the overall TEOAE recordings (figure 4.1). These results differ from the slow recovery of DPOAE amplitude observed after longer CAS durations (Moulin & Carrier, 1998). In their study they reported that DPOAE amplitude reduction continued for over one minute after the CAS offset at a rate of 0.32 dB/min in human subjects. This was attributed to the persistence of an efferent effect on the OHC's after the CAS is terminated. The present study in humans showed no continued reduction in overall TEOAE amplitude after the first minute of CAS offset (figure 4.3). However, the results of the current study suggest that lower half-octave frequency (1 kHz) revealed different effects within one minute after CAS termination. Amplitudes in the lower, 1 kHz half-octave frequency continued to decrease one minute after stimulus offset, although this decrease was small (0.54 dB) and not significant. Moulin and Carrier (1998) measured 2f1-f2 DPOAE stimuli with F2 fixed at 1501 Hz, measuring this specific area in the cochlea. It may be that different areas in the cochlea respond differently after prolonged OCB stimulation and that efferent neurons on OHC's surrounding lower frequency areas are able to maintain their discharge beyond CAS, leading to a slow recovery at the offset of CAS.

Nevertheless, the overall TEOAE amplitudes and the majority of half-octave frequency amplitudes in the experimental condition indicated complete recovery when measured at one minute after CAS offset. A quick amplitude recovery after

CAS termination correlates with a study conducted on animal models, concluding that suppression disappears roughly 80 ms after the contralateral suppressor is turned off (Warren & Liberman, 1989). Moreover, in the current study, amplitudes in the higher half-octave frequencies (2, 3 and 4 kHz) further increased, to values exceeding corresponding amplitudes in the control condition (figure 4.7). However, this increase was small and only 3 kHz showed a statistically significant difference ($p>0.05$) between the conditions. An interesting finding was that the amplitudes after three minutes of CAS offset, in the overall TEOAE and some half-octave frequencies (2 kHz & 4 kHz), continued to increase above control values. The overall recording revealed a significant ($p>0.05$) increase in TEOAE amplitude above the control, three minutes after CAS termination.

Elevated TEOAE amplitudes in the experimental condition of the post-noise periods lead to the impression that emission amplitude, after a prolonged CAS, increases even more than it would in total absence of noise over the same duration, up to at least three minutes post-noise. This raises the question of improved OHC sensitivity after prolonged contralateral stimulation. No studies have been done to investigate these findings, and thus further investigation into OAE amplitude changes after stimulus offset may be needed to confirm these results.

5.3 Sub-aim 2: Relationship between the duration of CAS and TEOAE suppression

The present study aimed to monitor TEOAE suppression over specific time interval recordings during the presentation of 15 minutes of CAS. Of particular interest was the change (increase or decrease) in suppression in response to continuous presentation of noise, observed by calculating suppression at each recording time interval.

5.3.1 Suppression as a function of CAS duration

Results of overall TEOAE's showed that there was no statistically significant ($p<0.05$) change in suppression between time interval recordings as the CAS duration increased, indicating a stable suppressive effect over prolonged stimulation. Therefore, it can be assumed that the efficiency of the MOC reflex in exerting its efferent effect on OHC's was the same throughout the 15 minutes of CAS. It can reasonably be supposed that acoustic stimulation has the same long-lasting effectiveness in OCB activation as sustained electrical stimulation of six minutes has been shown to have (Wiederhold & Kiang, 1970). The results of the present study also agree with the continued decrease in CAP suppression observed in guinea pigs during efferent electrical stimulation, which was ascribed to the continual fast effect on efferent neurons (Shridar, Liberman & Brown, 1995). Furthermore, it was found that the suppressive effect on the EBA brought about by two hours of CAS revealed no decrease for the entire stimulation duration (Da Costa, et al., 1997). This sustained suppression over time was also seen in other studies using evoked OAE's on human subjects for a duration of up to 20 minutes of CAS (Moulin & Carrier, 1998; Giraud et al., 1997). In the study by Moulin and Carrier (1988), the sustained suppressive response on DPOAE amplitude was attributed to the MOCS being capable of a sustained efferent effect on OAE's (Moulin & Carrier, 1998).

Though no significant change ($p<0.05$) in overall suppression was observed over time, a definite trend was noted amongst overall and half-octave frequencies. From the initial recording to the second recording at five minutes CAS, the majority of half-octave frequencies (1, 1.5, 2 and 3 kHz) and the overall TEOAE measurement showed a small decrease in suppression. From then on, a slow increase in suppression was observed from five minutes up to the last recording, made at 15 minutes of CAS. This continued increase in suppression over time was present in the overall TEAOE recordings and all half-octave frequency recordings (figures 4.6 and 4.8). The decrease in amplitude may be attributed to the slow effect reported in guinea pigs (Shridar, Liberman & Brown, 1995), which consisted of an increase of the CAP efferent suppression during prolonged electrical MOC stimulation. A similar slow effect was observed in EBA of the VIII nerve of guinea pigs when stimulated with a low-level contralateral broadband noise (Da Costa et al., 1997). It is believed that this slow effect is caused by OC fibres slowly increasing their rate of discharge during repeated electrical stimulation of the brainstem due to direct or indirect effects at their cell bodies in the brainstem (Shridar, Liberman & Brown, 1995).

However, this slow effect of the MOC was only measured during one minute after efferent electrical stimulation onset in guinea pigs (Shridar, Liberman & Brown, 1995) and not for longer durations. Differences in methods of MOCS stimulation could account for the difference in the duration of this slow efferent effect. Electrical stimulation of the MOC could shorten the duration of this slow effect by influencing natural acetylcholine discharge patterns, whereas acoustic stimulation could result in a more physiological activation of the MOC. A slow amplitude decrease after stimulation onset with a longer duration (3 to 10 minutes) has also been demonstrated in DPOAE's on animal subjects (Brown, 1988).

5.3.2 Suppression across half-octave frequencies

Statistically, no significant differences in suppression were found between frequencies at each time interval recording. It was also found that there was no significant change ($p<0.05$) in suppression as a function of CAS duration between these frequencies. Nevertheless, a clear trend was observed amongst these half-octave frequencies. Results showed evident suppression in the lower half-octave frequencies bands (1 to 2 kHz), where the effect is the greatest. As the frequency increased, a clear decrease in suppression was observed, with the least suppression in higher half-octave frequencies (3 and 4 kHz). This difference can be seen in figure 4.8. This was also discussed in section 5.2.2 in the TEOAE amplitude differences between conditions, where this observation was reported in previous studies (Berlin et al., 1993; Collet et al., 1992; Norman & Thornton, 1993; Veuillet et al., 1991) and possibly ascribed to a greater density of MOC efferent innervation in this frequency area (Guinan et al., 1983, Liberman & Guinan, 1998; Warr et al., 1986). In such a case, the efferent effect on OHC's in the lower frequency area of the cochlea is expected to be less than in higher frequency areas. This may also imply that the efferent protective function against acoustic trauma is less in lower frequency areas (Rajan, 1995). It is generally known that noise-induced hearing loss is a result of hair cell trauma in the region between 4 and 6 kHz. The greater impact on this area of the cochlea is ascribed to the fact that broadband noise (with equal energy across low to mid frequencies of 2 to 3 kHz) damage is found to occur in the octave-band above the band of the noise, as a result of natural resonance of the external ear (Ward, 1973). The reduced ability of the MOC efferent system to protect OHC's against acoustic trauma in higher frequencies may contribute to this area being more susceptible to noise damage.

5.4 Sustained suppression over prolonged stimulation durations

The results have important implications for understanding the physiology of efferent auditory system and more particularly, efferent inhibition. The current study shows that the MOCS is capable of a sustained suppressive response on TEOAE's over the duration of 15 min and that MOC neuron adaptation during prolonged stimulation is unlikely. Minimal adaptation of the MOC to neurons has been reported in anesthetized guinea pigs by measuring the adaptation of a single olivocochlear neuron's response to noise stimulation of 10 second durations (Brown, 2001). It has also been found that there are minimal declines in the response rate to continuous tones for MOC neurons (Liberman and Brown, 1986). Compared with auditory nerve response to long-term stimulation, the MOC response was found to be much more sustained over a period of several minutes. It was hypothesized that the decline in input provided by the auditory nerve fibres, as they adapt over time, may be compensated for by elements within the MOCS at a more central location (Brown, 2001). The lack of long-term adaptation suggests relatively constant effects on the MOC targets when the efferent system is activated by a contralateral noise.

Sustained efferent suppression for prolonged contralateral stimulation supports the possibility that the role of the efferent system is predominantly for ongoing stimuli, which corresponds with a role as a permanent gain control of the cochlear amplifier, adjusting the gain to the level of background noise and with a role in hearing protection against overstimulation. Indeed, the suppression effect of MOC efferent neurons has been found to exert its protective function from acoustic overstimulation for sound exposures of hours in duration (Kujawa & Liberman, 1997; Zeng et al., 1997 a, b). A study measuring OAE suppression in individuals with occupational exposure to noise showed that suppression was decreased in the experimental, exposed group when compared with suppression in the control, non-exposed individuals (Sliwinska & Kotylo, 2002). It was reported that efferent auditory neurons were damaged in the individuals exposed to noise, which may suggest a weakening of the protective function of the MOC efferent effect over time. It should be taken into consideration that these noise-exposed individuals had abnormal hearing thresholds in higher frequencies (4 kHz, 6 kHz and 10 kHz) and poorer OAE's (Sliwinska & Kotylo, 2002). The decrease in OAE suppression in the exposed group as compared with the control group may have been a direct result of noise exposure damage to the cochlea, and not as a result of a declining efferent protective function due to prolonged noise exposure.

Indeed, the definite trend of increased suppression over time, as was found in the current study (figure 4.6 & 4.8), may suggest the exact opposite of Sliwinska & Kotylo (2002) findings. An increase in efferent suppression may be caused by a slow increase in the discharge rate of MOC fibres during prolonged CAS (Shridar, Liberman & Brown, 1995). In such a case, the protective function of the efferent auditory neurons is expected to not only remain stable, but to also strengthen when the cochlea is exposed to noise for long durations.

5.5 Conclusion

The main effect of efferent stimulation is the physiological alteration of outer hair cells. It is reported that efferent innervation of OHC's probably controls the dynamic range of the cochlea, reduces the masking effects of noise, and protects the cochlea from the negative effects of acoustic overstimulation (Geisler, 1974; Rajan, 1995). This study shows a stable TEOAE suppressive effect over 15 minutes of contralateral stimulation, indicating that the MOCS is capable of a sustained efferent effect on OHC's for prolonged durations. This supports a sustained MOC role of protection against acoustic overstimulation, and adjusting the dynamic range of the cochlea with no adaptation of MOC neurons over longer periods. Moreover, a slow increase in suppression over time is observed, which may be a result of the slow effect after stimulus onset described by Shrider et al. (1995) in guinea pigs. However, one minute after CAS offset, TEOAE suppression is found to completely vanish, suggesting the absence of the slow recovery after stimulus offset that has been observed with DPOAE's (Moulin & Carrier, 1998). In addition, TEOAE amplitudes in the experimental condition were found to exceed corresponding control amplitudes in the recordings three minutes after CAS offset, suggesting a possibility of increased cochlear sensitivity minutes after stimulus offset.

5.6 Summary

This chapter discussed and interpreted the significance of findings in line with previous reports that studied similar characteristics of efferent suppression by either electrical or acoustic stimulation of the MOCS. It shed light on TEOAE amplitudes as a function of the duration of CAS for both conditions, by discussing the differences in TEOAE amplitude between conditions at corresponding time interval recordings with and without CAS and in the post-noise periods after CAS offset. It also discussed TEAOE suppression as a function of different CAS durations and provided possible physiological reasons for significant suppression over different time recordings. This chapter included previous literature describing the importance and different roles of the MOCS stimulation and attempted to discuss the current results according to these roles.

Chapter 6: Conclusion and Recommendations

The main aim of this study was to investigate TEOAE suppression as a function of prolonged contralateral acoustic stimulation (CAS). This was done by comparing replicated recordings of TEOAE amplitude obtained over identical recording periods in conditions with and without CAS and by defining the relationship between the duration of CAS and TEOAE suppression amplitude.

The aim of this chapter is to draw conclusions from the reported results and to critically review the research process. Implications of the research are presented along with recommendations for further research

6.1 Conclusion

The research process described in this report was successful in attaining the main aim set for this study, namely describing TEOAE amplitude suppression over prolonged periods of CAS. The purpose of the present study was to evaluate the relationship between the duration of contralateral acoustic stimulation and the suppression of transient evoked otoacoustic emissions (TEOAE's) in normal-hearing subjects. TEOAE recordings with specific time intervals were measured in two conditions, namely 1) in the presence of 15 minutes of continuous 45 dB SL contralateral white noise, followed by two recordings at different time-intervals after the noise was terminated, and 2) identical interval recordings without any noise to serve as a control condition. Results revealed visible reduction in TEOAE amplitude for the entire duration of contralateral acoustic stimulation. Although not statistically significant, suppression tended to increase as contralateral noise duration increased. After noise termination, TEOAE amplitudes increased to values above control recordings.

It has been reported that the main effect of efferent stimulation is the physiological alteration of outer hair cells (OHC's) and that efferent innervation of OHC's may control the dynamic range of the cochlea, reducing the masking effects of noise, and protecting the cochlea from acoustic overstimulation (Rajan, 1995).

The current study revealed the following effects on TEAOE amplitude suppression as a result of prolonged CAS:

- A stable TEOAE suppressive effect over 15 minutes of contralateral acoustic stimulation was observed, indicating that the MOCS is capable of a sustained efferent effect on OHC's for prolonged durations (up to at least 15 minutes). This result suggests a sustained MOC role of protection against acoustic overstimulation, and adjusting the dynamic range of the cochlea with no adaptation of MOC neurons over longer intervals.

- A gradual increase (though not statistically significant) in suppression over time was recorded, which may be a result of the slow effect after stimulus onset described by Shrider et al. (1995) in guinea pigs. This may imply/suggest that the protective function of the MOC can also be expected to strengthen when the cochlea is exposed to noise for long durations.

- In the recordings one minute after CAS offset, TEOAE suppression is found to completely abolished, which may suggest the absence of a slow recovery, or much faster recovery (within one minute) after stimulus offset, as has been documented with DPOAE's (Moulin & Carrier, 1998).

- In the recordings three minutes after CAS, TEOAE amplitudes in the experimental condition were observed to exceed corresponding control amplitudes, suggesting the possibility of increased cochlear responsiveness minutes after stimulus offset.

Sustained suppression over a prolonged duration of contralateral stimulation may imply that the MOCS has a reasonably consistent and sustained effect over prolonged periods of time, supporting the role for this efferent system during ongoing stimulation.

6.2 Implications of study

Apart from the clinical applications of OAE's, advances in the field are a continual area of research interest. Recently numerous studies have investigated the suppression of OAE's by CAS, because of the ability of OAE suppression to measure alterations of cochlear micromechanics by the medial olivocochlear bundle (MOCB), activated by acoustic stimulation of the contralateral ear (Maison, Micheyl & Collet, 1995). One of the purposes of the current study was to shed light on the relationship between OHC integrity, as measured with TEOAE's, and the duration of efferent inhibition in an attempt to understand the MOCS more thoroughly. The auditory efferent nerve fibres are known to have an inhibitory influence on the auditory periphery, which in turn serves as a protective reflex against loud, damaging sounds. The proposed study investigated the inhibitory effect of the efferent system to determine if it remains unchanged over a prolonged period of acoustic stimulation or if the medial efferent neurons adapt or show fatigue. The results of the present study indicated a sustained MOC role of protection against prolonged acoustic stimulation, and in adjusting the dynamic range of the cochlea with no adaptation of MOC neurons over longer intervals. The current study thereby provided information of the duration characteristics of CAS. This knowledge may be useful in our understanding of the exposure durations for which MOC protection is effective and the duration for which the MOC system plays a role in reducing the effects of noise masking. The definite trend of increased TEOAE suppression over time may provide evidence for an increase in the discharge rate of MOC fibres during prolonged CAS. This is an interesting finding and may be an indication of an increased or strengthened protective function of the MOC during prolonged exposure durations. The significant increase in TEOAE suppression amplitude after stimulus offset may also be important knowledge for clinical use. With total TEOAE suppression recovery within one minute after noise termination, it may complicate suppression measurements using a forward masking paradigm, where the suppression amplitude is usually measured directly after stimulation. It should be acknowledged that this paradigm is used mostly in the case of ipsilateral or bilateral acoustic stimulation.

Table 6.1 Critical evaluation of test method variables as applied in current study

	Test variable	Option chosen for current study	Strengths	Limitations
STIMULUS	OAE Type	*TEOAE broadband click*	*A single TEOAE measurement takes ± 1 minute to collect whereas DPOAE's require more time and are often inconsistent. Using DPOAE's would have complicated the test procedure (Figure 3.1). Click TEOA'Es could be measured every few minutes during continuous contralateral stimulation, because the responses could be collected rapidly.*	*DPOAE measurements can provide more frequency-specific information. DPOAE's have been used in a similar study (Moulin and Carrier, 1998), but F2 was fixed at frequency 1501 Hz in order to shorten the time to collect responses. The use of an broadband clicks ensured that the components of the TEOAE across a broad frequency range could be elicited*
	Time interval between TEOAE recordings	*4 minutes in between recordings in the with and without noise measurements and 1 minute between recordings in the post-noise periods*	*As mentioned in the above section, TEAOE responses took ± 1 minute to collect. Thus time intervals between recordings needed to be more than 1 minute. A 4-minute interval was chosen to investigate the suppression over a time.*	*If TEOAE's could be recorded more rapidly, it would provide more specific information on the changes over time, for example, a TEOAE recording every minute. It also would have been very useful to record directly after the noise was terminated.*
	Stimulus polarity	*Linear*	*A constant linear stimulus polarity can be used, because lower click intensity levels are used in the evaluation of contralateral suppression effects.*	*Nonlinear stimuli have the advantage of largely eliminating the stimulus artefact* *Although nonlinear stimuli are most often used for TEOAE recordings, they may result in some growth in the emission and they also have a higher level of residual noise.*
	Stimuli intensity	*60 dB SPL*	*A contralateral BBN stimulus is most effective in suppressing TEOAE's when the intensity of the click stimulus used to evoke an emission is between 55 and 65 dB SPL (Hood et al., 1996)*	*In some individuals, the use of such low stimulus intensities reduced the response reproducibility and stability. When the intensity was increased during the pilot study this problem was eliminated. Nevertheless responses were only accepted if the reproducibility was above 70% and the stability above 80%.*

	Test variable	**Option chosen for current study**	**Strengths**	**Limitations**
SUPPRESSOR	Contralateral vs. Ipsilateral and Bilateral	*Contralateral suppressor*	*A contralateral suppressor made it possible to present the continuous noise suppressor simultaneously with the TEOAE-evoking recordings in the opposite ear.* *With ipsi- and bilateral suppressors two approaches of assessing are used. Firstly, a forward masking paradigm, where a suppressor signal is presented to an ear prior to the presentation of an OAE stimulus. In this case, the suppressor must be terminated before the OAE recording, which thus makes it impossible to measure the effect of continual CAS on OAE's. The second approach is to use a simultaneous masking paradigm. Here the suppressor is presented simultaneously with an OAE, but a special custom-made dual probe is needed.*	*In relation to contralateral stimulation, ipsilateral and contralateral suppressors can result in more pronounced suppression of evoked OAE's (Kemp & Chum, 1980; Travartkiladse, Frolenkov, Kruglov, Artamasov, 1994; Wilson, 1980)* *In order to measure the effect of continual CAS on OAE's by using ipsilateral and contralateral suppression measurements, special equipment (custom-designed acoustic probes, consisting of a microphone and two electroacoustic transducers which provide the same ear with the suppressor signal and the recording-evoked OAE) is required.*
	Suppressor intensity Suppressor presentation	*Sensation level intensity of 45 dB* *Noise generated by a clinical audiometer*	*Sensation level intensities of 30-50 dB SL have been found to be low enough to prevent any crossover and contraction of the contralateral stapedius muscle (Berlin et al., 1994; Ryan et al., 1991).* *Sensation level intensities of each subject could be estimated by determining the threshold for white noise and presenting the suppressor 45 dB above the threshold.*	*Click stimulus intensities of below 65 dB SPL have been found to be the most effective in suppressing TEOAE amplitudes when using contralateral white noise stimuli (Hood et al., 1996a:117). Hood et al. (1996) suggested using 55 or 60 dB peak SPL with the overall intensity level of the noise set at or 5 dB higher than the click intensity (Hood et al., 1996a:117),. The click intensity used in the current study is 65 dB SL. It is imperative to avoid using high click intensities (e.g. 70 dB SPL) in order to minimize the risk of major participation of the middle ear muscle reflexes* *White noise generated by a GSI 61 clinical audiometer is presented in dB HL and not in SPL. SPL's in the ear canal during noise presentation could not be measured, because of lack of appropriate equipment.*

	Test variable	Option chosen for current study	Strengths	Limitations
SUBJECTS	Subject characteristics	*Auditory characteristics: Thresholds ≤ 15 dB HL from 250 to 8000 Hz, normal otoscopic examination, tympanograms and otologic history, no history of noise or ototoxic exposure or complaints of middle ear problems* *Age range: 20-30 years*	*Selection criteria ensured homogeneity of research sample and controlled factors that could possibly affect TEOAE recordings*	*Required a series of selection procedures.*
TEST PROCEDURE	Suppression measurements	*The entire procedure was repeated three times, each on separate days, in all the subjects, to increase the reliability of the results.*	*One session of data collection took approximately an hour to conduct. The experiment is a lengthy procedure and thus it was decided to do the recordings over three different days to decrease subject discomfort.*	*Subject exposure to noise during this period of days could not be closely controlled. If the subject were to be exposed to excessive noise during these three days OAE results could be negatively influenced. It is well known that OAE's are highly sensitive to noise damage, even before threshold changes are observed with audiometric measurements.*

6.3 Recommendations for further research

The experimentation conducted in this project provided insight into the effect of prolonged CAS on TEOAE's and the effects after CAS offset. Investigating the TEOAE amplitudes, in the presence and absence of CAS, provided a non-invasive, objective, approach for investigating MOCS efferent feedback in subjects (Giraud, Collet, Chery-Croze, Magnan, & Chays, 1995). However, additional research could prove valuable in further refining the test methodology. The current research findings could also stimulate further research. The recommendations for further improvement on the current study and new findings that may be worth investigating are summarized in Table 6.2.

Table 6.2 Recommendations on improving test method and new research areas to be investigated

		Current study	**Recommendations for futures studies**
METHODOLOGY	Suppressor transducer	*In the current study prolonged continual contralateral acoustic stimulation was used to investigate suppression on TEOAE's. It has been found that ipsilateral and contralateral suppressors can result in more pronounced suppression of evoked OAE's than contralateral suppressors (Kemp & Chum, 1980; Travartkiladse, Frolenkov, Kruglov & Artamasov, 1994; Wilson, 1980). The reason why this approach was not followed in the current study is mainly due to the lack of a dual probe consisting of microphone and two electroacoustic transducers, which provide the same ear with the suppressor signal and the recording OAE.*	*With the use of a custom-made dual probe, prolonged continual ipsilateral and bilateral suppression on TEOAEs can be investigated using the simultaneous masking paradigm. The use of ipsilateral and bilateral suppressors may result in more robust suppression, which may show clearer effects of acoustic stimulation on TEOAE's. It is important, however, to take into consideration that bilateral and ipsilateral suppression of TEOAE's may not be attributed only to the MOC bundle but also to intracochlear processes.*
	Suppressor intensity level	*White noise was generated by a clinical audiometer which presents the noise in dB HL and not in dB SPL. SPL's in the ear canal during noise presentation could not be measured, because of the lack of appropriate equipment.*	*Some OAE apparatus are equipped with noise generation software, which presents noise in SPL. Often in the literature, research on OAE suppression was done by using noise presented in SPL. It would be useful to conduct similar studies using suppressor intensities measured in SPL in order to compare the results with these studies and to ensure that the level stays under 70dB SPL in order to minimize the risk of major participation of the middle ear muscle reflexes.*

		Current study	Recommendations for futures studies
NEW RESEARCH	Slow effect of MOC stimulation	*A slow increase (though not significant) in suppression over time is recorded, which may be a result of the slow effect after stimulus onset described by Shrider et al. (1995) in guinea pigs. This slow effect may be caused by a slow increase in the discharge rate of MOC fibers during prolonged contralateral stimulation (Shridar, Liberman & Brown, 1995). However, this slow effect of the MOC was only perceived during one minute after efferent electrical stimulation onset and not for longer durations, as in the current study.*	*Differences in methods of MOCS stimulation could account for the difference in the duration of this slow efferent effect. Electrical stimulation of the MOC could shorten the duration of this slow effect by influencing natural acetylcholine discharge patterns, whereas acoustic stimulation leads to a more physiological activation of the MOC. It would be interesting to investigate the slow effects by measuring the discharge rate of MOC fibers by acoustically stimulating the MOC*
	TEOAEs after CAS termination	*In the post noise periods two interesting results were found:* • *Firstly, one minute after CAS offset, TEOAE suppression was found to have been completely eliminated, suggesting the absence of a slow recovery after stimulus offset as been documented in previous reports (Moulin & Carrier, 1998).* • *Secondly, in the recordings three minutes after CAS, TEOAE amplitudes in the experimental condition were found to exceed corresponding control amplitudes, which may suggest the possibility of increased cochlear sensitivity minutes after stimulus offset.*	*It would be interesting to conduct a experiment recording OAE responses before and after prolonged noise stimulation, to investigate if there are changes in the OAE amplitude. I, this were to happen, and a slowly increasing OAE amplitude, as has been found in current study, were observed, these results would be confirmed. If a slow increase were observed, as compared with recordings before noise stimulation, it might suggest that there is increased cochlear sensitivity after prolonged noise stimulation.*

6.4 Final conclusion

The research project described in this study has been successful in answering the research questions posed in the first two chapters. The different methods that were used by previous researchers in the investigation of OAE suppression, especially TEOAE's, were extensively explored and critically discussed to provide a framework that served to guide the methodology of the present study. The experiment provided new information on the effect of prolonged CAS on TEOAE's in normal-hearing subjects, which indirectly provides insight in the efferent response of the MOCS to constant acoustic stimulation. These findings provide further support for the protective function of the efferent auditory system, even when the auditory system is subjected to acoustic overstimulation for long periods.

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Appendixes

Appendix A: The interview

Personal information

Name:	Subject file:
Date of birth:	Gender:

Information regarding hearing status

Do you have any problems with your hearing? ☐

Did you suffer from any pain in your ear/s within the last 6 months? ☐

Did you have any discharge coming from your ear/s recently? ☐

Did you suffer from or are you suffering from any other ear, nose or throat problem? ☐

Does anyone in your family have a childhood history of hearing loss? ☐

Do you hear any unusual sounds or noises in your ear/s? ☐

Do you practice any hobbies that involve exposure to very loud noise? ☐

Have you been exposed to very loud noises? ☐

Did you injure your head and/or ear/s that affected your hearing? ☐

What types of medication are you currently using?

____

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Appendix B: Informed Consent

University of Pretoria

Department of Communication Pathology
Speech, Voice and Hearing Clinic
Tel : +27 124202355
Fax : +27 124203517
Email : brenda.louw@up.ac.za

Researcher: Altelani van Zyl
Tel: 082 925 0830
E-mail: s23030799@tuks.co.za

Date: ____________

To Whom It May Concern:
Thank you for showing interest in this research project being conducted at the Department of Communication Pathology, University of Pretoria.

We are currently investigating the effects of prolonged contralateral acoustic stimulation on Otoacoustic emissions (OAEs). This will give us a better understanding of the way the outer ear hair cells of the inner ear react to prolonged stimulation of broad band noise. This procedure is completely harmless and non-invasive. Participation in the study is voluntary and you may withdraw at any time if you wish to. If you do participate the following procedures will apply to you:

- An otoscopic examination, followed by immittance measurements, will be carried out. You will be asked to sit quietly, while the researcher examines your outer ear canal, eardrum and your middel ear functioning. These procedures do not require any response from you and will take approximately 5 minutes.

- You will then undergo a standard hearing evaluation (pure tone behavioural audiometry), where you are required to respond to the presence of a sound. This procedure takes approximately 10 minutes.

- An otoacoustic emission (OAE) test will then be conducted. This procedure is also objective and does not require a response from you. During the TEOAE measurement a small probe will be placed in one ear while an earphone will be placed on your other ear. The test will be repeated two times without and with noise presented to the non-test ear. It is important to know that the noise level that will be used will be at a comfortable level. The entire procedure will last for approximately 1 hour.

All the procedures (tests) are non-invasive and only the behavioural (pure tone) procedures require responses from you. All acquired information will be treated as confidential and no names will be used. The results will be used for research purposes as part of a dissertation and possibly future articles and presentations. The data will be stored for archiving and research purposes for 15 years. By agreeing to participate in this study you acknowledge that future research using the acquired data may be conducted at a later stage. A copy of your results will be made available to you, should you request it. You are free to withdraw from the study at anytime without any negative consequences.

Should you require any further information, you are welcome to contact us.

Sincerely,

Altelani van Zyl
Researcher

Dr De Wet Swanepoel
Supervisor

Professor Brenda Louw
HEAD: Dept of Communication Pathology

UNIVERSITEIT VAN PRETORIA
UNIVERSITY OF PRETORIA
YUNIBESITHI YA PRETORIA

University of Pretoria

Department Communication Pathology: Audiology

The effect of prolonged contralateral noise on the amplitude of TEOAE suppression

Surname______________________ Name________________________

Age__________________________

<u>Please complete the following:</u>

I ___________________________ hereby agree to participate in this project and acknowledge that the data may be used for research purposes. I am aware that I can withdraw from this project, at any time, should I want to.

______________________ ________________________

Signature Date